

ESHRE



The First 21 Years

Simon Brown

With an Introduction by Basil Tarlatzis

PREFACE

It was at the 77th meeting of ESHRE's Executive Committee in April 2002 that the prospect of writing the society's history was first formally discussed. In fact, the seed of the idea had been sown a few months earlier by ESHRE's new chairman at the time, Hans Evers, and chairman elect Arne Sunde. After their nominations had been approved at the 2001 annual meeting in Lausanne, both Evers and Sunde had immediately set about the composition of a 16-point strategy report for the Executive Committee, designed to take ESHRE's management forward over the following three or four years. Section 16 of that report, under the heading of "other items", was a proposal that ESHRE's past chairmen should collect "the important documents and illustrations from their term of office" with a view to recording the society's history.

Now, in the spring of 2002, as the Executive Committee sat down at ESHRE's Central Office in the suburbs of Brussels to battle their way through the strategic plan, they too recognised the huge advance in reproductive medicine reflected in ESHRE's history. A record of that history would indeed represent ESHRE's place within that advance - and ESHRE's contribution to it. The Executive Committee thus did what it always did when faced with a proposal which required consideration and planning: it formed a committee. The ESHRE History Task Force was set up at that meeting in April 2002 under the chairmanship of Basil Tarlatzis; joining him on the committee were his fellow past chairmen Jean Cohen, Pier Giorgio Crosignani, Klaus Diedrich and André Van Steirteghem.

All except Tarlatzis had been formally involved with ESHRE since its formation in 1984, Cohen as a founding member.

For a year, ESHRE's history continued ticking, until May 2003 when I received a message from Basil Tarlatzis asking if I might be interested in helping out. The Task Force had hoped that one of its members might assemble the documents and record what happened, but the archives were simply too large, the events too many for a weekend labour of love. The Task Force thus turned to me as a professional writer.

The ideas I put to Tarlatzis during ESHRE's annual meeting in Madrid that year were essentially that ESHRE's history would be best recorded in book form and within a broad framework of reproductive medicine. We thus agreed that the text should provide a document of record, but should also be a lively read in which ESHRE's history evolves alongside progress in reproduction and in the context of those individuals who made it all possible. Hence, the sources of the book would be ESHRE's own archives and the personal recollections of those involved.

I should therefore express my appreciation to ESHRE's managing director Bruno Van den Eede for maintaining such a thorough and well organised archive. Bruno joined ESHRE in March 1987 as a part-time assistant, but from that time on his reporting of meetings was scrupulous, his use of English without fault. The details, events and dates recorded in the following pages are derived almost exclusively from Bruno's minutes.

However, what follows is not just a chronology of events. It is also a personal record and a reflection of the sheer human energy given by so many individuals to ESHRE's progress. Jean Cohen, Pier Giorgio Crosignani, Klaus Diedrich, André Van Steirteghem, Basil Tarlatzis, Lynn Fraser, Hans Evers, Arne Sunde, Paul Devroey and Liz Corrigan all gave up their time - and many of their own personal papers - to me.

I regret that the name of Robert Edwards is not on that list. As the following pages will show, Edwards's contribution to ESHRE, both as a founding member with Jean Cohen and as editor of *Human Reproduction*, was enormous; between 1984 and 2000, when he resigned from the editorship of the journals, there was little that happened in ESHRE which did not involve Edwards. However, despite requests from me and from many of his former colleagues, Edwards chose not to contribute personally to this book. He never formally declined to co-operate, but simply said that he didn't have the time. Nevertheless, the presence of Robert Edwards runs through these pages, and I hope that his contribution to ESHRE has been accurately recorded and appropriately acknowledged. Despite his

personal absence, ESHRE's own archives contain many of Edwards's papers and correspondence, and I have liberally drawn on these, particularly to record events from ESHRE's early years. Edwards's founding-father colleague Jean Cohen was also immensely helpful in explaining how those early years unfolded.

There are two or three details of this book which I should also here explain. The first involves money, which - in ESHRE's early years especially - was frequently at the top of the agenda. ESHRE's official currency started as Swiss francs, switched to Belgian francs, and is now Euros. However, the accounts of many annual meetings were also run in the currency of the host country, and the finances of the journals managed in UK pounds. In my first draft I recorded these currencies at their original face value, noting revenues in deutsch marks or krona, expenditures in guilders or US dollars. It was Hans Evers who suggested that, as exemplary Europeans, ESHRE should express its finances in Euros - which in most cases I have now done. However, in the belief that even the most ardent Europhiles recognise the value of a dollar and a pound, I have left these two currencies in their original form.

Readers may also note some discrepancies in the numbers I have used for attendance at ESHRE's annual meetings. The graph on page...represents the official number of registrants for each meeting; however, I have on occasions noted total numbers of attendees, which is invariably larger.

Finally, I should warn readers that this is not a textbook and I have not followed Vancouver style in the use of references and footnotes. Where a reference is, I believe, applicable, I have added it briefly in parenthesis within the running text. Appendix D provides a full list of references to all publications associated with ESHRE.

The text has been liberally illustrated, and I am once again grateful to those past chairmen who dug out old photographs from their collections. However, I am particularly indebted to the photographer Dieter Jausovec, Organon's own in-house paparazzo, for access to his considerable picture archives. Dieter is now retired but on Organon's behalf has covered all ESHRE meetings from 1991 onwards; many of the illustrations in this book are Dieter's photographs and we are grateful to him and Organon for granting us rights to use them. I am also indebted to the *Daily Mail* in London for rights to reproduce their front page of 27th July 1978. Billed as a "world exclusive", the *Mail's* front page was half occupied by a picture of Louise Brown, "bright-eyed at 18 hours old", such was the public impact of her birth. Jenny Hope, the *Daily Mail's* medical correspondent, also

confirmed details of many dates and headlines for me from the paper's library.

However, while the gratitude is mine - and my name sits squarely on the cover - we should not forget that this is essentially ESHRE's book. I was commissioned to research the archives, interview the personalities, and write the text. But what is published here *is* on ESHRE's behalf and with the approval of its past chairmen. Some of ESHRE's past and present committee members - notably Berndt Kjessler, Karl Nygren, Françoise Shenfield, David Barlow and Luca Gianaroli - have seen selected sections of the text and made suggestions. Others have offered numerous anecdotes and details from the past. One evening in Berlin last year, for instance, I found myself surrounded at dinner by Pedro Barri, Tony Rutherford and Gab Kovacs. Next morning, my pockets were stuffed with scribbled notes on scraps of paper - what *was* happening in Melbourne in 1980, who *was* the first to use transvaginal ultrasound . . . and much more.

I have tried to introduce them all, the facts, the comment and the anecdotes. And I hope that, on ESHRE's behalf, I have achieved what we set out to do in Madrid in 2003, to put ESHRE's history on the record and recognise its monumental achievement within the progress of reproductive medicine. Few will disagree that ESHRE - and certainly its annual meeting and journals - are at the forefront of that progress today, and I hope this book is fitting testimony to the vision and effort which made that possible.

Simon Brown
February 2005

INTRODUCTION: THE EUROPEAN DREAM

Major accomplishments begin with visionaries who dream and, most importantly, have the will to realise their dream. The history of the European Society of Human Reproduction and Embryology (ESHRE), as well as that of in vitro fertilisation itself, is indeed the history of a dream shared by several prominent European clinicians and scientists who joined forces to make it work.

Although many breakthroughs in the field of reproductive medicine - for example, laparoscopy and laparoscopic surgery, ovulation induction with human menopausal gonadotropins and particularly IVF - all started in Europe, there was no established European forum before the early 1980s where these innovations could be publicised. By contrast, across the Atlantic the American Fertility Society had been organising an extremely successful annual meeting since 1944 and publishing a monthly journal, *Fertility and Sterility*, the only prestigious journal in the field, since 1950. Thus, based on the principle of “publish or perish”, the only way for Europeans to describe and achieve international recognition of their work was to have it presented or published in the USA. However, this was not so easy; while the amount of new data on IVF from various European centres was increasing exponentially, there was at the same time an abundance of papers flowing from the American institutions.

These frustrations, shared by many clinicians and scientists from different backgrounds and different European countries, served as the star which led them to Hall B of the Finlandia Hall, Helsinki, in May 1984. And it was the aspirations presented here by Bob Edwards and Jean Cohen that became the seed from which ESHRE grew and flourished. Here in Helsinki they described their idea of a democratically elected and governed “European” society, with its own journal, an annual meeting and training workshops which would all serve as a forum for the exchange of scientific knowledge between clinicians and scientists in Europe. It was exactly these “dreams”, so passionately presented by Bob to make them sound as if they were already happening, that attracted this first handful of people and convinced them to devote time, energy and money to this new endeavour.

The first years of ESHRE’s foundation phase were indeed very difficult. There were no resources, no institutions, nothing. Everything had to be planned from scratch: the name, the logo, the by-laws, the annual meeting. It is now impossible to imagine how difficult it was for a young society like ESHRE to organise activities, and especially an annual meeting, with no firm commitment from the pharmaceutical companies. But we managed to gain their confidence and support, striving to balance their interests with ours, by ensuring democracy, transparency and high quality science. It is exactly this trio of principles which has played such a key role in ESHRE’s phenomenal growth in the 1990s.

This second phase in ESHRE’s history, the phase of growth, is characterised by a proliferation of scientific activities and an impressive increase in the number of delegates attending the annual meeting (rising from almost 1000 in Milan in 1990, to 1600 in Thessaloniki in 1993, 2178 in Maastricht in 1996, and reaching 3700 in Bologna by the end of the decade), paralleled by a similar increase in membership. Another sign of this growth was the significant enhancement of ESHRE’s international recognition at the time, as evidenced by its numerous collaborations with other scientific societies - for example, the American Society of Reproductive Medicine or Middle East Fertility Society - or professional bodies like the European Board and College of Obstetrics and Gynecology. However, nothing epitomises better this period of ESHRE history than the evolution of the journal.

The journal... Who could really imagine the success of *Human Reproduction* when the first slim pilot issue was presented in 1985? Nobody - or almost nobody - with the exception of Bob Edwards. Some of our

colleagues, especially the young ones, tend to take the success of the journal for granted. They think that it came easily, automatically, or even that it was always there. Yet, those of us who were fortunate to be there from the beginning vividly remember Bob asking all of us, in his polite and friendly but also persistent way, to submit our work to this new, unknown, uncited and no-impact-factor journal. We all remember Bob attending meetings and soliciting papers from colleagues with the best presentations. We all remember Bob trying his very best to be fair with every author, especially the younger ones. "We are here to help our young colleagues to get their work published," he always said, "not to destroy them." After all, Bob was himself reading every single paper submitted, first to *Human Reproduction* and subsequently to *Human Reproduction Update* and *Molecular Human Reproduction*, setting an extraordinary precedent. We all remember the agony of the Executive Committee in its efforts to ensure the financial health of the journal and the endless hours of comparing on a blackboard the calculations made by Bob and me.

Bob was always ahead of everyone as far as the journals were concerned. He was continuously coming up with new ideas, proposals and initiatives. He was undoubtedly their driving force. On the other hand, we in the Executive Committee took a more pragmatic view, and had the unpleasant but crucial duty of balancing his vision with the hard financial realities of the publisher. Over the years, this was the only cause of disagreement with Bob, but one which led to the final dispute in the late 1990s. He firmly believed that it would be better for the society itself to undertake the publication of the journals, whereas the Executive Committee was afraid that this was a far too risky option. All of us involved in the debate had the best possible intentions, the benefit of ESHRE. Who was right and who was wrong? It is still too early to know, and only time will give us the answer.

Now, ESHRE has entered its third phase, the management of success, which is extremely important and equally critical. It involves strategic planning to sustain growth without loss of quality, to meet the needs of an expanding membership and to be at the forefront of educational, ethical and social issues in a rapidly expanding Europe. The leadership of ESHRE is doing a wonderful job to meet these new challenges and lead the society into the new millennium. I am sure they will be absolutely successful, because they share the same ideals and principles with those who founded ESHRE 21 years ago and made it what is today. Moreover, they share the

same drive so appropriately described by T. S. Eliot in the final section of his *Four Quartets*:

*We shall not cease from exploration
And the end of all our exploring
Will be to arrive where we started
And know the place for the first time*

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Past-Chairman of ESHRE
Chairman of the ESHRE History Task Force
February 2005

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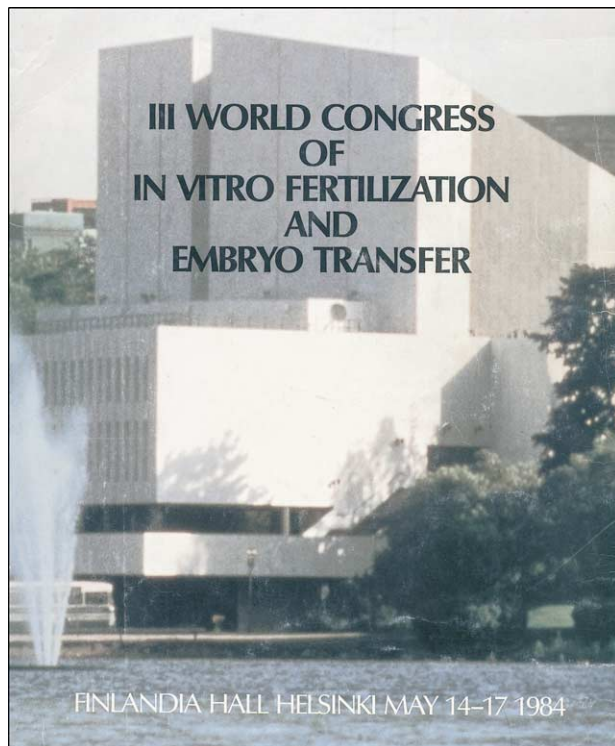
I

THE PIONEERS

On the final day of the third World Congress of IVF held in Helsinki in 1984 a young Norwegian scientist new to reproductive medicine wandered into a meeting room to pass a little time. There, he found 30 or so people he vaguely recognised, some sitting on tables, some talking idly in groups. The research scientist didn't know why they were there, but, before he could slip away, was spotted from the front of the room and asked to make himself welcome.

The voice from the front – as genial and persuasive as ever - was that of Robert Edwards, who was sitting at a table alongside the French gynaecologist Jean Cohen. Earlier in the week, at the opening ceremony, the congress president Markku Seppala had agreed for Edwards to announce plans for the formation of a European society of reproductive medicine, and both Edwards and Cohen had been busy posting notices of a foundation meeting around the Finlandia Hall. Now, in Hall B on that final day of the congress, 17th May 1984, the young Norwegian scientist Arne Sunde had stumbled into the first meeting of what would become the European Society of Human Reproduction and Embryology, or ESHRE .

ESHRE was then, of course, not much more than an idea, a growing awareness that Europeans, like the Americans, should have their own learned society and access to a journal which would gladly publish their work. But no-one at that meeting, and certainly not Arne Sunde, who in 2003 would be elected chairman of ESHRE, could have foreseen



At the third World Congress of In Vitro Fertilization and Embryo Transfer in Helsinki in 1984 Edwards and Cohen announced plans for the formation of a European society of reproductive medicine.

the impact which the society and its journal would make on reproductive medicine over the next 20 years. Throughout that time ESHRE would stage a scientific meeting each year, which in 2004 in Berlin was host to more than 6000 participants. From 1986, when three initial workshops and study groups were organised, ESHRE would be involved in more than 200 training courses, some as pre-congress events, some as "Campus" workshops, some as symposia - and indeed there can be few clinicians or scientists now working in reproduction whose learning has not been shaped in one way or another by ESHRE's training programmes. Membership since the society's formal foundation in 1985 had risen to 4543 by June 2004, with members distributed over all continents, though predominantly from western Europe. And ESHRE's journal, *Human Reproduction*, by 2004 had for several years been ranked among the highest in the field of obstetrics and gynaecology in the Journal Citation Reports of the Science Citation Index, and was recognised throughout the world as Europe's leading journal in the field.

This huge achievement is in no small measure due to the drive and energy of Robert Edwards. By 1986, remarkably, Edwards was chairman of ESHRE, editor of *Human Reproduction*, a director of Bourn Hall Clinic near Cambridge, and Professor of Human Reproduction at the University of Cambridge. He was in addition a Fellow of the Royal College of Obstetricians and Gynaecologists and of the Royal Society, as well as an active member of Bourn Hall's clinical and research programmes in assisted reproduction - in 1986, for instance, he was the author or co-author of at least ten scientific papers. And in 1987 Edwards almost single handedly and at short notice organised the third annual meeting of ESHRE in Cambridge. No wonder that in March 1987, having been invited to Toulouse for ESHRE's first conference on the ethics of assisted reproduction, he wrote to Jean Cohen: "I am still very doubtful about coming to Toulouse since I have been so totally wrapped up as chairman, Cambridge editor, and congress organiser. I must find time for my own things." And a few weeks later he wrote again to Cohen: "I am still worried about coming to Toulouse. I am trying to drop my commitments, yet already find I am on ten lectures next autumn alone! I also find that I am not present as much as I should be in Cambridge, with my students, in the university, or at Bourn Hall, and this is worrying me immensely at the moment."

Moreover, when Edwards did find himself in his office in Cambridge - either at Bourn Hall or in the university's Physiological Laboratory in Downing Street - he was a tireless correspondent, some days firing off more than 50 letters to colleagues on ESHRE's executive and advisory committees or to potential contributors to the journal. "You are such a compulsive letter writer," wrote ESHRE committee member José Egozcue in June 1986, "that I have a tableful to answer just because I am guilty of going on a one week vacation." Those letters were always courteous, complimentary and succinct, invariably ending with a request for support, action and commitment.

Edwards had first met Jean Cohen in 1968 at a conference on immunology in reproduction in Bulgaria, and later, in 1972, at the International Federation of Fertility Societies (IFFS) congress in Tokyo. There, both had been invited to a reception and both, having misunderstood the time of the appointment, had arrived an hour early. "So we had an hour to wait," Cohen later recalled. "We didn't know each other too well, but we did talk about the possibilities of IVF in humans, preimplantation diagnosis, cryopreservation - he said it would all be

possible. At the end of that hour I felt that I'd met someone like a prophet, and wondered, 'Is he really serious, or just a dreamer?' But later, when I got back to Paris I looked at his publications and realised that he was very serious."

By then, as those publications would show, Edwards had long progressed from mouse models to reproductive biology in humans. His essential interests were in human oocyte maturation, but had been largely frustrated by a paucity of human oocytes to work with. Thus, for six weeks in 1965 - through their mutual acquaintance with the geneticist Victor McKusick - he had joined gynaecologists Howard and Georgeanna Jones at Johns Hopkins University in Baltimore, primarily to avail himself of a supply of human oocytes which were there available from wedge biopsies. It was here in Baltimore that Edwards confirmed the precise timings of human oocyte maturation when, in one experimental series, 46 of 48 oocytes cultured for 36-37 hours reached metaphase-II at 36 hours, and thus the stage in their development at which they could be fertilised. It was, he would later recall, the breakthrough which paved the way for human IVF. These early attempts to fertilise human oocytes matured in vitro were described the following year (1966) in the *American Journal of Obstetrics and Gynecology* (96: 192-200) and in 1969 (with Patrick Steptoe and postgraduate student Barry Bavister) in *Nature* (22: 632-635). "Not bad for six weeks!" Edwards later noted.

Reading between the lines of those papers, Cohen may well have realised at this time that the lack of human oocytes was a continuing frustration to Edwards. He tried collaboration with clinicians at the Hammersmith Hospital in London, but again many journeys to the hospital to utilise ovarian tissue from gynaecological operations proved wasted and frustrating. Fortune, however, finally turned.

"Even as I was making fruitless journeys to the Hammersmith Hospital," Edwards later recalled, "I was browsing one day in the library of the Physiological Laboratory in Cambridge and discovered a little article in *The Lancet* written by a surgeon named Patrick Steptoe. He worked in Oldham, North England, and described a technique called laparoscopy. With it he could visualise and carry out some operations on the oviduct and on other internal organs... If he could reach the oviduct without difficulty he could also reach the ovary. This meant that he could reach the Graafian follicles and collect oocytes for studies on fertilisation in vitro." Edwards phoned Steptoe, who asked without demur: "When do we start?"

Edwards headed north for Oldham, and the pair agreed immediately to work together.

The story of Edwards's collaboration with Patrick Steptoe (who incidentally was a founder member of the British Fertility Society in 1974), which culminated in the birth of Louise Brown on 25th July 1978, has been often told: the tiny laboratory at Oldham & District Hospital, the long drives north from Cambridge every Friday night, the frustrations of failure, and accusations of malpractice by colleagues in Britain's medical establishment. But Cohen, in his literature review, would surely be impressed by the 1970 *Lancet* paper (4: 683-689) in which Edwards and Steptoe described the laparoscopic recovery of preovulatory human oocytes after ovarian stimulation with gonadotrophins, and, later that same year, their *Nature* report with Jean Purdy (265: 1307-1309) announcing the fertilisation and cleavage in vitro of preovulatory human oocytes.

As the latter paper would suggest and as Edwards recalled, these were "exciting times", for even in 1970 the pair were not far away from the transfer of embryos back into the mother and the creation of a pregnancy. So it was time, they agreed, to scale up from the tiny Oldham laboratory to a clinic dedicated to the treatment of human infertility. They thus applied to the Cambridge and Oldham health authorities for ethical approval – which they got – and to the Medical Research Council for research funding – which was turned down on the grounds that the project was unethical and laparoscopy dangerous. It was, said Edwards, a "brutal" rejection.

In fact, their only visible support came from the authorities in Oldham, who allocated to them the small laboratory and operating theatre (plus one bed) of nearby Kershaw's Hospital. What followed, however, were further difficult years – many eggs, high rates of fertilisation and embryonic growth, but no pregnancies after transfer. Not until 1975 – three years after Cohen had met Edwards in Tokyo – was a pregnancy achieved at Kershaw's Hospital, in the last of a series of eight patients given gonadotrophins and hCG. That pregnancy, however, was ectopic and had to be removed at ten weeks, but it did confirm that embryos cultured in vitro could implant and grow to the advanced stages of differentiation. It would be three more years – this time in a natural cycle in one of three patients admitted to Kershaw's Hospital for laparoscopy – before a pregnancy would progress to term and, in the birth of Louise Brown, prove to the world that here was indeed a

FIRST EDITION

Daily  **Mail**
THURSDAY, JULY 27, 1978 8p

**WORLD
EXCLUSIVE**

And here she is...

**THE LOVELY
LOUISE**



LOUISE BROWN, bright-eyed at 18 hours old: The test-tube baby in hospital yesterday
Daily Mail world exclusive picture by BILL CROSS. © World Copyright Associated Newspapers Group Ltd. 1978. Full story and more pictures inside

The birth of Louise Brown, on 25th July 1978, attracted huge media coverage throughout the world. Before then, Edwards had kept news of the ongoing pregnancy a closely guarded secret, and even his associates Jean Cohen and Howard Jones heard of Louise's birth on the radio.



The Brown family at a press conference in 1995. From left to right, Lesley Brown, younger daughter Natalie (also an IVF baby), John Brown and Louise.

technique in which human infertility could be treated and the opportunity of parenthood given to couples who otherwise faced childlessness or, at best, adoption.

Indeed, in 1993 John Brown, Louise's father, said in an interview that continued infertility had put such a strain on their marriage that he and his wife Lesley would in 1977 contemplate anything for a cure – even as they thought a tubal transplant along the same lines as Christian Barnard's heart transplantation in South Africa. "Steptoe did explain everything to us," John Brown said, "but we didn't really understand what he was talking about. To be honest I thought he was talking about artificial insemination. But we were desperate – here was one glimmer of hope so we grasped it." Steptoe aspirated Lesley Brown's one leading follicle during the morning of 10th November 1977, and by late evening fertilisation had taken place. Two days later Edwards called Steptoe in from home at his wife's birthday party, and by midnight the embryo consisted of eight even blastomeres. Within the hour that embryo was transferred to the uterus of Lesley Brown - and so began the most celebrated pregnancy of modern times.

In France, meanwhile, Jean Cohen had also long faced the conundrum of treating infertility in couples desperate in their childlessness - and, while still a gynaecologist at the Hôpital St Antoine in Paris, had headed an

BIRTH AFTER THE REIMPLANTATION OF A HUMAN EMBRYO

SIR,—We wish to report that one of our patients, a 30-year-old nulliparous married woman, was safely delivered by caesarean section on July 25, 1978, of a normal healthy infant girl weighing 2700 g. The patient had been referred to one of us (P.C.S.) in 1976 with a history of 9 years' infertility, tubal occlusions, and unsuccessful salpingostomies done in 1970 with excision of the ampullæ of both oviducts followed by persistent tubal blockages. Laparoscopy in February, 1977, revealed grossly distorted tubal remnants with occlusion and peritubal and ovarian adhesions. Laparotomy in August, 1977, was done with excision of the remains of both tubes, adhesiolysis, and suspension of the ovaries in good position for oocyte recovery.

Pregnancy was established after laparoscopic recovery of an oocyte on Nov. 10, 1977, in-vitro fertilisation and normal cleavage in culture media, and the reimplantation of the 8-cell embryo into the uterus 2½ days later. Amniocentesis at 16 weeks' pregnancy revealed normal α-fetoprotein levels, with no chromosome abnormalities in a 46 XX fetus. On the day of delivery the mother was 38 weeks and 5 days by dates from her last menstrual period, and she had pre-eclamptic toxæmia. Blood-pressure was fluctuating around 140/95, œdema involved both legs up to knee level together with the abdomen, back, hands, and face; the blood-uric-acid was 390 µmol/l, and albumin 0.5 g/l of urine. Ultrasonic scanning and radiographic appearances showed that the fetus had grown slowly for several weeks from week 30. Blood-œstriols and human placental lactogen levels also dropped below the normal levels during this period. However, the fetus grew considerably during the last 10 days before delivery while placental function improved greatly. On the day of delivery the biparietal diameter had reached 9.6 cm, and 5 ml of amniotic fluid was removed safely under sonic control. The lecithin: sphingomyelin ratio was 3.9:1, indicative of maturity and a low risk of the respiratory-distress syndrome.

We hope to publish further medical and scientific details in your columns at a later date.

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P. C. STEPTOE

R. G. EDWARDS

The letter of Edwards and Steptoe to the *Lancet* (1978; 2: 366). The report notes that pregnancy was established after laparoscopic recovery of an oocyte, in vitro fertilisation, normal cleavage in culture and the re-implantation of the 8-cell embryo into the uterus 2.5 days later. Delivery took place 38 weeks and five days after Lesley Brown's last menstrual period.

animal IVF project for INSERM, France's national medical research institute. Cohen had maintained his connections with Edwards since Tokyo, corresponding on their separate projects and meeting at conferences. Cohen had even shown Edwards pictures of monkey oocytes from the INSERM programme, only to be told that monkeys were difficult, and women easier.

In the spring of 1978 Edwards had accepted Cohen's invitation to come to France to explain to the French fertility society, the Société Française de l'Étude de la Fertilité, more about human fertilisation in vitro - but he never mentioned the then ongoing pregnancy of Lesley Brown. He was, Cohen later suspected, acutely aware of its sensitivity and was reluctant to make any public announcements, especially in France. In the event, Cohen - like the rest of the world - heard the news of Louise's birth on the radio and knew immediately that this was a development likely to change the whole course of infertility treatment throughout the world. Cohen's new boss at the Hôpital Sèvres outside Paris, Vincent Loffredo, agreed, and quickly gave permission for Cohen to go to London and hear Edwards's imminent report to the Royal College of Obstetricians and Gynaecologists ("Pregnancies following implantation of human embryos grown in culture" on Friday 28th January 1979). Recognising the importance of the news for France, Loffredo also promised that Cohen, from September that year (1978), could take charge of a new infertility centre at the hospital; Charles Thibault, who was then Professor of Biology at the University of Paris, recommended two protégé students, Michelle Plachot and Jacqueline Mandelbaum, in support. Cohen duly went to London for Edwards's RCOG presentation, which was received first in stony silence, but finally, as the enormity of the achievement sank in, to huge applause. "But this was the first time I really understood the opposition they had had," Cohen says.

From then on Cohen's relationship with Edwards developed, and became very close. Cohen would later visit Bourn Hall several times, and he continued to meet Edwards at congresses. But at the Hôpital de Sèvres Cohen's group still met with little success. They achieved their first fertilisation in vitro in 1979, but no successful transfers until 1980. "We had no experience, and no laboratory," explains Cohen, "just oocytes. And we had to transport the oocytes by thermos flask to the laboratory of the Hôpital Necker for fertilisation."

It was evident that Cohen's problem in the late 1970s was the same as Edwards's in the 1960s, but in reverse. Edwards had stalled for a want of

clinical support in the supply of oocytes and ovarian tissue, and now here was Cohen struggling for want of laboratory services. Success in IVF – as the collaboration of Edwards and Steptoe would attest – could only be achieved in a marriage of science and clinical medicine, where the laboratory’s new sciences of embryology and andrology worked alongside the investigations, diagnoses and procedures of the gynaecologist. It was a theme which both Cohen and Edwards recognised from experience, and one which they would bring to the table of their first discussions about ESHRE. It was a theme too which would persist throughout ESHRE’s history and in the pages of *Human Reproduction*, a recognition that reproductive medicine was dependent on both the scientist and the clinician, and that each should have equal place in the record of progress. This recognition is no better reflected than in ESHRE’s continuing requirement that the professional discipline of its chairmen alternates between a scientist and a clinician.

Edwards, of course, would never relinquish his role as a scientist and would always insist that even the triumph of IVF was no more than a milestone on the way to bigger things. “As a scientist,” he said, “my main interest has always been to arrive at a thorough understanding of human conception. It was my interest in this type of research – work on controlling sex determination, developing genetically tailored stem cells to treat disease and typing embryos for genetic defects – that really drove me to develop IVF.” By contrast, he added, infertility treatment was always the primary goal of Steptoe the gynaecologist.

While the birth of Louise Brown may have been met by a frown of opprobrium from some of Britain’s establishment stalwarts, in the press and among infertility groups elsewhere in the world it shone like a beacon of triumph. Thus, while Steptoe’s retirement from Britain’s state health service and consequent switch to the private establishment of Bourn Hall forced a two-year hiatus on him and Edwards, clinics overseas – especially in Australia – rapidly moved forward. In France the group of Jacques Testart and René Frydman at the university hospital at Clamart had obtained fertilisation of human oocytes (but no implantation) by 1980. One pregnancy from Cohen’s group (from a natural cycle oocyte sent to Testart’s lab for fertilisation) did implant but aborted. Eventually, the Clamart group was the first to announce an IVF birth in France – baby Amandine born in February 1982. Cohen’s group at Sèvres followed four months later with the birth in June of baby Alexia.

In the USA, following their retirement from Johns Hopkins, the gynaecologists Howard Jones and his wife Georgeanna were moving to a new division of reproductive endocrinology at the Eastern Virginia Medical School in Norfolk, Virginia, on the very day of Louise Brown's birth. The Joneses too had heard the news reports and from his new office Howard phoned Edwards to offer congratulations - and later arranged for Steptoe to visit Norfolk and give consultative advice on their own plans for an IVF programme in the USA. (And shortly after, Jones, like Cohen, flew to London for the RCOG meeting.)

From its beginning in 1980, and at the suggestion of Edwards and Steptoe, the Norfolk programme was built upon the natural and not the stimulated cycle, but frustratingly, after work in more than 40 natural cycles, there were still no pregnancies in Norfolk. At the end of this fruitless first year Georgeanna proposed that a switch to a gently stimulated cycle for the recruitment of multiple oocytes might be more effective, and, by May 1981, Norfolk finally achieved its first pregnancy in their 13th patient to receive gonadotrophins. Delivery by Caesarian section followed on 28th December 1981.

However, with Bourn Hall's clinical programme still on hold, the biggest strides in IVF were to be found in Australia. It was here that the Monash, Melbourne, group of Carl Wood and Alan Trounson - which with reproductive physiologist Alex Lopata had begun work in 1972 - treated 272 patients by IVF between January 1980 and February 1982, with 45 live births or ongoing pregnancies. "We are presently maintaining a constant pregnancy rate of 20-25% of patients laparoscoped," Trounson reported in 1983 with characteristic understatement, "which, given the variety of infertility conditions, makes IVF a very acceptable clinical treatment." And nearby, at the Royal Women's Hospital in Melbourne, the group of Ian Johnston had started clinical IVF in 1979 and in 1981 would perform more than 100 embryo transfers - with Australia's first live birth, Candice Reed, recorded in June 1980.

The first public descriptions of the IVF technique - even before Edwards's report to the RCOG - came at the fifth ESCO congress held on the Isola di San Giorgio Maggiore, Venice, from 2nd-6th October 1978. ESCO, the European Congress on Sterility, was at the time a congress-only organisation without members or elected officers run under the direction of its secretary-general, Kurt Semm from Kiel, Germany. Semm, whose history would later become more closely entangled with ESHRE's, had like many others recognised the impact of

The natural or the stimulated cycle in IVF?

By the early 1960s it was known that in animal models hormone treatment with gonadotrophins could stimulate oocyte maturation and ovulation. At the same time the Israeli endocrinologist Bruno Lunenfeld and colleagues showed that human menopausal gonadotrophin, derived from the urine of menopausal women, could induce ovulation (and a subsequent pregnancy) in hypopituitary-hypogonadotrophic amenorrhoeic women.

The first clinical work of Edwards and Steptoe in Oldham followed the lead of Lunenfeld with “two or three injections of hMG” to stimulate ovarian response early in the cycle – and to “prime” the ovaries to a convenient schedule. Ovulation was triggered by human chorionic gonadotrophin (hCG) (as Edwards had done in mouse models 20 years earlier). Initially there were no problems – as Edwards recalled, “ripe human oocytes aspirated from their follicles just before ovulation occurred”, and fertilisation achieved exactly as with oocytes matured *in vitro*.

Edwards and Steptoe achieved their first pregnancy in 1975, although ectopic. Attempts with other stimulation protocols followed, including clomiphene and hMG – as well as attempts in the natural cycle, which finally proved successful in the birth of Louise Brown. A second healthy birth soon followed.

Thus, the state of knowledge at the time suggested that the natural cycle offered the best opportunities with fewest disruptions to the endocrine environment – and this is the advice Edwards and Steptoe gave to the Joneses in Norfolk. However, faced with 12 months of failure and the model before them of hMG’s ability to induce ovulation in anovulatory women, the Joneses took a chance with a modest regime of hMG in ovulatory women for the recruitment of multiple oocytes. Pregnancies soon followed.

This was also the position reached independently in Australia, where nine successful pregnancies – after many attempts in the natural cycle – were reported by Carl Wood in 1981 from cycles stimulated by clomiphene. In Australia, further trials followed using clomiphene and different doses of hMG, and these produced pregnancy rates comparable with those achieved in Norfolk – which indeed would set the benchmark for ovarian stimulation protocols in the years ahead.

Louise Brown’s birth and had persuaded Steptoe to speak – so here in Venice, billed on the second day in Hall C as a “main lecture”, was “Pregnancy following IVF technique in humans” by PC Steptoe. Basil Tarlatzis, who had then not yet completed his residency training in gynaecology in Thessaloniki, Greece, was there in the audience, keen to learn more about reproduction (it’s more than just “push, push”, a colleague had told him) and already inspired by the news reports from England. “People were jammed into one long room of the Piccolo Teatro,” Tarlatzis recalls. “Steptoe walked down the centre aisle to the podium. All eyes were on him. He gave no scientific details, just a description. But even then I was gripped by what he said, and I knew already that this was what I wanted to do.”



Patrick Steptoe, who would set up a new clinic with Edwards at Bourn Hall in 1981, at ESHRE's first annual meeting in Bonn in 1985. Steptoe was made an honorary member of ESHRE in 1986.

By the time of the sixth ESCO congress, which was held in conjunction with the third World Congress of Human Reproduction in Berlin in March 1981, Steptoe was the meeting's honorary president and Edwards chairman of its scientific programme committee; Semm, as ever, was congress president. It was also clear from the programme just how far the technique of IVF and its attendant science had moved on in just a year or so. Now there were entire sessions on cryopreservation, ovarian physiology and controlled ovarian hyperstimulation. But to many of the participants in Berlin the most memorable paper came from Australia when Alan Trounson described in detail the techniques of "successful" IVF and embryo transfer in a stimulated cycle. "It was a major event," Tarlatzis remembers. "They simply said, that's how we did it... the media we used, the instruments, the stimulation protocol... so for me this was a huge event. People were standing outside because they couldn't all fit in the room. I went home and said, this is it, the new era is finally here, because it was the first time that hard scientific evidence had been presented at an open meeting. So far it had only been Bob and Patrick, and they only reported limited descriptive details. But now I was very clear in my own



According to many of the pioneers, the most graphic accounts of the IVF technique and procedures came at this time from Alan Trounson and his colleagues in Melbourne.

mind what I wanted to do, and immediately after Berlin I went home and started writing letters.”

It was indeed, as Edwards had said, an exciting time, a time that Arne Sunde would later describe as “electric”. And it was against this background of remarkable progress – where progress in science was so rapidly evident in real clinical results – that conversations between Edwards and Cohen slowly moved towards the idea of a society for reproductive medicine in Europe. The first catalyst for the idea, according to Cohen, was a meeting Edwards arranged at Bourn Hall in September 1981 for the few groups worldwide then making tangible progress in IVF. Cohen himself spoke, as did Carl Wood, Trounson, Johnston and Lopata from Melbourne, Wilfried Feichtinger from Vienna, Liselotte Mettler from Kiel, Lars Hamberger from Sweden, Howard Jones from Norfolk, Testart, Plachot and Frydman from France and

Edwards's own colleagues Steptoe and Jean Purdy. Many of the sessions took place outdoors in the grounds and it was here that Cohen was first persuaded – by the Australians – that induced cycles would give better results in IVF than natural. But more importantly, in Cohen's eyes, this was also the beginning of an inspirational time for reproductive medicine, and one in which the contribution of Europe was visibly ahead of the USA.

It was also a time when those gynaecologists determined to pursue the IVF route sought out from the dark corners of their hospitals reproductive biologists and lab technicians for help with hormone assays and sperm assessments. How long would it take to measure oestradiol... how much would it cost for progesterone? It was in such a way that Arne Sunde found himself engaged in infertility and not – as his career might then have determined – in research into prostatic cancer. "I came into infertility by sheer accident," Sunde explains. "I was working from 1975 in androgen metabolism, as a research scientist in a cancer group in Trondheim and we had just developed a new – and for us exciting - technique of quantifying androgens. At the same time – although I was unaware of it – the gynaecologists were planning an IVF programme, and they were still thinking of natural cycles. They needed to detect the LH surge, so the professor phoned me and asked, how long does it take to measure a 'hormone'. Of course, he was thinking about LH, but I thought he was referring to our new androgen assay - so I replied, 'two hours'. The professor was deeply impressed by this, especially in 1982. There were a lot of misunderstandings between us, believe me, but I was still fascinated by what he had to say. Eventually we set up a clinic in a small office, and we borrowed and begged microscopes, an incubator - even a bench - from around the hospital. We painted the office with paint we bought ourselves. Then we borrowed an ultrasound machine on the pretext that we were going to test it. But we started to show results and things moved quickly from then on."

And there were similar starting points for an equally important partnership in ESHRE's history. In 1977 André Van Steirteghem, whose certifications were first in paediatrics and later in clinical pathology, had returned to Brussels after a three-year term as a visiting scientist at the National Institutes of Health in Maryland, where he had worked in basic research in protein chemistry. He had returned to a post at a newly opened Hospital – of the Dutch speaking Free University of Brussels, or VUB - to organise a clinical laboratory for the provision of hormone assays. And,

just as Arne Sunde had been approached by his gynaecologist colleagues in Trondheim, so was Van Steirteghem now asked to provide hormone assays for the VUB's newly instituted infertility programme. The gynaecologist who asked was Paul Devroey, who at the time had just taken over in the department from Robert Schoysman. "I was not a reproductive biologist," says Van Steirteghem, "nor an embryologist, but I had in my time at the NIH done a lot of tissue culture work, and I guess that's why Paul got in touch."

Devroey had joined the VUB in 1980, three years after the hospital opened. He brought with him a broad interest in gynaecology and reproduction, and an already vast experience of microsurgery and sperm banking for donor insemination. Surgery, of course, was still the cornerstone of treating infertility in women, and Devroey with his new boss at the VUB had trained in microsurgery with Robert Winston at the Hammersmith Hospital in London. (Winston, incidentally, had himself trained in nearby Leuven with two of the pioneers of microsurgery, Ivo Brosens and Willy Boeckx.) So Devroey's first priorities at the VUB – where, he recalls, there were still no formal structures in place for reproductive medicine – were to maintain the strong Belgian traditions of surgery and implement a new donor insemination programme. "We didn't even think about IVF until December 1980," says Devroey. "I did ask several professors here about it, but I was still very new and nobody really knew me. They all seemed puzzled at these strange questions. The only one who showed any interest was André Van Steirteghem, and he was willing to help. Our first efforts together were work on urine and then serum assays for oestradiol - and that's how our collaboration started."

The real cue for a more determined effort in IVF at the VUB came after Frydman and Testart announced the birth of baby Amandine in France in February 1982. Shortly after, in June, gynaecologist Bernard Hédon from Montpellier had organised a short meeting of French microsurgeons in nearby La Grande Motte, and had hurriedly introduced a Saturday morning session into the programme in which Frydman would describe France's first success in IVF. "We were presenting a little of our endocrine data and André and I drove through the night from Brussels to be there," says Devroey. And on the Saturday evening, once the meeting was over and the discussions had stopped, they got back in the car and drove back to Brussels. "We were very motivated," smiles Devroey. But what happened on that Saturday lunchtime in La Grande Motte would make

the long hours of driving more than worthwhile. Luca Gianaroli, a young Italian scientist at the meeting who had already secured a two-year fellowship with Trounson in Australia, told Devroey and Van Steirteghem over lunch of a short hands-on workshop the Monash group was about to organise in Melbourne. Gianaroli, who would later be dispatched by Trounson to an outback sheep station to learn ovum pick-up and embryo transfer on an industrial scale, gave them a phone number in Melbourne. "What we were missing at the time," says Devroey, "were the hands-on experience and the hard scientific details. And here was Trounson ready to explain his work. So we went to a public telephone with a handful of French francs, and dialled Luca's number." What they heard at the other end was the answering machine of the Monash gynaecologist Gabor Kovacs, who evidently took the message and replied by mail that their places on the two-week workshop were booked. "From then on," Devroey recalls, "we were able to convince the board of directors at the VUB that we should proceed with IVF. After Monash, we began work on the mouse model, and, with everything in place, started treating patients in January 83." The first 30 cycles at the VUB – all stimulated cycles with the Monash protocol of clomiphene and hMG - yielded just four pregnancies. But even then, results deteriorated, prompting Van Steirteghem's return to Australia to examine their procedures once more and refine their techniques.

Of course, Brussels was not alone, and now, in the early 1980s, there were many other European groups organising IVF initiatives, with several looking to Bourn Hall, Australia and the USA for their training. Thus, many had established thriving programmes with several live births well before that third World Congress on IVF in Helsinki in May 1984 – notably the groups of Gerard Zeilmaker in Rotterdam, Hamberger and Matts Wikland in Sweden, Seppala in Helsinki, Ian Craft in London, Feichtinger in Vienna, and Safaa Al-Hasani, Klaus Diedrich and Liselotte Mettler in Germany.

Moreover, in the USA other groups were now following the Norfolk lead and orchestrating substantial programmes of their own – Martin Quigley in Houston, Richard Marrs in Los Angeles and Alan DeCherney at Yale. And here too were Europeans in abundance, notably Basil Tarlatzis working night and day with DeCherney, Neri Laufer and Fred Naftolin in Yale, and Pier Giorgio Crosignani on short NIH secondments in reproductive endocrinology to UCLA and the University of Southern California. However, progress in the USA had

been slower than might have been expected, even though - like the rest of the world - the Joneses had been keen to set up an assisted reproduction programme in the autumn of 1978. What held them back was not their new hospital, nor funding, nor appropriate staff. Firstly, as noted above, their entire work in 1980 had been almost wasted when 41 attempts in a natural cycle all ended in failure. Eggs were obtained from only 19 patients, and no pregnancies were achieved before switching to stimulated cycles in 1981. Secondly, the Joneses were restrained by local (not national) protests over the ethical issues of IVF. There was at the time in the state of Virginia a requirement that any new hospital programme should be granted a Certificate of Need. Hearings for all such applications were held in public, and the Norfolk application was met by loud local protest, which inevitably delayed the granting of the Certificate. In the interim Steptoe, Carl Wood and Alex Lopata all paid visits with advice from Europe and Australia, but Norfolk did not begin treating patients until March 1980. However, once the Joneses were successfully on the move from mid-1981, the pace in the USA quickened - and here, as in Europe and Australia, it became a time of huge excitement.

Basil Tarlatzis, who had joined the Yale programme in 1982 on a NIH fellowship, remembers the few months of that summer and autumn as truly inspirational and rewarding: "At the time the specialty of clinical embryology was non-existent and we were doing everything. We had to calibrate the media, the pH, look after the incubator, clean the benches . . . everything. Norfolk had set the standard with clomiphene and lower doses - two amps - of hMG. But at Yale we were more aggressive, and thought more eggs would give better results. So we were starting with three amps and increasing to four - and all this was part of our research. I think in the three years I spent at Yale we must have published 50 papers in peer reviewed journals. We were extremely productive, working day and night. There were no holidays. At that time we could not programme the cycle, and we were going to many meetings as well. We were writing papers on the plane and it was a very prolific time. We had a lot of basic science on top of the clinical work and we had papers in all the major congresses."

In the USA as in Europe the stars of those congresses were predominantly the Australians, notably at the fifth FIGO congress in San Francisco in October 1982, where for Tarlatzis "it was like a revolution, with free communications sessions on IVF which had phenomenal

attendance. People were even standing outside the rooms, straining to hear what was going on inside." And immediately after FIGO the circus moved down the California coast to the resort of Carmel, where a Serono "clinical colloquium" on IVF and embryo transfer had been organised by Pier Giorgio Crosignani, then working as an NIH research fellow in Los Angeles. It was a hugely popular event with all the main groups – including the two from Melbourne – presenting detailed scientific and retrospective data. "Once we arrived at Carmel," Tarlatzis recalls, "everybody was saying, you must get there early to get a seat, so we were there hours before the sessions started. Everybody doing IVF was there. At the time it was like this at every meeting. It was such an exciting and challenging time to live through. Everything was new. A single observation was new, whatever you saw, you could publish it immediately. It was only a matter of finding the time and the energy to do it. It's a rare privilege that we had. Very few people, especially clinicians, have this privilege."

And now, just a year or so later, the congress circuit was back in Europe and here were the same individuals, bouncing on the same waves of enthusiasm, assembled in the Finlandia Hall in Helsinki for the third World Congress of In Vitro Fertilization and Embryo Transfer. The same individuals who too would hear Robert Edwards on the opening day announce plans for a European society of reproductive medicine – and a proposal that those interested should assemble in Hall B at 11.00 am on the final day.

2

THE TEMPORARY COMMITTEE: 1984-1985

In March of 1984, just two months before the Helsinki congress, Robert Edwards phoned Jean Cohen from his office at Bourn Hall. IVF in France - with fewer than ten live births - was not going as well as elsewhere. Would Cohen like Edwards to come over and take a look? There were evident explanations to Cohen for his modest progress, not least the difficulties faced by his biologists in having no laboratory at the Hôpital Sèvres and having to learn their embryology alone as they went along. The success of Edwards and Steptoe's new venture at Bourn Hall - which had opened as a private clinic in 1981 after more than two years of organisation - was also a reminder to Cohen of how important biology was to the achievement of high pregnancy rates in IVF. Although his colleagues Plachot and Mandelbaum were cautious, Cohen agreed and Edwards duly arrived by car from Cambridge. He was allocated a room at the hospital and stayed 15 days, working closely with Plachot and Mandelbaum - and with Jean Purdy who arrived later from Cambridge.

Over dinner one evening at Cohen's 16th arrondissement apartment the conversation turned to the "bigger picture" of reproduction and their own concerns that the only way to publish their results with any impact was through the journal of the American Fertility Society and at meetings which were predominantly in the USA. "We both knew how important this was," says Cohen. "Ninety-five per cent of the world's gynaecologists

were still hostile to IVF. But there was no way we could reach them, no international audience unless we went to *Fertility and Sterility* or the AFS meetings." It was a concern, of course, shared by many others working in IVF in Europe or, like Pier Giorgio Crosignani, seeing for themselves at first hand how potent the US structures were. "In Europe," says Crosignani, "we are divided by history, not by geography. Whereas in the USA, whether you're in California or in Florida, you're still in the USA, and this gave the American groups a great advantage. This is why I was so keen on the idea of bringing together the few groups in Europe then working in reproduction."

It's a view expressed by many others of the pioneers who met that May in the Finlandia Hall in Helsinki, but it was, nevertheless, in that conversation of Edwards and Cohen at dinner in Paris that emerged the determined idea of a European society able to give to European scientists and clinicians the same advantages then enjoyed by the Americans.

If the huge advances of the previous few years in IVF were the ostensible driver of the idea, recognition that real progress could only be made on strict scientific principles - basic research, the proper reporting of results, full discussion of any ethical issues - lay firmly at their roots. Success, as the experience of Edwards and Cohen demonstrated, was dependent on the partnership of science and clinical medicine, and now, Cohen recalls, in March 1984 in this Paris apartment, "we knew what we wanted to do. I was the clinician Edwards needed to form the society we wanted, but, as Steptoe said, it was not always easy to work with him. It was the same with me. I could be difficult, but I was a good ally, and we always worked in an alliance of biology and clinical medicine."

What Edwards and Cohen had in mind was a society which would be steered in a formative first year by a temporary committee representative not just of science and clinical medicine but also of the geography of Europe. The essential responsibilities of the temporary committee would be to finalise a name for the society, formulate constitutional by-laws, and oversee the election of a committee which would take over the running of the society. The ultimate goals, of course, were a journal and an agenda for scientific meetings, but first there were the formalities.

In his first announcement in Helsinki Edwards had explained the principles of national representation, and some countries in the next few days of the congress had nominated their own delegates for the temporary committee - Robert Schoysman and André Van Steirteghem for Belgium, Aarne Koskimies and Lauri Saxen for Finland, Henning Beier and

Klaus Diedrich for Germany, Harry Massouras for Greece, Neri Laufer and Shlomo Mashiach for Israel, Crosignani, now back in Milan from Los Angeles, and Ettore Cittadini for Italy, Bert Alberda for The Netherlands, Pedro Barri for Spain, and Lars Hamberger and Percy Liedholm for Sweden. It was a good start, Edwards thought, but there were still some representative gaps, particularly among the scientists - which is why, in Hall B of the Finlandia Hall, all eyes turned towards the young Norwegian researcher now sitting at the back of the room. The name of "S. Arne" was duly added to the list.

There were some names, however, not on the list, despite their strong feelings in favour of a European society. Paul Devroey, although registered as a delegate in Helsinki, was detained at the VUB by an emergency in the labour ward, and Basil Tarlatzis, although presenting papers at the congress with his Yale colleague Alan DeCherney, was heading right back to New Haven and was not yet sure where his academic future lay, in Europe or the USA. However, for the "delegates" now assembled as the temporary committee in Hall B, Edwards and Cohen had four items on their agenda: the name of the society, its aims, its constitution, and the



Arne Sunde with Robert Edwards in 1985. Sunde, a fledgling embryologist, was surprised to be invited to join the temporary committee in Helsinki in 1984, and even more surprised to be asked on to the first Executive Committee as special advisor for training the following year.

election of officers. Without hesitation Edwards himself was elected chairman and four names for the society were proposed for discussion: the European Society for Human Embryology; the European Society of Biological Reproduction; the European Society of Human and Animal Reproduction; and the European Society of Human Reproduction and Embryology. No decisions were taken, but, as far as Edwards was concerned, the working name - and one which he would use in tabling the agenda for the next meeting and drafting proposed by-laws - was the European Society for Human Embryology. As for the by-laws, Edwards asked each member to forward the details of other societies' constitutions "to serve as a model for our Society". Members of the temporary committee were also asked to identify any other European societies whose areas of interest - developmental biology, placentology, paediatrics, andrology, fertility, genetics - might be shared.

Before going their separate ways, the members agreed to meet next in London on 2nd September 1984, an interim of more than three months which would give them time to promote the society and consider the proposed by-laws which Edwards would draft. On the 12th July, less than two months after the Helsinki meeting, Edwards did indeed mail the draft text to his colleagues on the committee, a 16-item proposal which primarily covered the constitutional formalities of the society but - in paragraph 2 - identified its purpose as "to facilitate the study and discussion of all aspects of human embryology from before conception until the birth of the neonate" and to "cooperate with other learned societies, interested organizations, universities and any organizations with related interests". These two issues more than any others would be fiercely discussed when the group next met in London.

The Ramada Plaza Hotel is today not one of London's best known landmarks. The 12-storey functional hotel overlooks London's historic cricket ground of Lord's and, lying at the north-west corner of Regent's Park, is just a five minute walk from the Royal College of Obstetricians and Gynaecologists. Throughout its 40-year history the hotel has had several owners, and several names, but in 1984 it was in the hands of the Ladbroke's casino group and was known as the Westmoreland Hotel. The second meeting of the temporary committee was scheduled for 11.00 am at the Westmoreland Hotel on Sunday 2nd September and by mid-July Edwards had raised £750 from Bourn Hall and \$1500 from UNESCO to cover expenses. Two other organisations, the British Council and Council of Europe, did not reply to Edwards's request for support. The proposed

by-laws - as "a basis for the formation of a Society" - had been circulated to all 425 scientists and doctors who had shown an interest or been recommended by others, with committee members asked to submit comments before 15th August.

Not everyone could make it to London, and apologies were received from Beier, the German "science" delegate, Egozcue from Spain, Floersheim, Hamberger, Lauritsen, Miras, Polani, Saxen, Schoysman and Testart. Klaus Diedrich, who in 1984 was moving base from Lübeck to Bonn, was not sure, but now as the sole German representative decided to go to London and home the same day. Jean Cohen and Pier Giorgio Crosignani, however, were more determined. Cohen had been visiting his daughter in California and flew in overnight to Heathrow from Los Angeles. Meanwhile, throughout the summer Crosignani had been ill with a thyroid problem and had lost 8 kilos in weight. He was still not active around the hospital, but the idea of a European society was important to him and he was determined to support the initiative. Thus, true to his word, on the Sunday morning Crosignani rose from his sickbed and headed to the airport. It was his first trip after recovery, and he too went out and back to London in the one day. Joining him, alongside Edwards, Cohen and Diedrich, were Barri, Domenico Geraci, Koskimes, Laufer, Liedholm, Massouras, Sunde and Van Steirteghem.

The minutes for that meeting note that there was "extensive discussion given to the proposed by-laws". And certainly, while the agenda was billed under the name of the "European Society for Human Embryology", the minutes were recorded as those of the "European Society of Human Reproduction and Embryology", the first time that "ESHRE" was formally employed. However, a final decision on the choice of name was deferred until "subsequent meetings". The initial draft of by-laws was also substantially amended, with the society's aims now modified to promote study and discussion in "human reproduction and embryology" without any definitions of time. It was also agreed in London that the society should consist of an executive committee and advisory committee whose members would reflect the geography of Europe and preferably comprise an equal number of scientists and clinicians. By the end of the year, with further discussion at the third meeting in Monaco, the by-laws would be described as "recommended", but would not be constitutionally ratified until the society's first annual general meeting in Bonn in June 1985.

European Society of Human Reproduction and Embryology

Minutes of the Second Meeting of the Temporary Committee, held on Sunday, 2nd September in the Ladbrooke Westmoreland Hotel, London.

Members present: R.G. Edwards (Chairman), P.N. Barri, J. Cohen, P. Crosignani, K. Diedrich, D. Geraci, A. Koskimies, N. Laufer, P. Liedholm, C. Massouras, A. Sunde, A. Van Steirteghem.

Apologies received from: H. Beier, J. Egozcue, Y. Floersheim, L. Hamberger, J.G. Lauritsen, C. Miras, P. Polani, L. Saxen, R. Schoysman, J. Testart.

Edwards's minutes from the second meeting of the temporary committee at the Westmoreland Hotel, London. Although there was yet more discussion to come about the society's name, this was the first time that the European Society of Human Reproduction and Embryology was formally used.

However, by that third meeting, which Edwards called at the Loews Hotel, Monte Carlo, to coincide with the seventh ESCO congress in late September, the by-laws were moving in concept towards a constitution which would define ESHRE to the present day - notably, an executive committee consisting of chairman, chairman elect, past chairman, secretary, and treasurer (with the addition then of publications secretary and membership secretary), with appointments lasting two years, and the membership meeting once a year at an annual general meeting to confirm by majority vote all recommendations and decisions taken by the executive committee. The minutes of that third meeting also note, as item 5, that "the Committee decided that the Society should be formed".

The 1984 ESCO congress in Monte Carlo where the temporary committee met had in fact been organised by Jean Cohen and Alain Audebert at the request of Kurt Semm. At the opening ceremony Cohen, as President of the Société Française de l'Etude de la Fertilité, noted in his address that ESCO was an important society doing important work, but was not a democratic organisation and the scientific programme of its congresses not decided by committee. Now, however, added Cohen, there *is* a young society in Europe with democratic principles, and he suggested that both societies would benefit from a merger. The suggestion caused huge consternation, with Semm complaining next day to Cohen's professor. And of course Cohen's suggestion of a merger caused prolonged discussion at the committee meeting at the Loews Hotel, which went on long after 9.00 pm.

There was also much discussion about the society's name - should "Embryology" be dropped, was "Human" too restrictive, was it a society

Robert Edwards

Founding father and ESHRE's first chairman 1985-1987

It's fair to say that without Robert Edwards there would be no ESHRE and no *Human Reproduction* as we know them today. ESHRE acknowledged these remarkable achievements in 1993 when Edwards was made an honorary member of the society and in 2000 when the R G Edwards lecture was instituted at the annual meeting in his honour.

After graduating in zoology in 1951 from the University College of North Wales, Robert Edwards completed his PhD in Edinburgh at the Institute of Animal Genetics. In the following 50 years Edwards was awarded honorary doctorates from the universities of Wales, Hull, York, Brussels (Vrije Universiteit), North Wales, Valencia, Mons-Hainaut and Timisoara.

His professional life began at the National Institute for Medical Research in London, working mainly in mouse models on the mechanisms of normal and failed reproduction. Ten years after his first mouse paper, he published his first report on humans, describing blood group antigens on sperm. The following year he began working with human oocytes in vitro, which took him for six weeks to the Johns Hopkins Hospital in Baltimore where, with Howard and Georgeanna Jones, he worked on the maturation and fertilisation of human oocytes in vitro. Back in Britain and now established at the University of Cambridge, he began collaboration with the gynaecologist Patrick Steptoe in 1968, achieving fertilisation and cleavage in human oocytes in vitro the following year. Ten years later, this same collaboration was responsible for the birth of Louise Brown, the world's first IVF baby, born in Oldham on 25th July 1978.

Throughout this time Edwards's work was recorded in a multitude of written papers and congress presentations, and acknowledged in countless chairmanships and honorary awards. With Steptoe he opened Bourn Hall Clinic in 1980, and in 1985 was made Professor of Human Reproduction at the University of Cambridge, until his "retirement" in 1989.

Robert Edwards, along with Jean Cohen, founded ESHRE in 1984, and became the society's first chairman in 1985. He launched ESHRE's journal *Human Reproduction* the following year, and *Human Reproduction Update* and *Molecular Human Reproduction* in 1996, all of which he edited until 2000. He is currently Chief Editor of *RBM Online*.

"of" human reproduction or "for"? - and about the by-laws and the society's range of interest. Edwards later wrote in the minutes: "It was felt that the scope should be restricted in general to the study of gametogenesis, conception, the first trimester of pregnancy, but with the inclusion of associated topics of relevance to the main subjects of interest, e.g., the birth of children conceived in vitro, ethics, the use of DNA libraries and other preparations."

However, Edwards had also proposed in his draft of by-laws that the new society should co-operate with other associations with related interests; so not surprisingly in view of Cohen's controversial remarks, ESHRE's relationship with ESCO remained at the top of the Monte Carlo

agenda. ESCO had been founded in 1967 by Kurt Semm. Semm had devoted his life - despite ridicule and criticism - to minimally invasive laparoscopic surgery; indeed, it was Semm who, according to his 2003 obituary in the *British Medical Journal*, was largely responsible for the advance of laparoscopy from a diagnostic to a surgical procedure. However, by the early 1980s Semm was also a prime mover in the conference world of gynaecology, with ESCO congresses scheduled every three years and Semm's own name imprinted on the mastheads of numerous other meetings. Semm, for example, was a member of the International Advisory Board of the same world IVF congress in Helsinki at which Edwards made his first announcements about ESHRE, and subsequently as honorary chairman of the International Academy of Human Reproduction, whose world congresses were also staged every three years.

However, as Jean Cohen had publicly implied in Monte Carlo, what set ESCO apart from the formative ESHRE was that the latter would be a society of members empowered by majority vote at an annual meeting to affirm or reject the decisions of its executive committee, while ESCO remained a non-democratic society whose only vote apparently was that of Kurt Semm. Klaus Diedrich, whose career in gynaecology had begun in Lübeck, not far from Semm's base at the University of Kiel, noted that "Semm was a man of many ideas, and shared some similarities with Bob Edwards in that he had ideas, was creative, but was not always accepted by the medical establishment". Liselotte Mettler, Semm's former colleague in Kiel and his apologist in most obituaries, later recalled several incidents reflecting the controversies which always surrounded him, especially in Germany: a slide projector unplugged in mid-lecture (on ovarian cyst enucleation by laparoscopy) with the explanation that such unethical surgery should not be publicised; the request of his colleagues in Kiel that Semm should have a brain scan because "only a person with brain damage would perform laparoscopic surgery"; and advice to Mettler herself that, "if you wish to advance in the German academic world, don't pay any regard to Semm's nonsense".

But now, here in Monte Carlo for ESHRE's third temporary committee meeting, ESCO appeared to be - at least ostensibly - some sort of complement to ESHRE, a clinical forum seeming to reflect Edwards's aim of co-operation with organisations with related interests. Moreover, Cohen at the time was still convinced, first, that there was not enough room in Europe for two societies in a similar congress field, and second, that

ESHRE might benefit from ESCO's relationship with clinicians. Thus, as the evening grew later and dinner appointments faded out of reach, the temporary committee finally agreed that three representatives of ESCO - Semm himself, plus Robert Schoysman and Anthony Comninos - should join ESHRE's temporary committee as full members with a remit to consider closer collaboration and the joint organisation of future meetings. The next question, therefore, was where and when would these meetings take place.

During the second committee meeting in London in early September the subject of an ESHRE congress had been briefly discussed under the item "activities in 1985". The chairman had asked if any of those present might consider organising ESHRE's first congress, and two hands had been raised - one by Klaus Diedrich and the other by André Van Steirteghem. Edwards suggested that the pair should get together and sort something out. They agreed to meet on a forthcoming Saturday in Cologne, Diedrich driving down from Bonn with his colleague Hans van der Ven, and Van Steirteghem taking the train from Brussels with Paul Devroey. The meeting was, of course, amiable enough, but initially inconclusive, with both sides keen to demonstrate their credentials. A compromise looked inevitable, and both groups retired to consider their positions - Van Steirteghem and Devroey to the nave of the ancient cathedral of Cologne to reflect. "We didn't know the Germans," says Van Steirteghem, "but we were impressed that they had promises of support from the industry and a pledge of 10,000 deutschmarks. We couldn't compete with them on budget so, when we returned from the cathedral, we said OK, but on one condition - that you organise the first meeting together with us and we organise the second meeting together with you. So we went back on the train to Brussels, and that's the proposal we made in Monte Carlo." It was an anxious time for Van Steirteghem, with a lot at stake for Belgium and the new centre at the VUB - so much so that on the train to Cologne he started nervously smoking his pipe again after many years of abstinence (and even today, at times of less stress, Van Steirteghem is still known to take an occasional puff from his pipe). The promise of DM10,000 (€6500), incidentally, came from Diedrich's new boss in Bonn, Professor Dieter Krebs.

Thus, just a week later in Monte Carlo it was agreed that ESHRE's first annual meeting would take place in Bonn on 24th, 25th and 26th June 1985, setting a three-day precedent which would persist as a congress format to the present day. The organising committee would be composed of

Diedrich, Beier, Al Hasani, Krebs, Van der Ven, Devroey and Van Steirteghem, while the scientific committee was nominated as the organising committee plus Cohen, Testart, Chist (president of the German Embryological Society), Saxen, Egozcue, Geraci, Schoysman, Zeilmaker, Hamberger and Edwards himself. Bonn would be followed by Brussels in 1986 and by Budapest in 1987, where ESHRE would jointly organise ESCO's eighth congress.

Jean Cohen, who from Paris had long run almost single-handedly a journal for French doctors called *Contraception Fertilité Sexualité*, was also asked in Monte Carlo to consider for the next committee meeting the design of stationery and a logo - one perhaps not dissimilar to that of his own journal. It was also suggested that all matters relating to the publication of proceedings from the first annual meeting should be referred to Cohen. Appropriately, therefore, the next meeting of the temporary committee would be in the offices of Cohen's journal at Gyn.Obs just two minutes from the Place de l'Opéra on Sunday 9th December 1984.

For a young researcher like Arne Sunde the commitments of time and money of a place on the temporary committee of ESHRE were not insignificant. Apart from the small grants Edwards had secured for London, there was no funding for travel or accommodation - and Trondheim was not the most convenient location in Europe. While many of his clinical colleagues on the committee would find funding for their expenses, it was more difficult for a young scientist, and Sunde was simply unable to raise the finances for Monte Carlo. (His colleague, Professor Kare Molne, who was a delegate at the ESCO congress, represented Norway on the committee.) For the fourth committee meeting, however, Sunde was relieved to find that two nights (as well as his place at lunch) had been booked at a small Paris hotel near the journal's offices in the Rue des Petits Champs, with one night charged to the account of Gyn.Obs.

In his 13th November letter Edwards urged all committee members to attend "because our Society will soon have many ongoing activities and we must make sure that our organization is strong enough"; a week later he also promised "some funds" for travel expenses. On the agenda for the fourth committee meeting were updates from the organizing committees for Bonn (which had already held its first meeting in October) and Brussels, as well as reports from Cohen on publications and the logo.

With 19 members present, the meeting room at the offices of Gyn.Obs was cramped, smoky and hot, even on this December day. And discussion

once again proved just as heated. Klaus Diedrich as secretary of the organising committee for Bonn reported that the congress venue, the Stadthalle in Bad Godesberg, Bonn, had adequate meeting facilities and would cost ESHRE around DM150,000 (approximately €100,000). Most importantly, Diedrich added, the congress fee would be kept as low as possible - at DM150 (€100) for participants and DM50 (€35) for students - once again setting a trend of minimal registration fees which still continues today. And true to his word in Cologne, Diedrich announced that financial support was in place from the local offices of pharmaceutical companies for commercial exhibit space. More than 4000 copies of the first congress announcement would be printed (with the support of a commercial sponsor) and 1000 sent from Germany to all participants in Helsinki and in Monte Carlo. A second announcement, ready for the New Year, would hopefully incorporate “the new ESHRE emblem”.

Edwards, as chairman of the scientific committee, reported that the programme would be composed of invited lectures, free communications and poster sessions. He added that all invited lecturers except one had agreed to take part, as had all chairmen and discussants. This indeed was rapid progress - agreement in Cologne on Bonn as a venue was only reached in late September.

The logo of Cohen’s journal *Contraception Fertilité Sexualité* had been developed by a graphic designer in Paris, and the same designer had been commissioned by Cohen to consider a logo for ESHRE. The designer had produced three possibilities, each of which Cohen showed to the 19 members huddled in the meeting room at Gyn.Obs. A vote was taken on each, and one chosen - and remarkably, this same logo of ever increasing spheres and tight italic script is the one which still symbolises ESHRE today and is recognised in reproductive medicine throughout the world.



The logo of Jean Cohen’s journal *Contraception Fertilité Sexualité*. The temporary committee asked Cohen if his designer might come up with something similar for ESHRE.

But most importantly, this was also the committee meeting at which the idea of an ESHRE journal was first seriously discussed. In Monte Carlo Jean Cohen had been asked to consider the publication of the first congress proceedings and had since then approached three publishing companies. Now, in Paris he reported that one of the publishers, IRL Press from Oxford, seemed the best proposition - they were experienced in publishing scientific journals and books, and were not too big that ESHRE's commissions would be lost in the crowd. However, the fact that all three of Cohen's publishers were already publishers of journals in gynaecology and related fields raised concerns among the committee about the relationship between ESHRE and these other journals. Would it not be better for ESHRE, when the time came, to publish its own journal? It was a matter of such importance and heated discussion that the chairman called for a vote on whether ESHRE should even start a journal of its own - with the show of hands overwhelmingly in favour (with just one dissent). Cohen immediately took up the initiative and proposed Edwards as editor, who after protest that his workload was already excessive, accepted with the provision that an editorial committee might be formed to help him along.

It was, of course, a momentous decision and one which would absorb Edwards for the next 15 years of his life - and immediately stamp ESHRE as a society committed to the science of human reproduction. It would also, in greater measure than anyone could imagine, fulfil those first pioneer ambitions of founding a journal in which European scientists and clinicians would find a welcome home for their work and where the eyes of the editor would look warmly and diligently on any paper submitted.

Among the other items on the Paris agenda - and of huge long-term consequence for ESHRE - were that André Van Steirteghem was elected treasurer and Klaus Diedrich membership secretary. Edwards also proposed that each year two distinguished figures in reproductive science and medicine might be honoured as Honorary Members - the first to be Dr Raoul Palmer, the French gynaecologist who had been the inspiration in laparoscopic surgery for Kurt Semm, and Professor Friedrich Seidel, a zoologist from the University of Marburg, Germany, whose pioneer work in developmental biology had achieved live births from isolated rabbit blastomeres. Both would be presented with their honorary membership at next year's first annual meeting in Bonn (though in the event neither could be present).

Jean Cohen

Founding father and ESHRE's second chairman 1987-1989

In recommending Jean Cohen as his successor as ESHRE's chairman, Edwards described Cohen as "deeply involved in many of the fundamental ethical and organisational activities in human reproduction both in France and internationally".

Cohen had qualified in Paris in 1959. From 1965 to 1974 had worked as an "assistant" in O&G to Professor Bernard Meier at the Hôpital Saint-Antoine in Paris, and from 1974 to 2002 as director of the Centre de Stérilité at the Hôpital de Sèvres.

As well as chairman of ESHRE from 1987 to 1989, Cohen was a past president of the Société Française de Gynécologie and Société Française pour l'Etude de la Stérilité, and chairman of IFFS from 1992 to 1995. Cohen was made an honorary Vice President of the American Fertility Society in 1992 and an honorary member of IFFS in 1998. He was editor of his own journal *Contraception Fertilité Sexualité* from 1963 and of *Gyn.Obs* from 1973, and an assistant editor of *Human Reproduction* from 1991 to 1997.

During ESHRE's early years it was Cohen who took the first initiatives for the formation of the journal, instigated contracts with publishers, put ethical issues high on the society's agenda, devised a structure for training, recognised the value of acceptable corporate sponsorship, and determined to put the society's finances on a sound basis.

By the time of the fifth meeting of the temporary committee - which took place in Brussels in March 1985 - Cohen and Edwards had continued negotiations with two of the three publishers identified for ESHRE and had furthermore sought an agreement whereby the journal *Acta Europea Fertilitas* (the *European Journal of Fertility and Sterility*) would cease publication in December and transfer its resources (including three editors and subscription list) to those of a new European journal produced by ESHRE. A publications proposal from IRL Press in November '84 with updates in February seemed to meet most of Cohen and Edwards's requirements, so, when the committee met at the Fondation Universitaire in Brussels, a representative from IRL was present and a draft contract in place for consideration. It was a detailed document, outlining the terms on which IRL would print, publish and distribute for ESHRE a bi-monthly journal comprising around 80 pages per issue. ESHRE would supply IRL with all copy for each issue. The draft proposal also indicated that, because the transfer of subscriptions from the European journal would reduce IRL's "funding risk", IRL would make a donation of £10,000 to ESHRE. It was thus hoped that the editorial committee would reach agreement with IRL for both congress publications and a journal at its next meeting in Bonn in April.

Members of the temporary committee after Helsinki, 1984

Belgium: Robert Schoysman, André Van Steirteghem

Finland: Aarne Koskimies, Lauri Saxen

France: Jean Cohen, Jacques Testart

Germany: Henning Beier, Klaus Diedrich

Netherlands: Bert Alberda

Israel: Neri Laufer, Shlomo Mashiach

Italy: Pier Giorgio Crosignani, Ettore Cittadini

Norway: Arne Sunde

Spain: Pedro Barri, José Egozcue

Sweden: Lars Hamberger, Percy Liedholm

Switzerland: Yonat Floersheim

UK: Paul Polani, Robert Edwards

The temporary committee also heard that 90 short communications were already submitted for the first annual meeting in Bonn, as well as 40 posters. Final selection, text editing for the programme and abstract books, and arranging the presentations would be completed the following month. It was thus evident that interest in ESHRE - despite the fact that the society still lay in the hands of a temporary committee - was gathering pace, and Klaus Diedrich reported that membership was now approaching 150. An appeal for participation in Bonn and for membership of ESHRE would be mailed out in April.

There were two other items on the Brussels agenda which would have lasting impact for ESHRE: first, Edwards's proposal for the formation of an ethical committee briefed to produce guidelines on the discussion of issues in assisted reproduction; and second, that Jean Cohen - who was unable to attend in Brussels - should be invited to be chairman elect. Both proposals were accepted unanimously. Cohen, wrote Edwards in his letter of recommendation to all committee members, "has helped to establish the Society, he is a leading French doctor and is deeply involved in many of the fundamental ethical and organisational activities in human reproduction both in France and internationally".

Incidentally, the venue for the Brussels meeting, the Fondation Universitaire, would also set a precedent for many future meetings in Brussels. Accommodation and meeting facilities at the Fondation were available to its members and academic guests and had lasting appeal to

ESHRE's executive - its creaky oak floors lent a collegiate atmosphere to meetings, there was a wood-panelled bar where discussion could go on long into the night, and it was not expensive! Indeed, Arne Sunde, who was present at those early meetings, says: "ESHRE has never been about five-star hotels. We always stayed in modest tourist hotels in Paris - it was much more important that the hotel was convenient for Jean Cohen's office. And there was an excellent atmosphere in the Fondation Universitaire. It was necessary to be economical then - and it's still necessary not to spend too much but to invest more, in the journal, in training, in the annual meeting."

It was now clear that, as the date of ESHRE's first annual scientific meeting and first annual general meeting (AGM) drew nearer, activity among the temporary committee was intense. Both Edwards and Cohen were under pressure from IRL Press to reach contractual agreement so that announcements on the proposed journal could be made in Bonn, but there were still major issues - particularly over the duration of the contract - with which Edwards was not happy. Cohen was also busy in devising a structure for the proposed European ethics committee and, if the temporary committee was to hand over administration to an executive committee, the society would need formal registration and adoption of its by-laws before Bonn.

It so happened that the father-in-law of André Van Steirteghem had been the chairman of the International Federation of Library Associations and had much experience in the formation of international societies (through his dealings with the International Federation of Societies in Belgium). Van Steirteghem now turned to him for advice and discovered that Belgium had become a "kingdom for international societies" because of their charitable status and tax concessions. The only requirements, Van Steirteghem learned, were the deposition of statutory by-laws, one Belgian national on the board, and an address in Belgium. It was this information which Van Steirteghem would now take to the next temporary committee meeting, and the reason why moves began to register ESHRE in Belgium. The "recommended" by-laws as drafted by Edwards and modified in subsequent committee meetings were amended by a local lawyer in line with Belgian legal requirements and finally accepted by the temporary committee - and these were the by-laws which the first AGM would ratify and which are largely in place today. The address of the International Federation at 40 rue Washington in Brussels would be

ESHRE's first registered address, until Central Office moved from the VUB in 1996.

As the articles of the by-laws show (see Appendix A), ESHRE would be regulated by Belgian law as a non-profit making organisation whose purpose was to "facilitate the study and discussion of all aspects of human reproduction and embryology". The society was composed of a General Assembly, an Executive Committee (EC) and an Advisory Committee (AC), with members defined as full, student and honorary. Article 9 noted that all recommendations and decisions taken by the EC were subject to confirmation by majority vote at the AGM or referred back to the executive. Any changes to the by-laws could be accepted by a two-thirds majority of a quorum of 60 per cent of the total membership. Article 15 explained the election of the AC by the AGM, which "should reflect the geographical basis of the countries of Europe"; in Bonn the AGM defined composition of the AC as two members from France, Germany, Italy, Spain, United Kingdom, the Benelux countries and Scandinavia, and one from Austria, Greece, Israel, Ireland, Portugal and Switzerland. These recommendations, based on the notion that countries with more than 20 million inhabitants (and 15 ESHRE members) could elect two representatives and countries with fewer than 20 million (and more than 15 members) could elect one, would need some adjustment over the ensuing years. The AC, however, could propose nominations for the EC and changes to the by-laws.

Time would also show that an individual's involvement in the AC was a sure proving-ground for subsequent membership of the EC. Certainly, by the time of Hans Evers' chairmanship in 2001, nominations for the EC could only be made from members of the AC or chairmen of ESHRE's Special Interest Groups - and these, says Evers, were already people whose involvement and commitment were known. "So today everyone can become active in one of these two groups," explains Evers, "and, by becoming active, can be selected for the EC. Though that's still a selection, and not an election, our opinion is that we should stick to this system. At least people now know how you can become a member of the EC."

In May 1985 the new secretary, Klaus Diedrich, advised members of the temporary committee that its next - and last - meeting would be in the Hotel Dreesen in Bad Godesberg, Bonn, on 23rd June, the day before ESHRE's first annual meeting opened and two days before ESHRE's first AGM. It was a huge agenda reviewing the society's progress so far and

considering how the formalities of the by-laws could be adopted with sufficient strength to put to the AGM - and would take up more time than the single day allocated. In fact, the temporary committee met for two other days during the congress, on both occasions before breakfast.

First, before a gathering of some 25 temporary committee members and invitees, membership of the future EC was confirmed as Edwards (chairman), Cohen (chairman elect), Diedrich (secretary), Van Steirteghem (treasurer) plus Egozcue, Crosignani and Sunde as members. Arne Sunde, who had been an active and committed member of the temporary committee since Helsinki, was more than surprised to be nominated for the EC. "I was certainly an outsider," he recalls. "And as a scientist I hadn't really been doing much embryology. There were other people from the Nordic countries who would be much more obvious than me - Hamberger, Seppala, Wikland. But the fact that I was there, and after a while did something for them, and was a comparatively young scientist from Norway, I guess that made a difference."

After reports on ESHRE's three scheduled congresses (Bonn, Brussels and the joint venture with ESCO in Budapest), there were other items of long-term importance for ESHRE. First, Edwards announced that in 1986 ESHRE would organise three workshops, each designed to offer hands-on training in reproduction where, so far in Europe, there was none - in IVF to be organised by Zeilmaker in Rotterdam, in clinical endocrinology (by Crosignani and Van Steirteghem) and in chorion sampling (by Bruno Brambati). Next, Jean Cohen was nominated as chairman of the ethics committee and charged to report back at Brussels next year on the ethics of embryo research. And finally Edwards reported that ESHRE and IRL Press had agreed on a contract for publication of the society's new journal. The niggling issues raised by Edwards and Cohen over the contract term (now seven years unless dissatisfaction was expressed after three) and profit share (now 50-50 up to £100,000 profit, 60-40 up to £150,000 and 75-25 up to £200,000 in favour of ESHRE) were now after lengthy negotiations resolved, with the first issue of the journal planned for January 1986.

Bonn was in fact an enormous test of Edwards's energy and resolve as a chairman, and a huge testament to his commitment to ESHRE. In the four days of 23rd, 24th, 25th and 26th June he chaired three sessions of the temporary committee's final meeting, the first meeting of the EC and the first AGM. He was in addition involved in discussions with the first editorial board of the journal and at a formal meeting of the AC.

It was indeed, as Arne Sunde recalls, a time in reproductive medicine when everything in Europe seemed to focus on Robert Edwards, and nowhere was this more evident than in his chairmanship of ESHRE and editorship of the journal. "I realised soon after I first met him that scientifically he was outstanding," says Sunde, "but on top of this he also had this charismatic personality. Looking back, the normal progression for ESHRE would be as an AFS lookalike because the natural tendency of the membership then was towards clinical IVF. But Bob's personality and his track record were strong enough to make it different and incorporate the sciences. Part of ESHRE's success today is because of that."

As it turned out, ESHRE's first EC meeting was little more than a distillation of the huge temporary committee agenda started the day before and a rehearsal for the AGM next day, with confirmation of the composition of the EC, resolution that ESHRE should be registered in Belgium, and agreement for acceptance of a draft contract with IRL Press for production of a journal (now, for the first time, detailed as the *Journal of Human Reproduction*). The EC also formally allocated responsibility for the ethical committee to Jean Cohen, for workshops to Arne Sunde, and for relations with the AC to Pier Giorgio Crosignani.

At the AGM next day Edwards introduced the society to more than 250 members, outlined plans for the next annual scientific meetings and for the journal. Thus, with a constitution now taking final shape in Brussels, an executive committee in place to fulfil its articles, and a first scientific meeting (with programme and abstract book) open and running, ESHRE had finally become a real entity and was on the move.

3

THE CHAIRMANSHIP OF ROBERT EDWARDS

Ask any of the 650 people in Bonn what they remember most about ESHRE's first annual meeting and the reply will be the same - Edwards, Cohen and Diedrich standing at the door of the opening reception in Bad Godesberg to welcome everyone with a handshake. Alongside, a photographer hired by Diedrich was on hand to record the event in what Hans Evers describes as "the Bob picture". "All the friends I know who were there have a Bob picture," says Evers. "He was very good at PR."

For Evers, however, who in that same year of 1985 had just started an infertility clinic in Maastricht and was about to switch his treatment interests from surgery to IVF, there was more to ESHRE's first congress than good PR; it was to him a revelation. "At the time," Evers recalls, "I was used to obstetrics meetings, and they were extremely dull. Nothing new happened... slightly different forceps, 2000 breach deliveries... and dull, dull, dull. But here there were new developments everywhere. Every single lecture I attended was something new. Before the 1980s, there was nothing much we could do. We could count the sperm, or do a basal body temperature chart and a lot of praying that your patient would become pregnant. So I was amazed by this meeting, that wherever you went there was something new. And everyone was there."



All 650 participants at ESHRE's first annual meeting in Bonn in 1985 were welcomed at the door of the opening reception by Edwards, Cohen and congress chairman Klaus Diedrich. On hand was a photographer to record the moment in what became known as "the Bob picture". Above, Edwards, Cohen and Diedrich welcome Marku Seppala, president of the world IVF congress in Helsinki in 1984 at which ESHRE was first announced. Below, Edwards welcomes Gerard Zeilmaker, the Rotterdam scientist who joined ESHRE's second Executive Committee in 1987; he became treasurer in 1989, and left the committee in 1991. Zeilmaker staged ESHRE's first workshop - on IVF - in February 1986, and was one of the first five associate editors of *Human Reproduction*.

Evers was not alone in his enthusiasm. Mike Hull, consultant gynaecologist from Bristol, UK, applauded the “economic style” of the meeting (“simple lunch, low-cost conference dinner”); Saxen and Koskimies wrote from Finland to congratulate Diedrich and Edwards, adding how the congress “really showed the need for a European society in the field and also the strength of such an organisation”.

The abstracts and programme book for the meeting - which had run to more than 50 pages and had been “published for ESHRE by IRL Press” - bore the title *Human Reproduction* and was, according to Edwards’s introduction, “a first proposal for the design of the new journal”. Remarkably, the page layout and typography are not much different from what we all recognise in *Human Reproduction* today. The programme book notes also that 11 German companies (mostly local affiliates of international organisations) made financial contributions to the meeting and that 18 companies were represented in the commercial exhibition.

Diedrich’s report to the Executive Committee (EC) would subsequently show that there were 34 invited presentations in Bonn, with each session of two speakers allowed time for debate under the guidance a chairman and two “discussants”. Diedrich later reported that all but one of 23 invited chairmen and all but four of 38 discussants took part. There were in



The first AGM in Bonn. Seated cente are Dieter Krebs, left, and Henning Beier, from the organising committee. The abstracts and programme book on the tables were intended by Edwards as “a first proposal for the design of the new journal”.

addition 121 free communications presented and 51 posters submitted, all recorded in abstract form in the congress book - with each one individually typeset and laid out in double justified columns. It was indeed a remarkable achievement to bring together such a full, stimulating and polished congress in such a short time (around eight months) and with such authoritative participants. Among the invited speakers during the opening day's two IVF sessions were David Baird (human follicle growth), Henri Alexandre (oocyte maturation), Allan Templeton (the ripening human oocyte), Pedro Barri (male infertility), Henning Beier (animal implantation), and Simon Fishel (human implantation). Subsequent sessions featured the placenta, sexual differentiation, ethics in reproduction (which Edwards himself chaired), and fetal development.

Diedrich's own estimates are that 650 took part in Bonn, with 340 registering before the congress opened. The congress fee of DM200 (€130) (which was reduced to DM100 (€65) for chairmen, discussants and students) and industry contributions made a total income of some DM146,000 (€97,000), which, after deductions of DM135,000 (€90,000) for costs, left ESHRE with a modest but real surplus of DM11,000 (€7000). Indeed, from now on every ESHRE congress - except one - would record a surplus for ESHRE's funds, and, as the annual meeting fell more and more under ESHRE's own organising umbrella, would prove in time a significant source of income.

When Edwards returned from Bonn to Cambridge to begin his two-year term as chairman, he first wrote (in one day) 37 letters of thanks to invited speakers, but there were two other immediate priorities on his mind: first, to finalise the details of ESHRE's registration as an international organisation in Belgium; and second, to sign and seal the contract for *Human Reproduction's* publication by IRL Press.

A copy of the proposed by-laws with modifications applicable to Belgian law had been distributed at the AGM in Bonn, and a recommendation made to the AGM that these should be accepted and the society registered in Belgium. There was, however, considerable discussion in Bonn over Article 15 of the by-laws, which describe the election of the Advisory Committee (AC) (and its membership defined by a "byelaw" acceptable to the AGM). As a result of these discussions, the AGM agreed that two members from France, Germany, Italy, Spain, UK and Benelux countries, and one member from Austria, Greece, Israel, Ireland, Portugal, Switzerland and each of the Scandinavian countries should be elected to the AC by members from each of those countries. The AGM's by-law also added

The Advisory Committee

The Advisory Committee, defined under article 15 of the by-laws, would become - alongside the General Assembly of Members and Executive Committee - one of three bodies in the constitutional structure of ESHRE. Members of the AC are (since 1992) elected by the membership and are nominated to reflect the society's geographical composition. Eligibility criteria were first amended at the 10th AGM in Hamburg in 1995 and next at the 19th AGM in Berlin in 2004.

Two representatives are now eligible from

* European countries with more than 20 million inhabitants and more than 15 members, and from

* European countries with less than 20 million inhabitants but more than 200 members.

One representative is eligible from

* European countries with less than 20 million inhabitants and more than 15 members.

At the first AGM in Bonn in 1985 the AGM elected the following to the first Advisory Committee.

Bert Alberda (Netherlands)

Pedro Barri (Spain)

Henning Beier (Germany)

Ettore Cittadini (Italy)

Anthony Comninos (Greece)

Paul Devroey (Belgium)

Yonat Floersheim (Switzerland)

Domenico Geraci (Italy)

Lars Hamberger (Sweden)

Aarne Koskimies (Finland)

Neri Laufer (Israel)

Glenn Lauritsen (Denmark)

Percy Liedholm (Sweden)

Shlomo Mashiach (Israel)

Harry Massouras (Greece)

Erich Muller-Tyl (Austria)

Manuel Neves-e-Castro (Portugal)

Paul Polani (UK)

Lauri Saxen (Finland)

Robert Schoysman (Belgium)

Jacques Testart (France)

R Winter (Austria)

David Whittingham (UK)

Gerard Zeilmaker (Netherlands)

Terms of membership of the Advisory Committee lasted for two years - until 2002 when the membership term was extended to four years.

that members of the AC cannot be members of the EC but can stand for election to the EC. The AC would furthermore have powers to propose nominations to the EC, amendments to the by-laws, and society activities. By November, each member of the EC had received a final draft of the by-laws for comment and, by the end of the year, the much amended text had finally been signed by each member of the EC and lodged for registration in Brussels.

Article 15 also implied a preferably equal representation of scientists and clinicians on the AC, a point fundamental to Edwards's view of ESHRE as a society "committed to a broader collaboration between these

two professional disciplines". It was, of course, a commitment he would pursue throughout his chairmanship and his much longer editorship of *Human Reproduction* - but it was not always easy to strike the balance he wanted. For instance, a few days before the Bonn meeting began, the French reproductive biologist Jacques Testart wrote to Edwards advising him that he could not attend (because of family circumstances) and could not meet his obligations as a member of the temporary committee and as a discussant. However, Testart - who with René Frydman had pioneered France's first IVF birth at the university hospital in Clamart in February 1982 and would later become director of research for INSERM, France's national institute for medical research - took the opportunity in his letter to warn Edwards of a trend he already sensed of ESHRE becoming "a new society of gynaecologists". Testart went on to find clinical bias in a Bonn session on oocyte maturation and, in the officers of the society and on the editorial board of the journal, that "numerous physicians have taken the lion's share". Testart concluded: "I'm afraid the scientists will find only poor interest to join the society if it develops in the way I fear".

In fact, Testart's enthusiasm for ESHRE had appeared no better than lukewarm, and he had attended only one of seven meetings of the temporary committee - in Paris at the smoky offices of Gyn.Obs, and even there, in the hubbub of that occasion, he had left early. Edwards replied to the letter, warning Testart that he would "speak directly", and explained his frustration: "I have been reserving places for scientists on various committees and on the editorial board, but it is difficult to invite them to take positions if they do not come to the organizing committee meetings. Inevitably, therefore, the names present on committees will reflect more medical men than scientists, since they are the ones who are prepared to travel, often at very inconvenient times." Financial support for travel expenses - as Arne Sunde would appreciate - would be one important use of any surplus funds, not least to make possible the participation of scientists in ESHRE's affairs. Testart, meanwhile, would later complain mischievously to Jean Cohen that "you the clinicians are up in the salon, while we the scientists are still down in the kitchens". Smoking, incidentally, was not banned in EC meetings until June 1991 - in Paris!

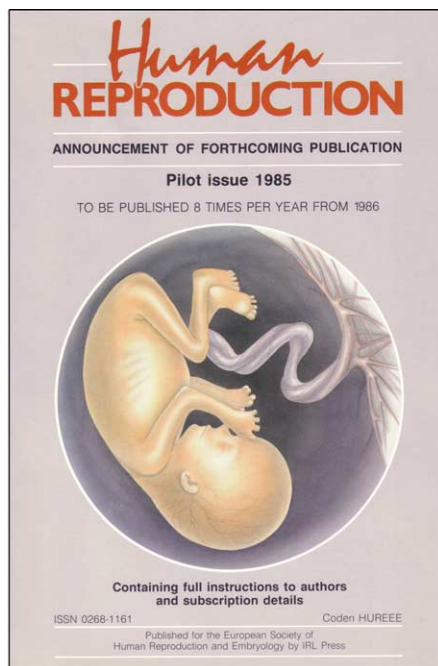
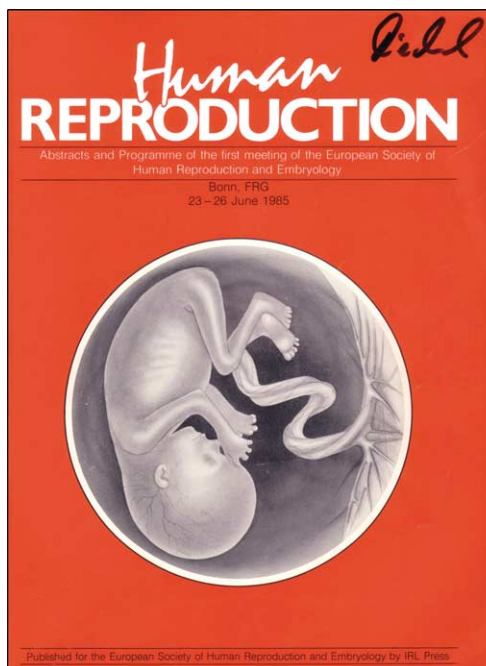
Edwards had reported to the AGM in Bonn that the first issue of the society's journal would be published in January 1986 (with eight issues a year) and had outlined the main points on which agreement had so far been reached with IRL Press. The final contract, however, was still not signed, and Edwards had had further meetings with IRL in Bonn on

accounting procedures and working budgets, subscription rates, and membership of the editorial board. Within two weeks IRL's solicitors had produced a further draft contract (the eighth draft!) - which prompted yet more negotiation. These, Edwards told Cohen, which took place on 9th July, "were very tough and lasted well into the night", concentrating on text editing, associate editors and the editorial board, and the proviso that ESHRE's accountants should agree to the estimated budget. Edwards duly asked his accountants, Whitmarsh, Sterland & Co of Cambridge, to meet with IRL's accountants and report back on the company and on the budget. Nevertheless, negotiations were clearly now in a final stage and Edwards felt confident enough in their outcome that he began making editorial plans.

The "tough" 9th July meeting with IRL had agreed that the first item of promotion for *Human Reproduction* would be a pilot issue which would contain the names of associate editors and the editorial board, an introductory article by Edwards, a 1983 paper by Edwards and Steptoe from the *Lancet*, a news section ("supplied by Jean Cohen"), instructions to authors and subscription information. The final deadline for all copy for the pilot issue, it was agreed, would be the end of July, just three weeks away.

Edwards went into overdrive. He first asked Cohen to help sort out a cover picture and then for editorial: "Could you write me immediately three paragraphs on news and views you may have from France. I shall need it urgently." He next fired off letters to Cohen again, Beier, Barri, Hamberger, Schoysman, Zeilmaker, Geraci, Malcolm Ferguson-Smith (Cambridge geneticist), Robert Williamson (London biochemist), Comminos, Mike Ashwood-Smith (Canadian colleague at Bourn Hall), Crosignani, Henry Leese (York reproductive biologist), Fraccaro, Hahn, and Etienne Baulieu in France asking if they would join *Human Reproduction's* editorial board; "associate editors will be appointed later," he added.

Duties for editorial board members would be "a commitment to the journal, a willingness to referee papers quickly, to submit manuscripts, and to encourage others to submit manuscripts". Towards the end of the month members of the EC received letters also asking for News and Views contributions for the journal proper scheduled for January. "I would be especially interested in any debates in your parliament about abortion, in vitro fertilisation, genetic screening, contraception, etc.," wrote Edwards, adding that news of any "industrial developments", "opening



The abstracts book for the 1985 annual meeting was printed by IRL Press and was intended to serve as a style model for *Human Reproduction*. A pilot issue of the journal was produced three months later in which the names of associate editors and editorial board were given.

of new research centres”, or “death of any well known colleague” would also be welcome. Indeed, over the next several years Edwards never lost any opportunity to convert meetings into manuscripts or to canvass his contacts for papers for the journal, often stressing urgency and a need to increase the submission rate. “We need four or five papers a week as a minimum to provide a good base,” he wrote to the editorial board in January 1986. And a few days later to all associate editors: “We have an urgent crisis coming up about papers for the Journal. Volume 1, numbers 1 and 2 are in press or published and we now urgently need papers for numbers 3 and 4... We have at the moment only six manuscripts, some of which may be rejected by the referees. It is urgent that I have another ten papers immediately... We must make a target of 20 papers per issue as soon as possible.”

At the second meeting of the EC - held in Brussels in mid-August 1985 - Edwards had announced a provisional list of five associate editors (Beier, Cohen, Fraccaro, Hamberger and Zeilmaker) and an

extended list of editorial board members, more than half of whom had not yet accepted their invitation to join. Responsibility for the journal, Edwards had added, would lie with himself as chief editor, the associate editors and the EC. He also informed the EC that 5000 copies of the pilot issue would be printed and mailed out as part of the promotion campaign. Deadline for copy for the first issue would be 30th September.

The first meeting of the editorial board took place at the Excelsior Hotel at Heathrow on 3rd November 1985, and by then 24 members had agreed to join. The copy deadline had now been extended to 8th November, and the meeting also agreed production schedules for the remaining seven issues of 1986. The journal's style - based on the pilot issue - was approved by the board, with detailed attention paid to references, abbreviations and the presentation of figures. A glance at the first issue is remarkable testimony to the layout planning at this time, for there are few stylistic or typographical differences between the pages of January 1986 and those of *Human Reproduction* today. Moreover, the contents page of that first issue similarly categorises original papers as today - "grouped into separate sections covering specific topics", as Edwards described it.

IRL Press outlined a huge marketing programme for the journal, with direct mailings, adverts, catalogue listings and presentations to advertisers. The print run of the first issue would be 3000 copies, with the majority scheduled for promotional mailing. True to his word, Jean Cohen had secured via Lars Hamberger a cover picture from Lennart Nilsson of the Karolinska Institute in Stockholm showing in colour and high magnification an ectopic pregnancy at eight weeks' gestation. Inside, there were 11 original articles plus several news items, including papers from the groups of Seppala, Devroey and Van Steirteghem, Diedrich, Feichtinger, Cittadini, Leese (with David Gardner) and Jacques Testart (on the relationship between embryonic cleavage rate in vitro and developmental rate after transfer).

One final issue to be resolved at the Excelsior Hotel was the relationship between members of the EC and the editorial board. The board believed that there should be no formal association between the two but agreed that, because the EC had been so instrumental in the journal's formation and were anyway all leaders in their field, members of the EC should be invited to join the board. Edwards added in a letter to the board the following day that "two women members" would be invited and that he would ask the London embryologist Anne McLaren and Anne Grete Byskow from Copenhagen; both names were present on the title page of the first issue.

This first issue of *Human Reproduction* also carried an announcement for ESHRE's second annual meeting, to be held the following June in Brussels. Because of the deal struck by Van Steirteghem, Devroey, Diedrich and Van der Ven in Cologne, the organising and scientific committees for Brussels would be the same as for Bonn. A two-day meeting of the two committees in Brussels in August (each chaired by Van Steirteghem) had set a schedule for deciding the scientific programme (invited speakers, subjects, new topics, plenary lectures, chairmen), terms of the commercial exhibition, registration, accommodation arrangements (through a professional agent), social events, transport, refreshments, audio-visual facilities, promotion, and finally budget. Eight topics were agreed for the scientific programme - andrology, cryobiology, teratogenesis, mammalian embryology, IVF, neuroregulation of hormone secretion, ethical aspects of reproduction, and ultrasound (which as a guide for transvaginal oocyte collection was at the time revolutionising IVF). The following month, those selected for invited lectures received letters from Van Steirteghem and Devroey asking for their participation and detailing a "tentative" title of their presentation.

The letter also offered to cover travel and accommodation expenses, noting that an apex or second-class ticket would be sent by ESHRE's travel agency. Expenses, in fact, would become an issue of continuing concern for ESHRE. It was clearly felt that those engaged on ESHRE business or those invited to fulfil ESHRE roles should not be out of pocket, but from the start the pioneers of the EC were unanimously opposed to the idea of first-class travel and fancy hotels. Indeed, André Van Steirteghem, in his new role as treasurer, told Harry Massouras, Greece's representative on the AC: "As you are aware of our critical financial situation, we insist that a reduced excursion ticket is used whenever possible." And shortly after Bonn, Edwards had written to Mike Hull in Bristol that "we intend to keep the low costs, by having an active group who can raise funds from anyone who can give them".

Thus, with a view to the bank balance and commercial support for the forthcoming annual meetings, Edwards in July 1985 had proposed to his colleagues on the EC that there should be one member with responsibility for forging links with industry, though at the EC's second committee meeting (in Brussels in August) Edwards proposed that commercial participants at next year's annual meeting might be best approached and encouraged by a professional congress organiser (PCO). Responsibility for industry liaison eventually fell on Jean Cohen, whose efforts bore fruit in

early 1986 when Pieter Van Keep, medical director of Organon International, promised ESHRE an annual grant of \$1250 for the next two years. "We hope that in two years' time the society will be able to stand on its own legs," wrote Van Keep encouragingly. At the 10th meeting of the EC - in Brussels in March 1987 - Cohen was also able to report promises of support from Serono and, following a visit of Crosignani to Berlin, of DM10,000 (€6500) for three years from Schering.

Another issue which Edwards took up on his return from Bonn was ESHRE's associations with other societies. The by-laws, now going through their final stages of agreement, had in Article 3 committed ESHRE to "co-operation" with other medical and scientific societies, and now, following the second meeting of the EC in August 1985, Edwards wrote to the chairmen of Europe's national fertility societies inviting them to a forthcoming meeting of ESHRE's executive in February 1986. Members of the EC, wrote Edwards, "had expressed a strong desire to form happy and constructive relations with the societies in each country of Europe. They felt this was important since the European Society is now organizing workshops, symposia and other activities which will be greatly assisted by the collaboration of members from various countries, and that a meeting should be organised for this purpose." Edwards also wrote to the chairman of the Society for the Study of Fertility (the Nottingham University agricultural scientist Professor Eric Lamming) and to a founder member of the recently formed European Association of Gynaecologists

First Executive Committee 1985-1987

Chairman

Robert Edwards

Chairman elect

Jean Cohen

Secretary

Klaus Diedrich

Treasurer

André Van Steirteghem

Members

Pier Giorgio Crosignani

José Egozcue

Arne Sunde

and Obstetricians (EAGO), Sir Rustam Feroze in London. Both these letters would have important repercussions for ESHRE and for Edwards.

While co-operation with national societies was one thing, it soon became clear to Edwards that EAGO might be something else - and a possible threat to ESHRE's immediate plans. Sir Rustam wrote back to confirm that EAGO had its initial meeting in Basel in early 1985 and was, like ESHRE, planning a journal and low-cost membership fees. What was most worrying, however, was that EAGO's next scientific meeting was scheduled for June 1986 in London, just two weeks before ESHRE's in Brussels. As ever, Edwards offered the hand of conciliation, promising to meet Sir Rustam at FIGO in Berlin in September "to talk over the details of our respective societies and to ensure a happy and fruitful co-operation".

However, a far more contentious co-operation was now building up with ESCO, with whom ESHRE had concluded firm plans for a joint congress (ESHRE's third) in Budapest in 1987. At its final meeting in Bonn the temporary committee had discussed its relationship with ESCO and agreed for Budapest that ESHRE "would take over all functions of ESCO, but would respect and retain the traditions of ESCO as much as possible". When Kurt Semm read the item in the minutes (he was not at the meeting and had sent apologies) he was not happy, and spelled out to Edwards his view of the competing and diverging interests of the two societies. "I think we have to handle the cooperation of contributions in these fields very carefully," wrote Semm sternly (who added that he would present Edwards with a copy of the 185-year history of O&G at the University of Kiel when they next met - in Athens at the fifth World Congress on Human Reproduction).

Semm's colleague in Kiel, Liselotte Mettler, had informed Edwards and Van Steirteghem in July that the chairman of the 1987 joint meeting would be the Hungarian gynaecologist Rezso Gimes, who was now invited to the August meeting of the EC but - not surprisingly - was unable to leave Hungary. Now, in Gimes's absence, the EC was increasingly anxious about the organisation and development schedule of the Budapest meeting and, in case of any more serious hitches, agreed that "a meeting would be organised by ESHRE itself at a different time and location in Europe".

Nevertheless, Edwards forged ahead with planning for Budapest, making several contacts with Gimes throughout the second half of 1985 and promising to decide the main themes of ESHRE's sessions at the next meeting of the EC (scheduled to coincide with the fourth World Congress of IVF in Melbourne in November). There it was agreed that Edwards,

Cohen, Diedrich, Crosignani and Van Steirteghem would travel to Budapest in the New Year to visit the convention centre and address the “problems” of the scientific programme, financial arrangements, and accommodation. Again, the EC reiterated its determination that, should agreement not be reached between ESHRE and ESCO on joint organisation, an alternative ESHRE meeting would be arranged.

The quorum from the EC duly met with Gimes, Semm and local colleagues in Budapest on 10th February with a whole raft of queries - and returned home with many still unanswered: payment of air fares, visas, disposal of any profit from Hungary to ESHRE, invitation formalities, ESCO’s role in financing, organisation of the commercial exhibition, publicity, and of course the scientific sessions. When a summary of the meeting finally arrived Edwards was still uncomfortable that so many issues - particularly financial - remained unresolved, and that the scientific programme appeared so vague. But once again, he drew on his contacts and fired off a pile of letters of invitation to nominated speakers.

However, it was not just one-way traffic. For his part, Gimes too was frustrated at the pace of the joint organisation, and also by the fact that his budget projection now forecast a \$60-70,000 shortfall; he complained repeatedly to Edwards and Diedrich that mailing lists (of ESHRE members and delegates in Bonn) to promote the meeting and the addresses of invited speakers had not been sent in time to produce an early second announcement. Certainly, for Gimes - with or without ESHRE’s full co-operation - Budapest was becoming a battle of the budget.

It was about now - in the early Paris spring of 1986 - that the bedside phone in Jean Cohen’s 16th arrondissement apartment rang one morning at around 2.00 am. Cohen woke with a start. “It was Bob,” he recalls, “so agitated about the Budapest congress that he couldn’t sleep. He couldn’t accept that the next year could pass without ESHRE’s own congress, so we discussed it there and then, at two in the morning, and agreed that we’d have to make a firm proposal to the committee.”

Edwards’s letters of request for co-operation to other fertility societies had prompted two sympathetic replies, both from Britain - from Sir Rustom Feroze of EAGO and from Professor Lamming of the Society for the Study of Fertility. And Edwards now saw in the latter’s willingness to co-operate with ESHRE - and in later encouragement from the British Fertility Society - the opportunity for an independent ESHRE congress in the UK in 1987 (in ESHRE’s regular time slot of June). Thus, in April 1986 - while the EC was still awaiting non-existent minutes from February’s site

meeting in Budapest - the EC heard Edwards's proposal and agreed that a third annual meeting of ESHRE would indeed be held in Cambridge. Edwards immediately took responsibility to contact the local city authorities and the university in Cambridge for lecture hall space. There were just 14 months to go.

Thus, by the time Kurt Semm travelled once more to Budapest for a further meeting with Gimes and his Hungarian colleagues (on 9th August) they were all fully aware that ESHRE was now committed to its own annual meeting in 1987 as well to the joint congress with ESCO. "We have to face the facts," Gimes noted ruefully, "that Cambridge will draw away a considerable number of participants." However, for Semm's colleague Liselotte Mettler - who had first suggested to Edwards the idea of a joint meeting en route to Monte Carlo for ESCO's seventh congress - the prospect of a separate ESHRE event was a severe blow. In October she wrote to Edwards: "A combined meeting of the two societies in Budapest would be fine for 1987, but to hold a similar meeting in Cambridge is a clear slap in the face for people working with ESCO. I am quite disappointed about your action, especially as you are the main figure in the establishment of the Cambridge meeting."

The letter was clearly upsetting to Edwards, who wrote back immediately reaffirming ESHRE's commitment to Budapest and his belief that both events would be "outstandingly successful". The Cambridge meeting, he explained, had arisen because of "circumstances in the UK which would have been a mistake not to capitalise upon". He urged Mettler not to be disappointed, nor to feel responsible for the turn in events: "My desire is to make Europe a coherent group in our field because we are so very strong. So thank you for suggesting the idea of joint meetings, and I will back them as hard as I can and prove that we in Europe can work together."

Of course, the local organisers in Budapest pressed ahead with their schedule and with the detail of the scientific programme, which was now taking firmer shape. To drum up more interest (and sponsorship) they decided to add ten round-table discussions to the programme (which by a further meeting in October had attracted eight commercial sponsors). The outlook, for the moment, seemed brighter.

Meanwhile, organisation of ESHRE's 1986 annual meeting in Brussels had been progressing without any apparent hitch. Van Steirteghem had reported to the third EC meeting in Melbourne in November that all invited speakers had accepted and that details of the scientific programme

ESHRE's joint meeting with ESCO took place in Budapest in September 1987. Organisation of the congress was not always a harmonious exercise, but the two groups agreed to continue their collaboration, with a joint organising committee put in place for Milan in 1990.



were sufficiently firm to distribute the second announcement in December. He also reported that Organon and Serono had agreed to sponsor two sessions, setting a trend of support from these two companies which would continue throughout the enormous growth of the annual meetings over the next two decades. Jean Cohen was already in touch with six other companies looking for financial support. While the scientific sessions in Brussels were to be held in conference rooms at the VUB, the commercial exhibition was planned “in a huge tent”, which would eventually accommodate 46 exhibitors.

There were two other features in the organisation of the 1986 meeting which would also become important in subsequent congress planning: organisation of the scientific programme by a local *and* an international scientific committee; and the planning of a pre-congress workshop for

members on the Saturday before the meeting opened. The workshop - on reproductive endocrinology, organised by Crosignani and Van Steirteghem - would also stamp Brussels as the leading forum for training in ESHRE. Not all such pre-congress workshops would be successful, as Arne Sunde, the first co-ordinator for training, would admit, but those organised at the VUB set standards to which all other ESHRE workshops would aspire. "I think all of us in the first executive committee had this idea of ESHRE as a learned society - which were Bob's words," says Sunde. "So we felt we had a responsibility to organise education, but there was also a pragmatic issue, because, from both the embryological and clinical side, there was at the time no practical training in fertility. In this respect Brussels has clearly been the flagship because they always organised extremely good workshops. And they've added a lot to the image of ESHRE's training responsibility." The one-day pre-congress course planned before the Brussels meeting featured lectures in the morning from David Baird (ovarian and testicular physiology), Pierre Jouannet (male infertility), Crosignani (hyperprolactinaemia) and Devroey (ovarian stimulation for IVF). Practical sessions in the laboratory in the afternoon covered immunoassay techniques, hormonal monitoring and the handling of data by computer. More than 90 members attended.

It was also clear from the Brussels scientific programme that ESHRE was even then keen to collect, collate and report data on new developments in assisted reproduction. Gerard Zeilmaker, whose centre at the Erasmus University in Rotterdam had recorded Europe's first live birth from a frozen embryo in late 1983, wrote to all members of the EC and AC asking for data on cryopreservation (clinical results, freezing protocols, thawing, synchrony of embryo transfer) to present a European review, while Ari Wisanto from the VUB also trawled European centres for a collaborative report on oocyte and embryo donation.

In just 12 months it was evident that the scale of the annual meeting was already escalating. At the final count, more than 800 took part in 1986 - with 650 registrations before the congress began and more than 300 papers presented. The opening ceremony was a more formal occasion, with this year's two honorary members - Patrick Steptoe and the Belgian molecular biologist Jean Brachet - each receiving a decorative scroll and specially commissioned sculpture; on the Monday evening, the mayor of Brussels hosted a reception for delegates at the City Hall.

In Brussels - as in Bonn - the main scientific programme included a session on the legal and ethical aspects of assisted reproduction, this time

chaired by Jean Cohen (alongside Dieter Krebs). Twelve months earlier the first AGM in Bonn had approved the temporary committee's decision to form a three-man ethics committee, with Cohen as its chairman. In Bonn Cohen had submitted a proposal for a European Ethics Committee and had been charged to report back on embryo research a year later in Brussels. Cohen's proposal in Bonn sought to "pool thinking" in Europe on new conception methods, prenatal diagnosis and gene transfer to produce "recommendations concerning both the research scientists (knowledge) and the public and its representatives (power)".

The ethical implications of assisted reproduction were of course central to Edwards and Cohen's original discussions about ESHRE - and would become a cornerstone of ESHRE's progress and interests over the next two decades. Indeed, the first issue of *Human Reproduction* contained a paper by the academic Anglican theologian Gordon Dunstan on the ethics of IVF. Dunstan had also presented a paper at the first annual meeting in Bonn and was, according to Klaus Diedrich, a frequent confidant and discussant with Edwards on numerous ethical issues. It was Dunstan's view, incidentally, that practitioners of IVF themselves "are to be defended as the proper moral agents" provided that they maintain corporate self-discipline, keep faith with patients and research, and safeguard the liberty of "disciplined enquiry". But Dunstan was also sensitive to the public's moral anxieties about IVF and other emerging techniques, as evident in the language and imagery sometimes applied to IVF by the popular press - "unnatural" practices shrouded by the spectre of clones, hybrids and "genetic engineering". Such public fears, of course, reflected the real battles which Edwards and Steptoe had to fight: accusations that their work was "unethical", grant refusals on the grounds of immorality. Howard and Georgeanna Jones in Norfolk had been similarly delayed in their work by public protests and controversy. And for many others of those ESHRE pioneers a consensus on the ethics of assisted reproduction was an important reason for their involvement.

"What interested me most about ESHRE at the time," recalls Arne Sunde, "was the idea of backing from European colleagues for the ethical debate which we already had in Norway about IVF." Such debate, in fact, would lead in 1987 to the world's first legislation on IVF, with Sunde taking a part in the public discussion. Similarly, Paul Devroey cites ESHRE's activities in the production of guidelines on ethical issues as landmarks in ESHRE's history, and as necessary today - when moral views on reproduction have

been written into the political agendas of governments in Germany and Italy - as in 1984.

At the second meeting of the EC in August 1985 it had been agreed that a workshop on ethical problems in reproduction would be valuable and that ESHRE should initiate some form of collaboration with the European Parliament on the provision of accurate background to the inevitable debates to come on IVF and embryo research. Ten months later, at ESHRE's second annual meeting in Brussels, Cohen had also presented his report on "the European response to nine questions on embryo research", and it was this presentation (as well as Wisanto's collaborative paper on oocyte and embryo donation and their ethical implications) which had sparked greatest discussion at the AGM. Edwards proposed that ESHRE should act quickly to follow up such interest and, at the EC meeting during the Brussels congress, called for suggestions. Cohen pursued the idea of a workshop before the end of the year, possibly in Bordeaux in September where AC member Alain Audebert was organising an international meeting on contraception. On his return from Brussels Edwards immediately renewed contact with Audebert, now arranging rooms (and air fares) for a hastily convened ethics workshop in Bordeaux. By the end of July, the date and times were fixed, and two subjects for discussion were on the agenda: the current legal status of contraception (this was, after all, a contraception meeting), and the ethical issues of oocyte and embryo donation (which Paul Devroey would lead as a follow-up to Wisanto's survey). Cohen and Edwards invited Frydman, Barri, Zeilmaker, Cittadini, Hamberger, Shlomo Mashiach, Van Steirteghem, Crosignani, Jacques Salat-Baroux and the Swedish gynaecologist Berndt Kjessler. Meanwhile, Edwards had corresponded with the European Parliament and promised to send a report from the Bordeaux discussions "to show that the Society was taking effective steps in this direction".

In fact, following his presentation in Brussels on embryo research Jean Cohen as chairman of the ethics committee had in July written to the Council of Europe to introduce ESHRE and offer its expertise to the Council's pre-legislation discussions. Both Edwards and Diedrich were known to the Council as independent experts and had each submitted evidence to the Legal Affairs Committee of the European Parliamentary Assembly in March 1986. Edwards had also been asked to make comments on the draft report of the Committee and had painstakingly identified ambiguities, inconsistencies and errors in the text, re-wording any text which would harm the scientific aim of research on embryos for

therapeutic purpose. Edwards was similarly in contact with his Cambridge colleague Mary Warnock, who from 1982 to 1984 had chaired the UK government's Committee on Human Fertilisation and Embryology. It was the recommendations of Warnock's report which formed the basis of the Human Fertilisation and Embryology Act of 1990, and the Human Fertilisation and Embryology Authority (HFEA), the regulatory body with responsibility for embryo research and assisted reproduction with embryos in the UK. Edwards consistently supported the position taken by the Warnock committee, and similarly applauded Lady Warnock's advice to the Legal Affairs committee of the Council of Europe. Indeed, two days after the Legal Affairs Committee briefing (held in Paris on 4th March 1986) Edwards wrote to Lady Warnock asking if her submission might be reprinted in *Human Reproduction* (which appeared in issue 7 of 1986 alongside other submissions to the European Parliament).

Cohen's letter to the Council of Europe was followed by a further communication from Edwards after the workshop in Bordeaux. "We have taken further steps to consult our members about the ethics of in vitro fertilisation, embryo research and other aspects of human reproduction," Edwards wrote. "We are seeking an initiative whereby our Society can be constantly in touch with your Committee, so that we can exchange information and concepts of value to all of us."

The requests bore fruit, and by March 1987 the chairman of the Legal Affairs Committee made two proposals for cementing ESHRE's relationship with the Committee: first, that ESHRE should request formal "consultative status" with the Council of Europe, which would give a legal basis to the relationship; and second, that the rapporteurs of the various advisory committees would consult ESHRE for advice along with other scientific societies. "It would be most valuable to have the advice of scientists and to be aware of their concerns before making recommendations to the Committee of Ministers of the Council of Europe," said the chairman of the Legal Affairs Committee. Edwards duly requested consultative status on behalf of ESHRE.

And there were yet further opportunities to come for ESHRE's ethics committee. The final two meetings of the EC in 1986 (held in Bordeaux in September and Strasbourg in December) had made plans to continue the ethical debate at an ESHRE-sponsored session at the Salon International de l'Energie et des Techniques du Futur in Toulouse in October 1987. ESHRE's session, *Ethics of the New Procreation*, would cover embryo research, biological and genetic identity, legal problems, and fetal screening.

Jean Cohen, as chairman of the ethics committee, was named as ESHRE's contact with the organisers in Toulouse, and it was now clear that his obligations to this committee - which also included a new five-page questionnaire on ethical issues in assisted reproduction - were substantial. Thus, with Edwards's two-year term of office as chairman drawing to a close and Cohen's new term imminent, Edwards in his EC reshuffle thus invited Berndt Kjessler to take on responsibility for the ethics committee after the annual meeting in Cambridge - to which Kjessler agreed. "One of your first duties," Edwards wrote, "will be to continue the organisation of the Toulouse meeting and the questionnaires."

However, there were other changes apart from this now required under the two-year rule of ESHRE's constitution, and in Strasbourg the EC had considered a chairman-elect to succeed Jean Cohen. With the principles of "continuity" and "renovation" before them, the EC identified two front runners for the chairmanship, Lars Hamberger and Pier Giorgio Crosignani, both well known to the EC as active, willing, wise and enthusiastic leaders in their field. As events transpired, Hamberger was about to become head of department in Gothenburg and considered himself unable to make the necessary commitments. So Edwards phoned Crosignani in Milan, who gladly accepted the honour. "We are all deeply impressed by the work you put in for the Society, the care with which you have attended the meetings and your most happy personality," Edwards wrote in his formal letter of invitation. Crosignani would thus become chairman of ESHRE from June 1989 to June 1991 following Jean Cohen, subject to approval at the AGM in Cambridge. Hamberger did agree to a place on the EC, replacing Arne Sunde whose two-year term was over, as did Anne McLaren and Gerard Zeilmaker; Van Steirteghem as treasurer and Egozcue were nominated for a second two-year term (which the articles allowed), and all five proposals were accepted unanimously at the AGM. (Sunde, like Kjessler, would in fact remain an ex-officio member of the EC as special advisor for workshops.)

With Edwards's intense term as chairman now drawing to a close, there were still several outstanding issues for the EC to face, not least ESHRE's brittle association with ESCO and the ever-pressing need for a permanent administrative home. By March 1987 the scientific programme for Budapest was in place and arrangements had been made to print the abstract books and programme in Hungary. The only major surprise to the EC had come with publication of the second announcement in January 1987 where, listed as a "Lecture of Honour" at the opening ceremony, was

Second Executive Committee 1987-1989

Chairman

Jean Cohen

Chairman elect

Pier Giorgio Crosignani

Past chairman

Robert Edwards

Secretary

Klaus Diedrich

Treasurer

André Van Steirteghem

Members

José Egozcue

Lars Hamberger

Anne McLaren

Gerard Zeilmaker

Berndt Kjessler (chairman ethics committee)

Arne Sunde (special advisor workshops)

found “The history of reproductive science reflected through ESCO” to be given by... Kurt Semm. In fact, notice of Semm’s “lecture of honour” had been in the minutes from the Budapest meeting (with Semm) of August 1986, but Edwards still insisted that an ESHRE lecture be given equal billing (with Cohen now speaking on “Horizons in reproduction” at the closing ceremony). However, by the time of Edwards’s final EC meeting as chairman in June in Cambridge, he seemed well disposed to the joint meeting, and even keen that such collaborative efforts should continue, primarily to avoid clashes with other congresses. There would now be one final meeting in Budapest (on 12th July) to finalise outstanding matters; with more than 300 abstracts already received, Edwards was sure Budapest would be a success.

Following the 1986 annual meeting in Brussels André Van Steirteghem wrote a long letter to Edwards correcting the June EC minutes and asking him to thank, first, the army of volunteers who worked behind the scenes in Brussels, and next the medical director of the VUB for the free use of an administration room during the congress. “We might have a chance to keep this room,” wrote Van Steirteghem, “for our ‘eventual’ secretariat.”

Despite the pressure of space at the VUB, a room was indeed found, which would become, for the next six years, the permanent administrative office of ESHRE. The room, just 4 metres by 4 metres, would be rent-free and located in the Department of Paediatrics. All it had was a window, a table, and an original Macintosh computer. There was also someone Van Steirteghem knew who might know someone who could do the administration. He had just finished his military service with the Belgian army in Germany working in communications and had now been temporarily teaching. His university background was German philology, and he seemed keen, literate and able. Van Steirteghem made contact and offered him a job... on trial and part-time. The young man's name was Bruno Van den Eede, and, when he joined ESHRE in March 1987, he was just 20 years old.

Van den Eede would immediately take over the everyday secretarial activities of Klaus Diedrich (though Diedrich would remain secretary of ESHRE on the EC), compile the first database of members, chase membership fees, deal with ESHRE correspondence, and take the minutes from the meetings of the EC and other committees. In his letter of welcome Edwards thanked Van den Eede for joining, and hoped "we will have a long standing relationship". Today, now as managing director of ESHRE's Central Office, Bruno Van den Eede remains at the everyday helm of ESHRE, to many the recognisable face of the society, and the first phone call for all committee members in distress.

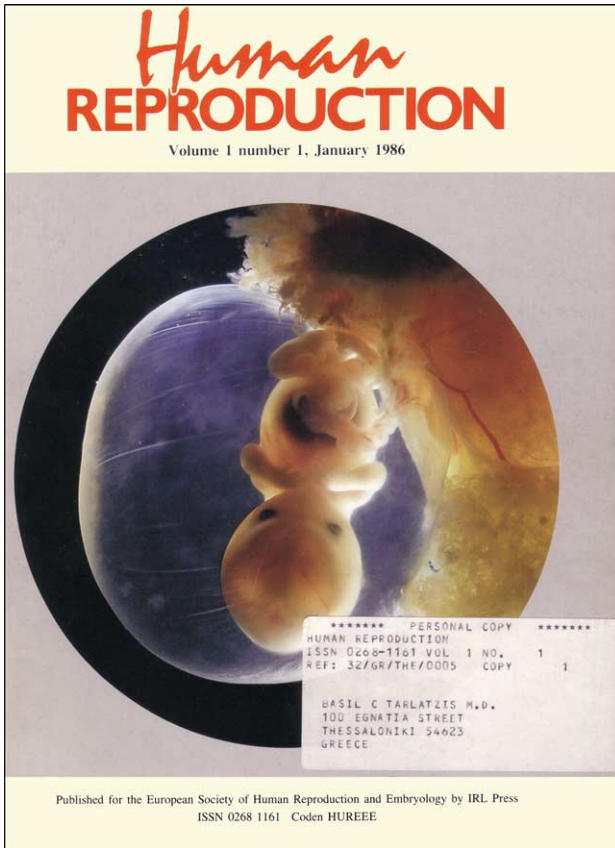
By the time Bruno had his feet properly under his desk at the VUB, ESHRE had made huge progress since its tentative formation at the Westmoreland Hotel in 1984. In May 1987, when Diedrich asked Van den Eede to alert all members of the AGM in Cambridge, there were 581 listed members of ESHRE, representing 32 countries. "Writing to them all takes a lot of time," Van den Eede told Edwards. And ESHRE's first proper balance sheet, which Van den Eede had prepared with the help of Paul Devroey's father, an accountant, would show a total surplus of almost 150,000 Swiss francs (€95,000). Now, a new executive committee was in place to take over the responsibilities of Edwards's chairmanship, with committees formed and active in ethical issues and in training. Not surprisingly, in welcoming his successors on the EC, Edwards had proudly told them that "our Society is flourishing mightily". Thus, with affairs of ESHRE in safe hands, and the congresses in Budapest and Cambridge finally moving forward, Edwards would now turn his attention to more pressing needs, *Human Reproduction*.

4

HUMAN REPRODUCTION 1986-1995

Almost all the pioneers of the temporary committee were attracted to the idea of a European society because it would allow them the same publishing opportunities as their counterparts in the USA. The American Fertility Society (AFS) had been founded in 1944 with the aim of advancing research into infertility, improving diagnosis and treatment, and spreading reliable information. The success of the society, said its founder Dr Walter W Williams, would - like ESHRE's - be "dependent upon the quality of its scientific productivity". The first issue of *Fertility and Sterility*, the official journal of the AFS, had appeared in January 1950 under the editorship of Pendleton Tomkins, "a man as skilled with the pen as with a scalpel", according to the AFS historians Walter E Duka and Alan DeCherney. *Fertility and Sterility* was an immediate success and within two years of its introduction had more than 2000 subscribers. Tompkins attributed such success not just to the journal's content, nor to individuals, but to the AFS as a whole. "Good journals do not happen," he said. "They are made by the membership."

And so it was that as *Fertility and Sterility* progressed through several new editors, the introduction of peer review in 1970, self-publication in 1974, and more than 10,000 subscribers by 1980, it was indeed perceived by many working in Europe as the journal of the AFS for the AFS. "That's what we wanted for ESHRE," says Klaus Diedrich, "to bring together



The first issue of *Human Reproduction* appeared in January 1986. Edwards's first editorial said the journal would be of interest to clinicians and scientists. The cover illustration was supplied by Lennart Nilsson.

European clinicians and scientists working in the field of reproductive medicine as something of a counterpart to the AFS." And Paul Devroey is even more explicit: "There was nothing like the AFS in Europe at the time. ESCO was not really a democratic society, and even before 1983 I had sent several papers to *Fertility and Sterility* and they were always rejected. There really was a need for a journal in Europe where European papers could be published. That's what Edwards wanted and what we all wanted. I still remember in Bonn, when *Human Reproduction* was announced on the last day of the meeting, Edwards emphasised the need for a journal where members of the society can publish their work. It was a vision then, but he realised it and it remains one of his great achievements."

In his editorial for the first issue Edwards opened the door of *Human Reproduction* to "original articles, reviews, news and views from Europe and elsewhere", with "a rapid rate of publication". Poor English, he

Human Reproduction Volume 1 Number 1

The first issue of *Human Reproduction* rolled off the press for publication in January 1986. The 56-page perfect-bound journal carried eight pages of commercial advertising (two from Serono, and one from Organon, Amersham, Boehringer Mannheim, Sigmater Diagnostics, Planer Biomed and Elsevier Publishing) and 12 scientific papers categorised on the contents page under the headings of:

- * Reproductive Biology (Bischof et al on response to RU486, and Seppala et al on endometrial proteins)
- * Reproductive Endocrinology (Van Steirteghem et al on delayed implantation, and Diedrich et al on ovarian stimulation in IVF with hMG and GnRH agonists)
- * Gametogenesis (Kemeter and Feichtinger on transvaginal oocyte retrieval)
- * Fertilization and Early Embryology (Gardner and Leese on nutrient uptake by mouse embryos, and Testart on the developmental potential of cleavage stage embryos)
- * Pregnancy (Geraci et al on immunomodulation, and Brambati et al on feto-maternal transfusion after CVS)
- * Ethics and Society (Dunstan on the ethics of IVF)
- * Mini Review (Adinolfi on recurrent abortion)
- * News and Views
- * From Other Journals

The first year of publication would comprise eight issues, with annual subscription for ESHRE members set at £33. The front cover illustration, which “will be changed occasionally”, was in colour, a macro photograph from Lennart Nilsson of an ectopic pregnancy.

added, would not be grounds for rejecting papers, “and attempts will be made to correct the wording and style of non-English speaking contributors.” Indeed, Edwards’s own notes and committee minutes bear testimony to the long hours he spent on every manuscript from overseas, personally correcting the text and putting into house style papers from non-English groups. Indeed, in 1988 he estimated that without his work on the texts the rejection rate would have increased from 25 to 35 per cent.

However, while support for the concept of *Human Reproduction* was enthusiastic and universal, its finances were a continuing source of anxiety to the Executive Committee (EC). The protracted negotiations over the initial contract with IRL Press in 1984 and ’85 were evidence that production costs and subscription revenue were a sensitive issue. The full subscription rate for eight issues in 1986 had been set at £84, with a reduction of 60 per cent for members of ESHRE (£33). Throughout the eight draft contracts proposed by IRL Press there were many revised profit-and-loss projections; the final one forecast an operating loss for the first three years, before hitting profit in the fourth. Sales revenues would be

largely comprised of subscriptions, which by year 10 were estimated at more than £100,000, and advertising. However, by the second meeting of the editorial board - on 5th June 1986 in Brussels - IRL had received only 183 subscriptions to the journal and gloomily predicted fewer than 150 more for the rest of year; by year's end this would be less than 40 per cent of the target.

In response to such forecasts, both IRL's marketing department and Edwards himself set about a determined direct mailing campaign, to ensure that "those who should subscribe *do* subscribe". Subscriptions were also less than anticipated because the transfer of subscribers from the *European Journal of Fertility and Sterility* had not materialised (and had in fact been written out of the cost estimates by the fifth draft of contract proposals).

The first two issues of *Human Reproduction* had contained 12 and 14 original articles respectively. Edwards had made it repeatedly clear - in urging his colleagues for contributions - that his goal was 20 papers per issue, and 12 issues per year. However, in June 1986, with four issues of the journal printed or put to bed, Edwards was aware that such targets could never be met with the current rate of submissions. Thus, as the journal's first year drew to a close Edwards had two pressing needs: to improve subscription rate (via the ESHRE membership and IRL's marketing efforts, particularly to institutional purchasers); and to increase the number of papers submitted for publication.

Shortly after the second meeting of the editorial board - in July 1986 - Edwards wrote to every member of the Advisory Committee (AC) asking them to read "the following points very carefully and do all you can to help me". What the AC members saw was a seven-point wish-list for the journal, ranging from news reports, to job vacancies, to original papers, to promotion of the journal at members' own libraries. And of course he continued as ever to canvass for papers at every opportunity, writing to investigators and clinicians at any hint of a manuscript. He also saw an opportunity in publishing supplements, not just the abstracts for ESHRE's own annual meeting, but now for other organisations too (*Human Reproduction* published as a supplement the abstracts of the sixth World Congress on Human Reproduction in Tokyo in 1987 at the request of Liselotte Mettler).

In fact, not until September 1987 and the joint meeting with ESCO in Budapest would Edwards report that subscriptions to *Human Reproduction* had passed 500 and were steadily rising. This was partly attributable

to a new sales initiative which offered a “combined” membership of ESHRE (which included a discounted subscription to the journal), and also to the quality of the journal itself. More and more papers were now being sent from established groups and overall numbers of manuscripts were finally increasing. Indeed, issues 1, 2 and 3 of 1988 (volume 3) would include around 25 papers in each, “some of excellent quality,” said Edwards.

However, despite the emerging editorial success of the journal, there now appeared the first signs from IRL Press that any hopes of moving into profit within three years were unlikely. Institutional subscriptions to the journal were growing too slowly, despite over-budget marketing efforts. And also over budget were print and production costs, largely because of the added pages. Thus, as the EC sat down for its 14th meeting in January 1988 in Brussels, just two years after the first issue of *Human Reproduction* had appeared, the journal was facing its first - and by no means last - mini-crisis, a familiar theme of abundant editorial quality, over-budget costs, and insufficient revenue. During the long discussions in Brussels, from many remedial ideas suggested in response to the crisis it was proposed that pharmaceutical companies might be persuaded to take bulk subscriptions for their own distribution, that supplements to the journal should only be accepted if the sponsor guarantees all costs, that André Van Steirteghem should act as a formal liaison between the EC and IRL Press, and that Edwards himself should have some full-time help in the form of a junior editor. In fact, until 1992 editorial assistance to Edwards was only on a freelance basis.

IRL’s review of the first two years reached Edwards in the New Year of 1988 and must have made miserable reading. “Should we simply invest more money in promotion,” asked IRL, “or should we dig deeper to discover a more fundamental reason for the journal’s under-achievement?” Whatever, IRL thought its original expectations “too optimistic”, and short-sightedly concluded that *Human Reproduction’s* appeal only lay with “a restricted audience of scientists” and “a small number of specialist clinicians”.

It was not what Edwards wanted to hear - and proved the start of what would become a strained working relationship between the editor and the publishers. It was, of course, a source of frustration to Edwards and his colleagues on the EC, editorial board and the journal to see such a dramatic surge in editorial quality counterbalanced by such negative reports on finance. Papers, Edwards reported to the EC in Paris in May 1988, were

now coming in at a rate of one a day, and around 75 per cent of them were published. Thus, what seemed at the heart of IRL's frustration was Edwards's editorial policy that, if a submitted paper had been judged acceptable by peer review, that paper had to be published.

In 1987 *Human Reproduction* went 120 pages over budget, and IRL saw Edwards's editorial policy as responsible. IRL questioned the policy and sought to reduce the number of pages, which Edwards could not accept. Cohen as chairman of the EC agreed with Edwards, and brushed aside all talk of page numbers as "irrelevant"; what was necessary was an improvement in sales - especially in the USA - to match the high editorial standards which Edwards had achieved. No-one on the EC that day considered Edwards's policy a problem and all applauded his remarkable progress in such a short time. There was also encouraging news from Cohen that Schering, Serono and Sterling-Winthrop were likely to take bulk orders and distribute their own copies. Indeed, bulk orders from Serono, which in the early 1990s reached around 300 copies per issue, would be a substantial cornerstone of the journal's progress. The EC would not be swayed by IRL, but did agree to some cost cutting from the editorial budget (a maximum 90 pages per issue) and a contribution from its own funds to make up the over-budget production costs.

A report on membership of ESHRE from Klaus Diedrich to the 16th meeting of the EC in Barcelona (at the 1988 annual meeting) also indicated what an impact the combined membership initiative had had on the journal. In 1987, after the offer was introduced in April, there had been just 100 takers, but now by mid-1988 that number had soared to more than 300 and was now the most popular membership option. Shortly after the meeting, a memo from Van Steirteghem to all members of the EC and AC set out details of a two-pronged attack on the journal's subscriptions - by direct mailings to potential members/subscribers and active promotion of the journal by members at all meetings in which they took part. If IRL couldn't improve the journal's profile and revenue, the EC itself was determined to do so.

However, before the year was out events took a turn of their own which would have an unforeseen and dramatic impact. At the end of August Cohen received a letter from IRL notifying him that IRL Press would soon be acquired by Oxford University Press; while the sale "should in no way affect the running of *Human Reproduction*", Cohen was told, the EC was immediately aware that this might resolve the difficulties with IRL and, of course, necessitate eventually a new contract with OUP.

Would circumstances now bring the changes the EC was looking for in the management of *Human Reproduction*?

The first evident change introduced by OUP was an extension to the page limit - from 90 pages up to 110 pages per issue. OUP later indicated that pages might be further increased if all members of ESHRE received the journal as part of their subscription. This was a contentious issue for the EC for, while it would inevitably drive up circulation beyond the 1000 mark, it would also impose a higher membership fee - when low-cost had been an abiding principle for ESHRE. Moreover, sales of the journal were steadily rising and were already over 600, not including the bulk orders from Schering, BioMérieux and Serono. There was also a feeling that, despite the runaway popularity of *Human Reproduction* as a medium for investigators to publish their work, the emphasis of papers submitted was more scientific than clinical. A greater clinical interest would surely extend the readership base - and to this end the editorial board had agreed that two members should be delegated to encourage more clinical submissions.

The sensitive question of compulsory or non-compulsory subscription to the journal was finally tackled by the EC at its 21st meeting in Malmo in June 1989. The EC and AC were split on OUP's proposal - with 13 voting against and eight in favour. But the matter was deemed so fundamental that a final decision was left to the AGM two days later; under the OUP proposal mandatory combined membership would be set at 144 Swiss francs (€90), and non-mandatory at 164 Swiss francs (€110). Discussion at the AGM - as at the EC - was animated, and eventually the AGM accepted the revised subscription charges but rejected the idea of mandatory combined membership. *Human Reproduction* would remain a non-compulsory option of membership.

Meanwhile, as a result of Crosignani's contacts in California, ESHRE had formed loose agreements with the Pacific Coast Fertility Society in the USA. An exchange lecture programme had been agreed with the PCFS, brokered by its President, Jeffrey Chang, and Ricardo Asch. Now, the PCFS was aiming to cement the relationship further with publication of their prize-winning exchange lectures in *Human Reproduction* in return for 50 library subscriptions in the USA. It was an opportunity for the journal to break into the USA, and the EC agreed to a two-year trial. It was also agreed to improve the journal's profile outside Europe and that "world-wide" associate editors might be appointed - to which PC Wong in Singapore, Alan Trounson in Australia and Anand Kumar in India subsequently agreed. Within a few years, as the overseas representation

expanded to be now called “international editors”, the names of Ricardo Asch (USA), Jacques Cohen (USA), Alan DeCherney (USA), Mori (Japan), David Mortimer (Australia), Rodriguez-Armas (Venezuela), Taylor (Canada), Tsunoda (Japan) and Ryuzo Yanagimachi (USA) were added to the list. This turned out to be an important initiative and a mark of the journal’s wide readership base, for at the close of 2003, 21 of *Human Reproduction’s* 59 associate editors were in fact from outside Europe.

However, such moves did little then to address the real financial crisis facing the journal. The profit and loss projections at the base of the contract with IRL Press had forecast revenue running into profit after three years. Yet now, a financial report from OUP to Edwards in late 1989 (three years after *Human Reproduction’s* launch in January 1986) saw no sign of profit, despite well over 1400 subscriptions. Accumulated losses were substantial, with the greatest costs found in production. The original contract with IRL - which OUP had now taken over - had largely left responsibility for editorial matters (contents and the appointment of editorial board and copy editors) to ESHRE; losses, the EC reasoned, were not ESHRE’s responsibility. Moreover, at a meeting of Edwards and the EC in Jerusalem in December 1989, it was felt that OUP had not been as diligent as it might in canvassing for subscribers and advertisers. While members of the EC and AC were forthcoming at their meeting next day with suggestions to face the crisis - but insistent that the editorial quality of the journal should not be compromised - the chairman, Pier Giorgio Crosignani, believed this was indeed a crisis and warranted professional help. Although it was clear in the contract that ESHRE was not responsible for OUP’s losses, the ongoing negative performance of the journal meant that ESHRE was denied any return whatsoever from the journal’s success nor from the huge effort which its publication involved. Was it now time, therefore, to consider an ESHRE buy-out, or time to renegotiate the contract?

Crosignani, Van Steirteghem and Edwards met for a crisis meeting in Brussels the following February. Two items were on the agenda: *Human Reproduction’s* financial situation, and concerns over revenue from subscriptions and advertising. However, when the question arose of sticking with OUP or moving on, Edwards seemed in favour of OUP, provided that the journal had more “permanent care”, perhaps in the form of a businessman “to handle matters in a professional way and seek funds in support of the journal”. But Edwards also made it clear that, because of the journal’s ever mounting editorial acclaim, the issue of pages would not go away, and even here in Brussels he was agitating to increase page

numbers for 1990 from 124 to 130. Manuscripts were still coming in to *Human Reproduction's* editorial office at Bourn Hall at a rate of 30 a month, and their quality was such that peer review would reject only around one in four.

The "professional help" which Crosignani wanted arrived in the form of William Metcalf, a Cambridge business consultant introduced to ESHRE by Edwards, who was briefed to look at the entire financial footing of ESHRE, including membership and the journal. In preparation for what would become a 30-point plan for ESHRE, Metcalf spent a day with Edwards and went through the balance sheets. In his final report, which was discussed by the EC in Milan in August 1990, Metcalf gave short shrift to the EC's complaints that *Human Reproduction* carried so little advertising. "It is hardly surprising," he said. "We do not have a membership base (customers for advertising) in the areas of maximum commercial interest. . . . It may be intellectually satisfactory, but will ensure that ESHRE is self-limiting." Indeed, the overall thrust of Metcalf's proposals would be to expand the membership base of ESHRE - and this would raise serious and long-lasting discussions in other areas of society activity. Thus, in order to secure a more solid financial basis, Metcalf advised that each of ESHRE's activities should be developed as self-contained business units, and as far as the journal was concerned he made three recommendations: that the drive for revenue from subscriptions and advertising was the responsibility of ESHRE (to be co-ordinated by a management committee); that more attention be paid to *Human Reproduction's* listing in the citation index (then ranked at number 17); and that a position statement for OUP should clearly describe ESHRE's requirements with respect to advertising, subscriptions and production costs. The last, he explained, should be seen as a first step towards renegotiating - or terminating - the contract with OUP when the first possibility arrived in December 1992.

Many of Metcalf's proposals - as the next chapters describe in more detail - were discussed by the EC in Milan and put to the AGM for ratification. In essence, there would be an overall change in ESHRE's structure whereby sub-committees would manage membership, training, finances and the newsletter, while the various clinical and scientific interests within the society would be allocated to "special interest groups". Gerard Zeilmaker, who had now taken over as treasurer from André Van Steirteghem (who was now chairman elect), added that responsibility for increasing journal revenue from subscriptions and advertising would

indeed be taken on by an ESHRE management committee, while Edwards himself announced that the number of issues per annual volume would increase from eight to ten and that additional editorial staff at the Bourn Hall office would be taken on.

In 1990, for the first time, *Human Reproduction* made a small profit, of which, under the terms of the 1985 contract, 50 per cent was due to ESHRE. It was a small amount (and was retained by OUP to offset cumulative losses) but it was the first tangible sign of the journal's potential as a revenue source for the society and a stark reminder that OUP's contractual control over the journal allowed ESHRE little room to manoeuvre production costs. It had also irked Edwards throughout the last years of the 1980s that so much of his time and energy spent on the journal appeared spent "merely to reduce OUP's investment". But there were more reasons for dissatisfaction with OUP than just revenue. "Every new initiative in the journal has come from the Editorial Office," Edwards complained. "The introduction of Editorials, Opinions, Updates, new print styles, the full colour cover, the introduction of more colour pictures and free reprints." And now, with the management sub-committee taking initiatives with advertising, OUP appeared to be failing with even these basic requirements.

There were other complaints too. As the next decade began and the number of manuscripts submitted to the journal continued to increase, so did delays in publication. Edwards had complained to OUP about the delays, and to Van Steirteghem, who agreed that "something has to be done about the problems we have with publication". There were also blatant production errors for which OUP was deemed responsible - omissions from the contents lists, pagination problems, inadequate reproduction of figures. It was also irksome for Edwards to find that OUP's allocation of "overheads" to the balance sheet was roughly equal to his estimate of costs for running the entire editorial office at Bourn Hall.

Thus, when in October 1992 the EC offered to increase Edwards's honorarium as editor in return for a three-year commitment to continue in post, Edwards graciously accepted but only on the condition that he could resolve "the matter of the loss of profit".

ESHRE's contract with IRL Press had been signed in June 1986 to be binding (for a minimum of seven years) until December 1995, with 18 months notice of termination. The contract had also provided for 50 per cent of profits to be paid to ESHRE once the journal was in cumulative profit; a further agreement between ESHRE and OUP in 1990

had revised those proportions into the 1990s and now - with sales (1700 subscriptions by 1992, 12 issues per year in 1993) and impact factor ranking (number 8 in O&G in 1991) both moving ahead - profit forecasts into the decade looked substantial. Thus, when Van Steirteghem on behalf of the management committee reported to the 36th EC in December 1992, he said that ESHRE would have to face two options: either negotiate a new and more advantageous contract with OUP or another publisher, "or publish the journal ourselves".

Edwards, not surprisingly, favoured the latter option, but OUP too was keen to retain the journal and submitted a proposal for a new contract. The EC asked Edwards for a business plan, and Edwards asked his accountants and lawyers to look into the prospect of self-publishing. What followed in the ensuing months of 1993 was a period of intense activity on Edwards's part in proposing to the EC and management committee valid financial reasons for self-publication and exposing possible flaws in the detail of OUP's proposals.

Incidentally, throughout this turbulent time and to whatever extent a reasonable financial return lay at the heart of his arguments, Edwards never lost sight of his editorial colleagues at Bourn Hall, and the need to secure their contracts of employment either with ESHRE or with OUP. Indeed, in December 1993 following a proposed freeze by OUP on editorial office salaries for 12 months, Edwards offered to fund a small rise to new staff after 12 months' service from his own salary. Loyalty among his colleagues - in particular Helen Beard, the assistant editor, and Caroline Blackwell, who had worked on the journal as Edwards's administration assistant since its launch in 1985 - was something he frequently referred to.

When the management committee met in Brussels in December 1993 it was faced with a huge volume of material from Edwards and his consultants in favour of self-publication for *Human Reproduction*. Overall, his arguments were that the journal's future prosperity would be more fairly held in ESHRE's hands than in OUP's. Given the escalating success of the journal, he did not see the financial risk as heavy. But Edwards had also gone through the proposed new contract with OUP and tightened up items where he saw financial loopholes. As ever, discussion was heated, but the committee finally decided that it was too early for *Human Reproduction* to be produced independently without a management structure in place and without a clear view of the legal implications. Thus, three days later Klaus Diedrich, now ESHRE's chairman, wrote to Edwards confirming that ESHRE would continue with OUP but on

a renegotiated contract based largely on Edwards's proposals. That contract, intended to compensate ESHRE for what Edwards later described as an "immense and uncosted" burden paid annually in recognition of OUP's overheads, was finally signed at the close of 1995, for a term of five years.

The nine years since *Human Reproduction's* launch in 1986 had seen remarkable progress. Total subscriptions had risen from 351 in 1986 to 2129 in 1994, annual page totals from 597 to 2472, and revenue from £30,000 to almost a half million. In addition, its impact factor ranking had risen year on year (and before the 1990s were over would reach number 1 in O&G, ahead of *Fertility and Sterility*), with the quality of papers published increasing all the time (as reflected in an increase in the rejection rate from 25 to 40 per cent).

Of course, as this progress suggests, Edwards's preoccupations throughout this time had not just been with the contracts with IRL Press and OUP or with the journal's finances. He had introduced editorial innovations to the journal and - above all - had surely met the ESHRE pioneers' fundamental aims of providing a home for the publication of European work. Among these introductions were Editorials, which Edwards conceived as very short-notice commentaries on "hard topics on relevant material". It was his hope that such Editorials would lead to debates within the journal. He had also introduced Updates in review form and had begun to assemble relevant papers under a molecular biology section.

Thus, in the eyes of its subscribers, *Human Reproduction* was fast becoming a repository not just of research reports but also of current opinion, discussion and debate. However, in its publication of scientific and clinical research, with many landmark papers published and all within a relatively quick lead-time, *Human Reproduction* had fast become a source of well cited and well read reports, whose quality was guaranteed and whose publishing policy seemed free of any bias or hidden agendas. Not least among those landmarks were those from the VUB in the early 1990s describing ICSI and results from the Brussels group's first experimental series. ICSI was without doubt a European initiative, and *Human Reproduction's* growth in the early 1990s rose in parallel to the emergence of ICSI in Europe.

However, there were also many practical issues for Edwards to deal with, not least the composition of the editorial board and associate editors. The terms of the contract with OUP stipulated that responsibility for the

Human Reproduction's associate editors and editorial board

Edwards's primary editorial support came from a small team of associate editors comprising Henning Beier, Jean Cohen, Marco Fraccaro (who in June 1992 was replaced by Marku Seppala), Lars Hamberger and Gerard Zeilmaker. In addition, during *Human Reproduction's* early years ESHRE had appointed an editorial board for manuscript review, which included Pedro Barri, Etienne Baulieu, Giuseppe Benagiano, Anne Grete Byskow, Pier Giorgio Crosignani, José Egozcue, Wilfried Feichtinger, Malcolm Ferguson-Smith, WL Herrmann, Glenn Lauritsen, Benno Runnebaum, Jacques Salat-Baroux, Robert Schoysman, Jacques Testart and André Van Steirteghem.

Under the 1992 rules the 15 appointments made to the editorial board in 1986 and '87 and the associate editors were due for retirement from the journal, but, at a meeting of the editorial board in on 27th June 1993, Edwards made a plea for the continuing place of former ESHRE chairmen and those whose contribution had been "immense"; thus, only Byskow, Ferguson-Smith and Lauritsen would go, the rest would stay on alongside an ever-expanding list of colleagues (which at the end of 1993 additionally comprised Jon Aitken, Joelle Belaisch-Allart, Gerhard Bettendorf, Bruno Brambati, Maurice Bruhat, Lise Cedard, Frank Comhaire, Paul Devroey, Wolfgang Engel, Steve Franks, Franz Geisthovel, Hendry, Roy Homburg, Martin Johnson, Liz Lenton, Fernand Leroy, Gerhard Leyendecker, Jacqueline Mandelbaum, Antonio Pellicer, Josef Schenker, Serio, Antonio Simeone, Gregoria Siracusa, Juan Tarin, Basil Tarlatzis, Allan Templeton, and Jan Tesarik). In the meantime, others, such as David Baird, Mike Hull, Pierre Jouannet, Henry Leese, Anne McLaren and Arne Sunde had joined and subsequently left the board (though Baird would later rejoin, as was allowed by the rules after a 12-month absence).

appointment of an editorial advisory board lay with ESHRE, and it had subsequently been agreed (in 1992) that the term of office should be fixed at five years. As reflected in his appointment of "international" advisory board members, Edwards looked to such appointments to offer practical help to the journal - in this case in its worldwide profile - but more importantly in the function of peer review. His policy was to send each paper submitted to two reviewers; and to a third if one report was unfavourable (or not forthcoming after eight weeks). Thus, two favourable reviews would justify publication.

The new contract with OUP in 1995 seemed to resolve many of Edwards's irritations with OUP's management of *Human Reproduction*, though he was still unhappy with OUP's initial budgets for 1996, particularly the "immense sum" allocated to "overheads". But the bumpy road to the new contract had been partly smoothed by OUP's proposal that ESHRE might take on two new titles under its *Human Reproduction* banner - and of course under the editorship of Edwards. The first title - *Human Reproduction Update* - had been proposed partly to save

space in the journal then given to review articles (which had started in 1993) and partly to absorb two of OUP's minority publications, *Bibliography of Reproduction* and *Oxford Review of Reproductive Biology*. *Update* was planned for six issues a year, with each to include a CD-rom of visual and text resources. A second new title, *Molecular Human Reproduction*, had also been mentioned at the 1994 AGM in Brussels. Again, it was intended by Edwards to filter off special interest submissions in molecular biology then occupying a section of the main journal - and thereby free editorial pages for scientific and clinical papers of wider appeal. Although the first circulation estimates for *Molecular Human Reproduction* were put at no more than 1300 per monthly issue, with the majority coming from a combined members' subscription with *Human Reproduction*, within a few months Edwards would note that the quality and quantity of contributions were such that demands on the editorial offices at Bourn Hall were high and getting higher.

Human Reproduction and its two sister journals were clearly a huge commitment for Edwards and his team, which now involved not just the editing of raw copy but most of the page production too (which had transferred to Bourn Hall from OUP in 1994). Edwards would later complain that at this time OUP "were not very supportive editorially", and of course management at a remote site - and with a remote accounting procedure - would remain a source of irritation to him. However, for the moment the prospect of the new journals and the maintenance of *Human Reproduction's* inexorable success were challenges enough, and, with a new contract lined up with OUP, Edwards was poised to take the titles into the next five years of their contracts, and to the top of their citation rankings.

5

BUILDING A FIRM FOUNDATION: 1987-1991

At ESHRE's third AGM - held during the 1987 annual meeting in Cambridge at the end of June - the following appointments to the Executive Committee (EC) were confirmed: Cohen as chairman, Crosignani as chairman elect, Diedrich as secretary, Van Steirteghem as treasurer, Egozcue, Hamberger, McLaren and Zeilmaker as members, Sunde as special advisor on workshops, and Kjessler as chairman of the ethics committee. That AGM, like most of the main lectures of the congress, was held in the Corn Exchange, one of Cambridge's few historic buildings whose origins alongside the marketplace owed more to local commerce than to the venerable history of the colleges. Edwards, once the venue and date of the meeting had been agreed by the EC at its fifth meeting in April 1986, had turned to both the university and the city authorities for support in finding conference locations, and the scientific programme was duly delivered in an assortment of university lecture theatres, an examination hall, and the Corn Exchange itself. The commercial exhibition took place in the Guildhall (another building whose origins were more town than gown), and delegates staying in the city were offered a choice of accommodation ranging from a single student room in college (at £17 per night) to the city's two best hotels. It was, in fact, Cambridge's first major conference within the city centre and arrangements were - as Edwards would admit - "novel".

Despite the short lead-time (just 14 months) and Edwards's huge commitments at this time to both the society and the journal, the Cambridge annual meeting was a great success. The scientific programme attracted around 850 participants, and drew universal praise for its range and quality. Edwards called it "a feast of lectures" and among them were four "guest lectures" guaranteed to generate publicity and topical interest both within and outside the meeting: Steptoe on the outcome of IVF pregnancies, Mary Warnock on the ethics of human conception in vitro, David Weatherall on fetal DNA analysis, and from France Luc Montagnier on the emerging fundamentals of AIDS. In anticipation of outside interest in the meeting - and in the authority of the speakers - Edwards had also organised a press room and press officer, a service not formally revived at an ESHRE annual meeting until 1999 in Tours. As Hans Evers would say, Edwards was good at PR.

In all, 277 papers were presented in Cambridge in 12 plenary and 17 free communication sessions, with subjects covering assisted conception, molecular embryology, sperm parameters in IVF, prenatal diagnosis, follicular stimulation, intrauterine insemination, fetal tissue grafting, oocyte physiology, ultrasound, embryology, ectopic pregnancy, polycystic ovaries, gestation as well as the menopause, contraception and sexually transmitted diseases. Edwards himself spoke on the prospects for prenatal genetic diagnosis. Two full sessions were allocated to "recent progress in infertility", which, even at this rush-to-publish time, included two papers on the management of multiple pregnancies following IVF. The session on ectopic pregnancy was organised jointly with the British Fertility Society, and other sessions with the British Society for Developmental Biology. These were the opportunities which - as Edwards told Liselotte Mettler - he could not ignore in contemplating an independent ESHRE meeting in the UK.

It is also interesting to see how the introduction of GnRH analogues at this time had such a heavy impact on the scientific programme; whole sessions were now devoted to "programming the cycle" and to results from comparative studies assessing the various newly introduced analogues. What we now see, for the first time, is a concentrated burgeoning effort to measure the efficacy of different stimulation protocols in a multitude of outcome measures: oocyte fertilisation rates, serum hormone levels, number of oocytes retrieved, embryo transfers, clinical pregnancy rates (per cycle, per transfer), ongoing pregnancy and live birth rates; with hMG alone or in combination with GnRH agonists, FSH alone

or with agonists, busserelin or goserelin, “pure” FSH or hMG, fixed or individualised schedule, clomiphene or not, in a short protocol or a long protocol? It was indeed a “feast” of lectures.

But despite its runaway scientific success, for ESHRE the Cambridge meeting, unlike its two predecessors, did not show a financial surplus. More than 30 companies were present in the commercial exhibition, several sessions were commercially sponsored, and even the mini-bus transport from the colleges to the city centre was laid on by Serono. But, when the accounts were finally completed and the dust had settled, there was still a shortfall of . . . well, no-one was ever quite sure. The congress’s treasurer, Edwards’s Bourn Hall colleague Mike Ashwood-Smith, had returned to Canada shortly after the meeting, leaving many promises of income unfulfilled and many bills still to be paid. By the time the EC met next in Budapest in September 1987 - under Jean Cohen’s first proper chairmanship - the arrears looked to be around £20,000. Edwards, in his characteristically generous way, insisted on retaining responsibility for the finances (and indeed over the next few months worked his way through the shortfall with a catalogue of contributions from his own lecturing and from benefactors). In the meantime, treasurer Van Steirteghem was instructed to allocate £10,000 from ESHRE’s reserves to pay pressing bills from Cambridge, and Anne McLaren reaffirmed ESHRE’s policy that the travel arrangements of invited speakers should be insistently confined to economy tickets.

Nevertheless, despite the temporary financial setback, the take-home message from the Cambridge congress was, according to Edwards at least, that its scientific quality and interest “proved the society’s positive appeal and that ESHRE was now in full expansion”. Thus, when Cohen took over as chairman at the third AGM he headed a society of more than 750 members from 39 countries, a society with a journal moving towards a readership of 600, with annual meetings planned for the next three years (in Barcelona 1988, Copenhagen 1989, and Milan 1990), and with a programme of training workshops beginning to take shape and attract substantial interest. Moreover, the society had just initiated its first multicentre clinical trial and, with its ethical committee now formed and active, was already formally accepted as an advisor to the European Parliament. Such a society must have given Cohen, one of its two founding fathers, huge satisfaction. Nevertheless, despite such visible progress, ESHRE was not as robust as it seemed, nor as Cohen might wish.

“We had done the hard work,” Cohen recalls, “we had created something which now existed. But I felt we had to give it more life, to give it the energy to find its own way, and that’s what I tried to do during my chairmanship, so the next chairman might inherit something with its own momentum.” Cohen knew, coming after three hectic years of Edwards’s drive and commitment, that his task would not be easy and his first priority was to address ESHRE’s worrying financial affairs.

At the EC meeting in Budapest in September 1987 Van Steirteghem had reported a loss of almost 15,000 Swiss francs (still ESHRE’s currency (€9500)) over the previous five months. Now, there was the additional loss from the Cambridge meeting to factor in. ESHRE’s financial aim, of course - then as now - was not to accumulate cash like a bank, but to generate the reserves necessary to run its training programme, support the journal and, most importantly, provide security to the society against unforeseen circumstances. So far, in ESHRE’s short history, there had been little forward or strategic planning - let alone disaster planning - except for consideration of forthcoming meetings. But now, to Cohen and the EC, a cushion of reserves at the bank seemed fundamental to ride the ups and downs of the society’s income.

Both Van Steirteghem and Cohen, having seen the congress crowds in Cambridge and their interest in the commercial exhibition, reasoned that the society’s first source of additional funding might be the pharmaceutical and equipment manufacturers. However, then as now, relations with commercial organisations posed difficult problems for the EC in striking a proper balance between financial support and the society’s independence. According to Klaus Diedrich, whose organisation of the Bonn meeting first brought ESHRE into contact with commercial sponsorship, industry support has always been a big issue within the society. There was always the uneasy recognition, he explains, that commercial sponsors have the power to provide financial backing but that their support should be encouraged and provided in an ethical way. “In a way we were all - scientists, clinicians, manufacturers - sitting in the same boat,” says Diedrich. “We all wanted the same thing, success for ESHRE and the scientific and clinical disciplines it represented. But it was very important to keep our scientific independence and we were always sensitive to the power of sponsorship. Today, ESHRE is strong enough for companies not to influence our decisions. But we still see the danger of too much influence from sponsors, and it’s essential that we keep our independence.”

At the time three members of the EC, Cohen, Crosignani and Edwards himself, had fruitful working associations with the pharmaceutical industry, and early support from Serono, Schering and Organon was largely brokered by them. But now, as the EC in Budapest contemplated a balance sheet heading down into the red, Cohen proposed a systematic approach to the industry whereby earlier grants might be renewed and companies made fully aware of ESHRE's progress so far. Thus, at the following EC meeting, in Brussels in January 1988, individual members of the EC and Advisory Committee (AC) were given personal responsibility for contacts with specific companies for potential support. Cohen also initiated a drive to encourage members to pay their fees on time. Membership fees provided around one-third of ESHRE's income, yet, as 1987 drew to a close, around one in four members had not paid their annual dues. Chasing fees would become an important and time-consuming role for Bruno Van den Eede, now settled in as ESHRE's assistant secretary in his tiny office at the VUB.

But there was more drama for Cohen and ESHRE in Budapest than merely cranking up the bank balance. And once again, centre stage was ESCO and Kurt Semm. When the EC delegation arrived at the Budapest Convention Centre for the joint congress with ESCO they were exasperated to find that the attendance certificates for participants bore only the name of ESCO and had been signed by four ESCO officers, Gimes, chairman of the local organising committee, Comminos and Schoysman for the scientific committee, and Semm. ESHRE was nowhere to be seen. Cohen was furious. At the EC meeting next day (and one day before the joint congress opened) he immediately reshuffled the agenda to bring the ESHRE-ESCO collaboration to the front, to find some last-minute way of presenting ESHRE's part in the congress's organisation. Cohen would first of all insist, therefore, that he be allowed to speak at the opening ceremony and that he would emphasise "the democratic principles which govern the organisation of ESHRE and our activities since 1984".

But more was to come. Berndt Kjessler, who was co-opted to the EC as special advisor on ethics, was double-booked that morning for ESHRE and a planning meeting of ESCO. Thus, once the EC had sat down to deliberate, Kjessler was dispatched to his ESCO meeting to raise ESHRE's frustrations and report back on any response. Two hours later, as drama turned to farce, Kjessler returned, with news that Semm was smarting from the "threat" of ESHRE in the belief that ESHRE was trying "to undermine ESCO's existence". So now what to do? Truce or war?

Most of the EC, notably Kjessler himself, Anne McLaren and Crosignani, favoured a conciliatory approach, arguing that the two organisations would make more progress together than in competition. Cohen, however, was still suspicious, reaffirming his objections to ESCO's non-democratic principles and finally proposing that ESHRE should simply take over ESCO. Van Steirteghem as treasurer also saw financial problems in two societies continuing to scrap it out in the same congress arena for a share of sponsors, speakers and participants. Finally, under McLaren's urging - and in a tradition of ESHRE which would become hugely important in its later organisational structure - it was proposed that the whole issue might best be put in the hands of a sub-committee with specific responsibility to find a practical solution. Thus, with this and other proposals on the table, the EC would now meet with Semm and an ESCO delegation next day. Whatever the outcome, Kjessler wryly observed that surely "we've now seen the last of the autocrats".

Overnight Kjessler worked behind the scenes to broker a deal, and next day at the joint meeting - chaired by Gimes - had firm proposals to improve the ESHRE-ESCO relationship. With ESHRE now committed to its annual meeting in a different European city each year and ESCO committed to its three-yearly congress, Kjessler proposed that a six-strong sub-committee (three ESHRE and three ESCO) could oversee the organisation of the respective congresses within their current schedule schemes. To safeguard even the possibility of future collaboration, added Kjessler, "past misadventures should best be forgotten".

Cohen, however, was still not happy and reiterated his misgivings - that the venue for this ESCO congress in Budapest was chosen without any agreement of ESHRE, that the content of the scientific programme had become ESHRE's sole responsibility, that an interruption to ESHRE's annual meetings every three years would be damaging... and then, of course, there were those attendance certificates. Cohen repeated his belief that the only route to harmony was for ESCO to recognise its non-viable position and step under the ESHRE umbrella.

Semm, however, would hear none of it and would not see ESCO capitulate. ESCO, he said, represented 26 national fertility societies; where would their representation be if ESCO joined ESHRE? It would be better, he said, if ESHRE joined ESCO and became the 27th represented group. It was stalemate, and the discussion to wriggle out of the impasse was long and heated. Finally, with McLaren, Kjessler and Edwards taking on the role of mediator, the debate slowly turned towards the idea of a joint

congress organising committee composed along the lines first suggested by Kjessler. So it was Kjessler who now sought agreement from the EC that ESHRE should be represented on this joint committee by the chairman, Cohen, the chairman elect, Crosignani, and the treasurer, Van Steirteghem. For ESCO, he negotiated agreements from Comninos (who had already represented ESCO on ESHRE's temporary committee), Mettler and Elizabeth Johannison (who from her base in Switzerland organised the ICRR, International Committee for Research in Reproduction).

As the meeting dragged on to the following day, Kjessler's six names were finally put forward for membership of the joint committee. Fine, they agreed, but, asked Mettler, where was the name of Semm. Surely ESCO's secretary-general should have a place? But that, reasoned Cohen, would give an unfair advantage to ESCO - and once again the meeting broke up in disarray, now for each party to retire and find time for review. So, when the delegates sat down once more, Kjessler yet again proposed a similarly composed six-strong voting committee but now with the addition of ESCO's secretary-general and ESHRE's chairman as ex-officio members. Finally, after a further adjournment and more objections from Cohen, the mediators swung agreement round to Kjessler's proposals - on the proviso insisted by Crosignani that there should be no unforeseen changes to the scheme. Thus, after three days of often acrimonious discussion, a protocol for the joint committee would be finally agreed and signed by all members - and its principles chiselled in stone.

So the new joint organising committee would be composed of Crosignani, Van Steirteghem plus one other for ESHRE, Mettler, Johannison and Comninos for ESCO, and in a non-voting capacity Semm and Cohen. And, once the dust of battle had settled, the new committee immediately turned to its most pressing problem, the next joint ESHRE-ESCO meeting scheduled for 1990.

It was quickly agreed that the congress would be held in Italy, and in September so as not to clash with the AFS's meeting in October. Choice of a specific venue - Milan, Taormina or Rome - would be left to the local organising committee, which would be chaired by Ettore Cittadini, a member of ESHRE's AC. Under the drive of Cohen and Van Steirteghem the joint ESHRE-ESCO committee also formulated the financial arrangements for the congress in Italy, which, in essence, would allow ESHRE 50 per cent of any surplus generated. In return it was agreed that in 1990 - unlike 1987 - ESHRE would not hold a separate annual meeting. All its congress efforts would be directed to the joint event, whose location in

Italy would be finally decided at the next meeting in Barcelona in July 1988.

A congress in Italy, especially in Milan, would inevitably pile more on the desk of Pier Giorgio Crosignani, who now as chairman elect was already heavily committed with other ESHRE activities. One of these was a multicentre trial of different techniques in the treatment of unexplained infertility. The original idea had been Edwards's, but at a meeting of the EC in Strasbourg in December 1986 he had passed on responsibility for the trial to Crosignani. By the next EC meeting - in Brussels in March 1987 - Crosignani had firmed up the range of the study (a comparison of superovulation alone or with GIFT, IVF, IUI or intraperitoneal insemination in unexplained infertility, ie, women with normal tubes and "normal" partners, each centre to compare two treatments), numbers, treatment duration and preliminary protocol. Dr Eurof Walters would be responsible for the statistical design and analysis of the study. Cohen had also reached a tentative agreement with Serono for funding, and Crosignani was now instructed to draw up a budget. Participants in the trial - around 20 centres in Europe - had met during the Cambridge annual meeting, where Crosignani explained the protocol and the forms for returning data.

When the first preliminary results were published (*Hum Reprod* 1991; 6: 953-958) 19 centres had completed the programme, presenting data on 649 cycles in 444 subjects. There was evidence that the use of one of the assisted reproduction methods enhanced pregnancy rate beyond that expected from superovulation alone, but there was no evidence of superiority from any of the individual invasive methods. However, Crosignani's trial in unexplained infertility would become a well cited authority in supporting the view that both intrauterine and intraperitoneal insemination achieve higher pregnancy rates with ovarian stimulation than without.

ESHRE, in fact, would organise only one further clinical trial (on treatments in male subfertility (*Hum Reprod* 1994; 9: 1112-1118)) throughout the next 20 years of its history, but instead concentrated its clinical efforts on training, guidelines and data collection. The findings of the second study incidentally, one of the few controlled trials ever to have been performed of several treatments in male infertility, were of course quickly superseded by the ICSI revolution.

Meanwhile, Cohen's focus as chairman remained firmly fixed on ESHRE's finances, and he took note from Edwards at the 14th meeting of the EC in Brussels in January 1988 that "the great weakness of the Cambridge meeting had been a lack of proper financial management".

The Second Advisory Committee 1988-1990

There was always some confusion over the election of the Advisory Committee and its function. The original by-laws stipulated that the AC is elected by the General Assembly, but in 1992 the procedure was changed to a nomination and ballot process with the full membership. At the 1986 AGM in Brussels, Edwards insisted that the AC was there to be consulted “on any matter that may arise during the rest of the year” and proposed that the first AC should remain in place for one more year. In the event, election of a second AC was not approved by the AGM until Barcelona in 1988, when elections fell into a two-year pattern. The second AC comprised:

Bert Alberda (Netherlands)	Freimut Leidenberger (Germany)
Alain Audebert (France)	Shlomo Mashiach (Israel)
Pedro Barri (Spain)	Jacques Montagut (France)
Henning Beier (Germany)	Erich Muller-Tyl (Austria)
Angeles Bielsa (Spain)	Ove Nillson (Sweden)
Anne Grete Byskov (Denmark)	Guido Ragni (Italy)
Anthony Comninos (Greece)	Marku Seppala (Finland)
Leda Dalpra (Italy)	Arne Sunde (Norway)
Paul Devroey (Belgium)	Peter Sydow (Germany)
Marc Germond (Switzerland)	Basil Tarlatzis (Greece)
Michael Hull (UK)	David Whittingham (UK)

Progress for this year’s annual meeting in Barcelona had moved smoothly under its local chairman, Juan Antonio Vanrell. However, despite such smooth progress, there was for the first time a seed of doubt expressed about the financial wisdom of using a professional congress organiser (PCO) to help with the practicalities of the event. ESHRE’s income at the time drew fairly equally on three sources - membership fees, educational grants from industry, and a surplus from the annual meeting. Cohen had already initiated his policy to develop better relationships with commercial organisations, Bruno Van den Eede had introduced a system for chasing non-payment of membership fees, so now, reasoned Cohen, why reduce any surplus from the annual meeting when many of the tasks now being undertaken by a PCO could be done from Central Office. Of course, there was nothing unusual in using a PCO; in Cambridge Edwards had recruited Thomas Cook to handle delegate travel and accommodation arrangements. And now, the Spanish local organising committee had hired a PCO at a fee of 10 per cent of the congress’s income - but, as Cohen and Van Steirteghem saw it, this was still 10 per cent off ESHRE’s potential revenue. In fact, the question of PCOs would be raised in discussions on every annual meeting, but it was not until Thessaloniki in 1993 that an

ESHRE congress would be organised quite independently of a PCO. Ultimately, self-organisation would become a cornerstone of the annual meeting and an important means of guaranteeing a uniform congress structure from one year to the next, as well as complete financial control. In the meantime, Cohen proposed the formation of a sub-committee to strengthen and maintain ESHRE's association with commercial sponsors at its congresses; the committee would comprise Cohen himself, Van Steirteghem and Pedro Barri.

There were, however, more immediate congress issues for the chairman and EC to resolve. Following proposals from Kjessler and colleagues in Scandinavia, ESHRE's sixth annual meeting in 1989 had been originally scheduled for Copenhagen, with Professor Nils Otto Sjoberg as chairman. Those original plans, however, had now been modified by the local organising committee because the Copenhagen conference venue was deemed inadequate and hotel prices were steep in the city in June. The committee's second proposal was to transfer the main conference site over the water to Malmo, a 45-minute ferry away, where the city authorities were keen to be host and guaranteed 250,000 Swedish kronas (€28,000) against any possible loss. The EC had accepted this modified proposal and the local committee had forged ahead with a Copenhagen-Malmo plan. Now, however, there was a further complication: the following year - 1990 - ESHRE would not only have to share its annual meeting with ESCO in Italy but would also have to compete with the seventh World Congress of Human Reproduction now scheduled for Helsinki. It was a severe blow to the EC, especially as Hamberger (a member of the EC) and Seppala (a member of *Human Reproduction's* editorial board) were involved in the organisation, Seppala as congress president.

Thus, Seppala was invited to the next EC meeting, at the offices of Gyn.Obs in Paris in May 1988, to discuss with the EC how the two congresses might best manage the overlaps of interest and date. There were all sorts of proposals raised to minimise the conflicting threat - even that ESHRE might co-host the event - but, when a decision was put to the vote, there was no clear response from the EC other than that Crosignani should join the organising committee for Helsinki and that each congress would be left to make the best of a difficult situation.

In fact, Seppala informed the EC that the original date for the Human Reproduction congress had been in 1989 but, out of deference to ESHRE's plans in Copenhagen, he had persuaded the organisers to push the congress back one year. Now, sponsors, speakers and participants would

have to make a choice between a world congress in Helsinki and a European meeting in Italy. "The companies will have to choose," said Lars Hamberger. "They decide in advance which meetings they will attend and make their choices. They'll choose Helsinki or Italy, or both." What such resignation masked, of course, was the far larger issue that already in this relatively new field there was a plethora of meetings, many organised without the support of a society of members and with few aims other than turning a profit. For his part, Cohen deplored the number of congresses in the field, which were now popping up like mushrooms, and the fact that, despite ESHRE's ideals, there was still no collaboration or co-ordination in congresses in Europe.

Cohen's mushrooming congress problems, however, were not over yet. ESHRE's sixth annual meeting in 1991 had been provisionally planned for The Hague during June or July, but it was now clear that at exactly the same time the seventh World Congress on IVF was due to be held in Paris. It would be impossible for the two congresses to be staged at the same time, and in Europe. The EC's first suggestion was that the Hague meeting should be put back to September, not just in order to attract delegates but particularly to attract sponsorship. However, the EC was not keen, and another idea began to take shape. Would it not make more sense if ESHRE "could be included in some way or another" in the Paris IVF congress? Cohen was positive about the idea, arguing that the organisers of the world congress - notably Frydman, Mandelbaum, Plachot, Salat-Baroux and Testart - "were very close to ESHRE". They might be persuaded. Cohen said he would investigate the possibility, which also had the support of Edwards, with his colleagues in France.

Thus, at the next (17th) meeting of the EC, which took place during the Barcelona annual meeting in July 1988, Cohen introduced as guests Testart and Frydman from the executive committee of the world congress, who by now had agreed in principle to a joint effort in 1991 with ESHRE. A joint meeting, Cohen reaffirmed to the EC, would remove any conflict between the two organisations and maximise response from participants and sponsors. The major concern, once an agreement in principle had been reached, was how to incorporate the scientific activities of ESHRE and the world congress into a unified whole - probably, as Edwards suggested, two days for ESHRE followed by three days of IVF. The Hague as an ESHRE venue would now be put back in its original format to 1992.

It was indeed a difficult time for Cohen, faced with a critical bank balance, a desperate need for funding and now sudden competition to



ESHRE's seventh annual meeting in Paris in 1991 was organised jointly with the seventh World Congress on IVF, whose executive committee was "very close to ESHRE". Four of them, from left to right, Michelle Plachot, René Frydman, Jacques Testart and Jacqueline Mandelbaum, speak to the French press.

ESHRE's congress schedule. At the AGM in Barcelona Van Steirteghem had described the society "running at a loss". With financial commitments to the Barcelona meeting itself, to Crosignani's multicentre trial, *Human Reproduction* and seed capital for Malmo, the society found itself spending much more than it was earning. Although membership of ESHRE had just reached 1000, there was still not enough in membership fees to cover outgoings, particularly as revenue from the previous year's annual meeting in Cambridge and from commercial sponsorship had both fallen well short of expectations.

While Cohen juggled with dates and clashing congresses to maximise sponsorship potential, his colleagues on the EC nevertheless still urged restraint in extending ESHRE's hand to sponsors. In Barcelona Henning Beier expressed concern at the influence of the industry on the scientific programme of the annual meeting; Lars Hamberger insisted that product

promotion should be reserved for the commercial exhibition, and not allowed to stray into the lecture hall; and there was also dismay that a lecture on “25 Years of Humegon” had been allowed into the programme of the opening ceremony. Indeed, sponsorship was always a two-edged sword for ESHRE, and it was an issue which the EC had often to address. But as a principle, and as Beier categorically affirmed in Barcelona, “companies should not be allowed to buy the society’s interests”; this was a position which ESHRE always tried to maintain, whatever the state of its bank balance.

Meanwhile, the joint ESHRE-ESCO congress committee had decided that its 1990 meeting would be in Milan after all, despite Semm’s protests “that I am not very happy to have Milan as a congress place for ESCO”. Semm would have preferred the more resort destination of Taormina in Sicily, but transport, costs and dates precluded its choice. Not surprisingly, when discussions began in earnest over planning for Milan, the budget was foremost on the agenda. Crosignani, now nominated as congress chairman, had appointed a PCO, whose commission was set at 18 per cent of budgeted expenses. This was, in fact, the largest item on the budget, just ahead of the 100 million lire (€50,000) estimated for an optional gala evening at La Scala. While debate was intense over the projected finances and the scale of the PCO’s commission, there was little disagreement with the scientific programme which the joint committee had developed - 12 sessions ranging from reproductive health, to implantation, unexplained infertility, new developments (including growth factors), gamete and embryo research, outcomes of assisted reproduction, iatrogenic infertility and ectopic pregnancy. In planning the scientific sessions Crosignani had adopted a structure that would become a hallmark of future ESHRE meetings, parallel sessions which tried to maintain separate scientific and clinical subjects. In this way, it was argued, there would always be papers of interest available to delegates, whatever their background. The budget for Milan had also been trimmed, with the gala evening at La Scala now replaced by a more modest concert in church.

Elsewhere on the congress front the news was similarly encouraging. The Scandinavia meeting in Malmo, with around 700 paying registrants, had proved yet another success, again applauded for its scientific content and earning ESHRE a small surplus for its reserves. Paris too - with Cohen now elected as chairman of the meeting for ESHRE - was forging ahead with its plans, working to a two-day ESHRE and three-day world congress schedule.

The focus of the EC at this time, however, was not only confined to the bank balance and congresses. The multicentre trial was up and running, albeit slowly, the ethics committee had taken part in one public meeting (in Toulouse) and was formally poised to offer consultation to the European Parliament, and there was already discussion about the possibility of ESHRE acting as a clearing house for the collection of IVF data within Europe in much the same way that FIVNAT was now doing in France. There was also a feeling among the EC and AC that ESHRE should become a focal point not just for data but also in the provision of guidelines for good practice and minimum standards in reproductive medicine. Thoughts on this latter issue were galvanised by events in The Netherlands in 1988.

In February and March of that year 177 IVF patients in Rotterdam had been exposed to the hepatitis B virus as a result of contamination in a batch of culture medium. All the patients had been informed and treated, with no serious consequences. However, the events had drawn severe criticism in The Netherlands and the integrity of the whole IVF procedure had been questioned. Gerard Zeilmaker, who had explained the events to the EC, said that assisted reproduction in The Netherlands would now need to rebuild its credibility. The events in Rotterdam proved a salutary lesson to everyone, and Zeilmaker proposed that ESHRE should take a lead in confronting the issue and setting good practice standards for IVF laboratories. This was, said Zeilmaker, a "real need". As a result, Cohen proposed the formation of a Safety and Standards Committee, to be chaired by Klaus Diedrich and composed of specialists in virology, genetic disease, hygiene, immunology and embryology. Its aim would be guidelines designed to avoid all risks of contamination in the IVF process, and its starting point would be Rotterdam, which already had had to manage its own emergency; two Dutch consultants, Boks and Peeters, became members of the committee.

By April 1989's EC meeting in Jerusalem the Safety and Standards Committee had met twice and produced an initial draft of recommendations. The text covered three broad areas of risk: the patient (from counselling to serological examination); the culture medium (from source to assessment); and laboratory hygiene (from basic cleanliness to handling and labelling of gametes). The draft was circulated to all members of the EC - and some outside specialists - for comment. There was an overall concern that the "recommendations" should not be perceived as too restrictive, but one clause of the draft did cause much discussion. Clause 5, offering advice on the number of embryos to be transferred,

said: "The Committee advises that as far as the number of embryos that are transferred are concerned the number should be limited to not more than 3 or 4; as far as age is concerned the limit should be 40 years." Some members thought the wording should follow the line of the Voluntary Licensing Authority in the UK (a forerunner of the eventual statutory body, the HFEA) and advise "a limit of three, or in some cases four"; others felt that four was a reasonable number in certain cases and should not be excluded. Eventually, the EC agreed that "the number should be limited to three, or in exceptional cases four".

Of course, the next 15 years, with ever mounting safety concerns over multiple pregnancies and births, would see this discussion further intensified, with the eventual but slow adoption of lower embryo transfer limits. In the UK a sixth HFEA Code of Practice reduced the limit to two in 2004 in women under 40, while in some Nordic countries elective single embryo transfer under trial conditions would show that live birth rates were no different from those achieved from higher order transfers. Thus, in couples with a good prognosis and the possibility of further funded cycles, single embryo transfer would quickly become routine practice in many Nordic and north European centres. Nevertheless, a retrospective analysis of all 5856 IVF babies born in Sweden between 1982 and 1995 would find multiple births in 27 per cent of all IVF pregnancies (compared to 1 per cent in the general population). The study thus found that in IVF pregnancies more babies were born pre-term (30.3 versus 6.3 per cent) and more had low birth weights (27.4 versus 4.6 per cent under 2500 grams). An editorial

Multiple pregnancies

An ongoing challenge

The number of twin, triplet and quadruplet births following IVF has been found to vary considerably between countries. In an ESHRE survey of European IVF and ICSI results for 2000 (Hum Reprod 2004; 19: 490-503) the highest multiple pregnancy rates were found in southern and eastern European countries, where triplet rates were still 7 per cent compared with only 0.8 per cent in northern European countries. Overall rates in Europe were 24.4 per cent twins, 2.0 per cent triplets, and 0.04 per cent quadruplets, making a total multiple rate of 26.4 per cent for Europe as whole. To its credit, ESHRE has continued to campaign for lower order embryo transfer limits and has publicly deplored the trend seen in some southern European countries - and in the USA - of transferring three, four or more embryos. In the USA, meanwhile the multiple pregnancy rate in 2000 was still found to be 39 per cent.

commenting on the study in the *Lancet* (1999; 354: 1572-73) described triplets as “an avoidable procedure-related complication” of IVF, and added a little more to the unease some were now beginning to feel about IVF.

There was also concern among the EC that the Safety and Standard Committee’s text should include some comment on the fate of excess embryos. Mike Hull from the AC stressed how important it was for couples to formally agree a policy before starting treatment, especially in those countries where there was no relevant legislation in place. Zeilmaker also disputed the recommendation that “the laboratory has to be as close to the operating theatre as possible”. The Netherlands was at the time pioneering “transport IVF”, a technique whereby oocytes collected locally might be transported in a small incubator to a central laboratory for fertilisation and transfer or storage. Zeilmaker was insistent that transport IVF was a safe procedure.

The committee’s final text appeared in ESHRE’s newsletter of January 1990. The Safety and Standards Committee continued its work and within a year had produced a follow-up set of guidelines on the cryopreservation of embryos (covering patient consent to freeze-thawing techniques), and oocyte and embryo donation (covering examination and procedures, including a recommendation to karyotype donors for genetic disease). This second series of guidelines was published in the first issue of the relaunched newsletter *Focus on Reproduction* in 1991.

Following the example of the Safety and Standards Committee, the Ethics Committee under Berndt Kjessler had in 1989 regrouped and also set itself the task of issuing guidelines relating to the practicalities of assisted reproduction and prenatal diagnosis. The committee, which comprised Henning Beier, Paul Devroey, Marc Germond, Anne McLaren, Jacques Montagut, Erich Muller-Tyl, Basil Tarlatzis and David Whittingham, set about its long task of assembling argument and counter-argument to finally arrive at what would become “Guidelines regarding medical practice related to assisted procreation and prenatal diagnosis”. It was a huge project, and was published in draft form for comment in the third newsletter of 1991. In essence, the committee assessed the full range of diagnostic procedures, treatments, prenatal diagnosis and research activities under a four-point grading system: A as acceptable, E empirical, R research and NA not accepted. Each procedure was described and graded, as a knowledge base for “authorities, professional and other societies as well as individual doctors and

scientists" for decisions about "acceptable benefits and unacceptable consequences". It was interesting that most investigation procedures were in 1991 deemed acceptable, while, among the treatments, only surrogacy was deemed unacceptable.

Preimplantation diagnosis, occupying its own section, was graded R. By then the procedure of pre-implantation genetic diagnosis (PGD) had been successfully applied in a patient at risk of an X-linked genetic disease at the Hammersmith Hospital in London. There, a blastomere removed by biopsy from an 8-cell embryo was "diagnosed" for gender by DNA amplification of a Y-chromosome-specific repeat sequence. Only female embryos (ie, without the possibility of having the X-linked defect) would be transferred. Despite the success of the technique, reported by Alan Handyside and colleagues at the Hammersmith (in a patient at risk of Duchenne's muscular dystrophy), and the apparent finding that biopsy does not impair the embryo's subsequent development, the Ethics Committee remained cautious about PGD. In time, however, PGD - and its more broadly applied preimplantation genetic screening for aneuploidy - would become important special interests of ESHRE, both in terms of their clinical outcomes and their implications for genetic counselling. The Ethics Committee's guidelines stood the test of time for just a few years in this rapidly advancing field, and were next updated in 1994/95 (Hum Reprod 1995; 10: 1246-1271).

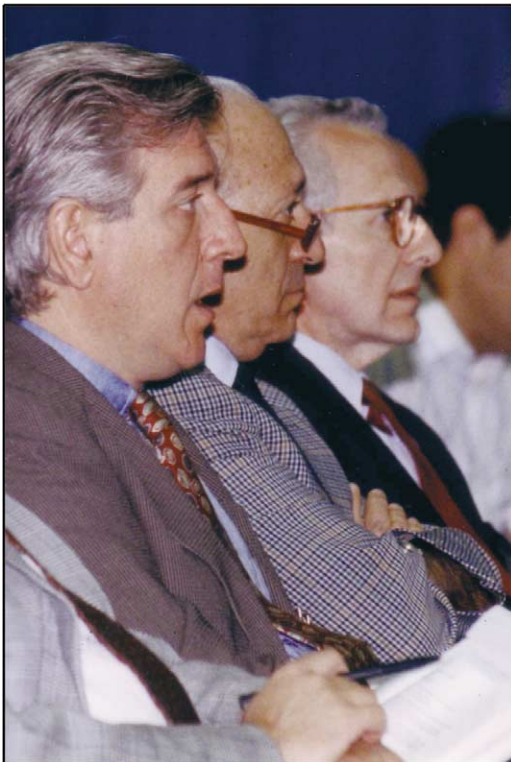
Jean Cohen's term as chairman of ESHRE came to an end at the AGM in Malmo in 1989. From the time those first ideas for a European society had been aired at dinner with Edwards in 1984, his contribution to ESHRE had been immense. His term as chairman had primarily focused on strengthening the society's financial basis and shaping its role as a reference point for reproductive medicine in Europe. His successor, Pier Giorgio Crosignani, took over a society which was still financially vulnerable, but there were now in place clearer relationships with sponsors, the structures for independent annual meetings and the interest to diversify ESHRE's role into the everyday working lives of its members.

In Malmo the AGM also had other EC changes to ratify. André Van Steirteghem had been nominated for chairman for 1991-93, and Gerard Zeilmaker was proposed as his replacement as treasurer. Lars Hamberger and Anne Maclaren, who had worked wisely and enthusiastically with the Ethics Committee and had been a moderating influence in the clashes with ESCO, were nominated for re-election to the EC, while Michelle Plachot, Pedro Barri, Henning Beier and the London reproductive

endocrinologist Steve Franks were newly proposed for membership. All of them had been active members of the AC and in the workshop training programme. Both Egozcue and Edwards would step down, though Edwards of course would still be heavily involved as editor of *Human Reproduction*.

The society which Crosignani inherited was short on revenue and long on expenditure, though Van Steirteghem had never been profligate with the society's purse. Beyond his control was the journal, which by now was operating under a huge deficit (of around £100,000) at OUP. Small but solid surpluses from Barcelona and Malmo, as well as the increase in membership, were reflected in a slight upward curve on the balance sheet, but there were still no strengths in reserve.

Crosignani's immediate practical priority, however, was next year's joint meeting in Milan with ESCO. As chairman, Crosignani had effectively organised the congress as an ESHRE event. Indeed, at a meeting of the EC in Barcelona in December 1989 Lars Hamberger had asked what ESCO had contributed to the organisation, to which Crosignani replied: "Nothing."



At the annual meeting in Malmo in 1989 the nominations of Pedro Barri to the Executive Committee, Pier Giorgio Crosignani as chairman, and André Van Steirteghem as chairman elect were confirmed. Barri would be co-ordinator of the Special Interest Groups from 1990 to 1994. Crosignani ran the 1990 joint meeting with ESCO in Milan during his chairmanship.

Third Executive Committee 1989-1991

Chairman

Pier Giorgio Crosignani

Chairman elect

André Van Steirteghem

Past chairman

Jean Cohen

Secretary

Klaus Diedrich

Treasurer

Gerard Zeilmaker

Members

Pedro Barri

Henning Beier

Lars Hamberger

Steve Franks

Anne McLaren

Michelle Plachot

Berndt Kjessler (chairman Ethics Committee)

Arne Sunde (special advisor training)

Hilde Olbrechts (paramedical)

There was already the identifiable stamp of ESHRE in the planning of the meeting's four parallel sessions and of course in the composition of the programme and speakers. Late additions to the programme in Milan included a workshop on the antiprogestogen contraceptive RU486, a presentation on "micromanipulation including microinjection and zona drilling", and a report from Kjessler on the Ethics Committee's guidelines in assisted reproduction. Crosignani also introduced a scoring system for submitted abstracts whereby a small scientific committee (this time composed of Beier, Diedrich, Franks, Hamberger, McLaren and Van Steirteghem) would review all abstracts with respect to study design, results, significance, quality and originality, and interest on a scale of 1 to 5. Final scores would determine whether the abstract was selected for oral presentation in a free communication, as a poster presentation, or rejected. This too would be a system which ESHRE would adopt (with modifications) over the ensuing years.

It was thus quite clear - certainly by the June 1990 EC meeting in Brussels - that ESCO's role in the Milan "joint" meeting would be minimal at best, and questions were inevitably raised about future collaborations. Most members of the EC were by now in favour of bringing the agreement with ESCO to an end and disbanding the joint committee. There was also the important consideration that ESHRE should hang on to its fixed congress slot in June each year, and not interrupt the pattern with triannual events at inconsistent times.

Although the Milan meeting was yet another success for ESHRE, attracting almost 1000 delegates and once more generating a small surplus (around \$30,000) for its bank balance, for ESCO Milan would be its swan song. Kurt Semm had in fact arranged a business meeting for his colleagues to clarify ESCO's substance and aims. And there, after much discussion among ESCO's usual quorum - which included Comninos, Mettler, Brosens, Johannison and Kjessler - it was indeed agreed that the interests of the various national fertility societies would be better looked after elsewhere (perhaps, it was suggested, within the International Federation of Fertility Societies, though IFFS's records show there was never any formal agreement with ESCO). Thus, after five years of tension, conflict and sometimes acrimony, ESCO finally left the stage, and with it went, as Kjessler had mischievously predicted, "the last of the autocrats". In fact, Semm would not be forgotten but would remain in the wings, still active in IFFS congresses, in the World Congresses of Human Reproduction, and even in ESCO's token representation at ESHRE's 1993 meeting in Thessaloniki. Of course, Semm's influence in microsurgery looks set to persist well beyond his death, which occurred in 2003.

ESCO was one irritation out of the way, but to Crosignani, Van Steirteghem and Cohen it was nothing compared to the financial crisis they believed ESHRE would surely face in the near future. The shaky bank balance (around \$40,000 in credit) and heavy deficit with OUP seemed out of proportion with ESHRE's escalating success - in its membership, at the annual meeting, in workshops, and of course in the pages of *Human Reproduction*. "At that time we were quite upset about it," Crosignani recalls, "because, despite the society's progress, we were still financially weak. We didn't really know what to do but felt we could approach the problem in two different ways. Number one was to reduce the expense of the journal and cut back the number of pages, but Bob and all of us were not keen to do that. The journal was now doing well and making a profit. Number two was to ask for more support from industry,

but again we were against this solution because it would undermine the freedom of the society. So this is why we accepted a third proposal made by Bob that we should try to solve the crisis by bringing in a business consultant.”

For ESHRE this was an unusual proposal - and an even more surprising decision to go ahead with it. It would in fact be the first time the EC looked systematically at its structure and ahead with any sense of long-term strategy. But the outcome of the decision would be immediate and long-lasting. The management consultant, whom Edwards knew in Cambridge and who was introduced to the EC's June 1990 meeting in Brussels, was called William Metcalf. His proposal was to look at ESHRE as a business, to evaluate its assets and its liabilities. As Henning Beier said, ESHRE had so far been a society “run by enthusiastic volunteers whose main concern was science and medicine”. Now, in an ever more demanding world, would enthusiastic amateurs have enough resources to meet the demands of young ESHRE members and safeguard the society's long-term future?

Not everyone on the EC was convinced that a more business-like approach was right for ESHRE - or even that a consultant would be a cost-effective solution. But finally, after much debate, Metcalf was commissioned to take a close look at ESHRE (to spend a day with Edwards in the *Human Reproduction* office, a day with Bruno Van den Eede at the VUB, and a day with a small ESHRE committee) and report back his initial observations.

By August 1990 Metcalf had submitted his investigation to the EC, who discussed it at the 26th meeting in Milan. His core advice was to restructure ESHRE under a management committee, with each of the society's activities co-ordinated and operated by sub-committees. Thus, there would be a management committee composed of the chairman, chairman elect, past chairman, treasurer and secretary, and then sub-committees for finance, special interests, membership, training, the newsletter, ethics, the journal and the annual meeting. All these committees would report to the EC.

Behind his development of the structure Metcalf would later explain that he had considered ESHRE as a business with products to sell (the journal, annual meetings, workshops), competitors (other congresses and other organisations), and customers (members and potential members). ESHRE's strengths, said Metcalf, were its association of members, an outstanding journal, burgeoning interest in the annual meetings, and

representation of a high level of science and clinical medicine. But strengths were counterbalanced by weaknesses - that membership fees were inadequately pursued, that both the journal and the annual meeting were not conditional on membership, and that the society was administratively inefficient.

Metcalf summarised his far-reaching 44-page report with a recommendation for ESHRE to broaden its base and provide its members with more value for their membership fee. In the end, his report came down to six key recommendations: to broaden the range of interests addressed by the society; extend the range of activities and services; improve publicity; change the administrative structure; improve the financial position; and increase membership. No-one on the EC disputed the wisdom of what Metcalf was proposing. There were some - like Mike Hull from the AC - who warned that ESHRE "should not lose its focus", but it was clear to all that for ESHRE to now move forward such issues as membership, management and members' interests should be taken care of in a more dedicated way. Thus, when the EC met two days later - still in Milan for the joint meeting with ESCO - it was already committed to the creation of sub-committees with responsibility for business management, training, a rejuvenated newsletter and membership, and to the formation of "Special Interest Groups" (SIGs) to develop the declared scientific and clinical interests of members. Beier, Montagut and Tarlatzis were nominated to the membership committee, Byskow, Diedrich (who in Milan retired from the EC as secretary to be replaced by Plachot) and Tarlatzis to the newsletter committee, Devroey, Dubuisson and Barri to the SIGs, and Sunde and Pellicer to the training committee.

It was a big step for ESHRE to take. ESHRE's drive to broaden its scope and give members more for their money would not come cheaply, and both Crosignani and treasurer Zeilmaker warned that expenditure would go up: the redesigned newsletter, additional pages to *Human Reproduction*, activities of the SIGs would all require funding - and in Milan the AGM accepted an increase in membership fees for 1991 (combined membership including the journal to \$150, ordinary membership to \$50, student membership to \$25, and life membership to \$500). To meet the estimated increase in expenditure, Zeilmaker proposed that membership of ESHRE would need to reach 4000!

But if the treasurer was cautious, the chairman was not, and saw in a restructured ESHRE the basis for a real move forward. "Before the meeting with Metcalf," says Crosignani, "we were all quite depressed and not very

Pier Giorgio Crosignani

ESHRE's third chairman 1989-1991

From the outset Crosignani had always been one of the keenest advocates of a European society in reproductive medicine, and he was there at the Westmoreland Hotel in London when ESHRE was founded. Like Jean Cohen, he had immense experience in the politics of gynaecology in Europe and was instrumental - with Cohen and Edwards - in establishing the financial security of ESHRE.

After qualifying at the University of Pavia in 1958, Crosignani has been associated throughout his working life with the Department of Obstetrics and Gynaecology at the University of Milan, first from 1962 as Assistant Professor, and since 1975 as Professor, where his special interest has been gynaecological endocrinology. During this time he was Visiting Professor in O&G at the University of Southern California (1970) and University of Chicago (1993).

Crosignani was and remains a tireless committee man, and, in addition to his commitments to ESHRE as chairman from 1989-1991, he was a member of the scientific programme committee of IFFS from 1989-1995, FIGO's advisory panel on reproductive medicine, the NIH's advisory committee on women's health and menopause, and on the board of the European Society of Contraception. He was on the editorial board of *Human Reproduction* from 1980 to 1997, and is presently a member of the editorial boards of *Human Reproduction Update*, *Fertility and Sterility*, *Contraception*, *Maturitas* and the *International Journal of Fertility*.

Crosignani served on many ESHRE committees - scientific and operational - and lectured on many courses, but will be long remembered for his co-ordination of two ESHRE multicentre clinical trials (in unexplained infertility and male subfertility), his co-ordination of the joint ESHRE-ESCO annual meeting in Milan in 1990, his commitment to resolve ESHRE's administrative problems, and his continuing organisation of the annual consensus workshops on Capri.

positive. We thought ESHRE was in a difficult position. But by the end of those two meetings in Milan our spirits were changed. We all felt this was a real turning point for the society." In fact, according to Crosignani it took less than a year for ESHRE to "sort out its problems", thanks largely to the surpluses from the Milan congress and the joint event with the World Congress of IVF in Paris the following year. At the same time, the renegotiated *Human Reproduction* contract with OUP saw the long-standing deficit absorbed and a stream of profit slowly turn towards ESHRE's own reserves. "Reaction was really very quick," says Crosignani.

However, the application of Metcalf's proposals for the SIGs was not as smooth or as immediate as Crosignani might have wished. The first suggestion was a SIG in contraception and its formation raised once more issues which had long been at the heart of ESHRE's identity. To explore the possibility of activities in contraception the EC had invited a delegation from the Society for the Advancement of Contraception (SAC) to Milan,

and now, as Metcalf unveiled his analysis, SAC offered the opportunity for collaboration and the formation of ESHRE's first SIG.

It was not an easy option for the EC: Mike Hull claimed that contraception really had little to do with ESHRE's central interests, while Jean Cohen insisted that, if ESHRE was to emulate the AFS, it had to broaden its scope. Edwards agreed, noting that the principles of fertility and contraception overlap and that ESHRE should represent this juncture of science and clinical medicine. However, the decision was made all the more difficult by second-guessing how the pharmaceutical industry might react to ESHRE's moves. Would manufacturers welcome ESHRE's interest? Or would they feel that their support would be better directed to groups with dedicated activities in family planning?

Moreover, the proposals from the SAC delegation raised fundamental issues of ESHRE's relationships with other societies. The collaboration with ESCO had been salutary at best. Would collaborations with other groups advance or dilute ESHRE's position? Would extending ESHRE's scope in the formation of new SIGs encroach on the activities of other existing societies? They were all difficult points of discussion for ESHRE and formed a basis for the first meeting of the SIGs sub-committee, which met in Brussels in November 1990. Pedro Barri had been asked to chair the committee and he insisted that ESHRE had to maintain its relationships with other societies and that ESHRE's SIGs should be mainly "for those specialties that were as yet unrepresented by any other group or society".

Thus, the committee finally decided that a limited number of SIGs would be formed, possibly in contraception, endoscopic surgery, reproductive endocrinology, assisted reproductive techniques, menopause, andrology, ultrasound, molecular biology, prenatal diagnosis and psychology. The committee also set the SIGs' terms of reference as a) to organise workshops, b) discuss papers at annual meetings, c) organise joint meetings with other societies, and d) organise postgraduate courses.

Once again, these were big steps for ESHRE to take, but still represented a determined effort to adopt Metcalf's recommendations. Nevertheless, the EC remained uncomfortable with the idea of SIGs in menopause and contraception, and there was added confusion in understanding the organisational role set out by Barri's committee and how it would overlap with the other activities of ESHRE. "I was in a minority," recalls Crosignani. "The only people really pushing in this broader direction

were Edwards, Cohen and me. As far as I could tell most of the others favoured a small society mainly concerned with IVF. I was strongly against this for one big reason - that you can't create a society based solely on one technique. IVF is not science, it's a technique. It's just one way to solve one particular problem for a minority of patients affected by infertility." Crosignani thus stood firm in his belief that the addition of interests in contraception and the menopause would indeed enrich the society, and should be pursued.

"The SIGs weren't popular with everyone," says Basil Tarlatzis, who had joined the AC as representative for Greece in 1988. "It later became clear that for the groups to be successful we needed motivated people who would give substance to them. Initially there was no single person responsible for the SIGs on the executive committee, and some of the groups - like the surgery group - didn't do well because of competition from other societies." Not surprisingly among such disagreement, the SIGs got off to a slow and bumpy start. Enthusiasm was only lukewarm among those members of the EC who feared their creation would break up ESHRE's homogeneity and its strength. In fact, the SIGs would not settle into a more successful pattern until Hans Evers was appointed co-ordinator in 1994 and they rumbled along for a year or two, unsure of their role and their relevance within the society's structure. In the meantime Barri reported to the March 1991 EC meeting in Bonn that SIGs would go ahead in andrology (chaired by Jon Aitken), assisted reproduction (Bernard Hédon), endoscopic surgery (Paul Devroey), contraception (John Newton) and reproductive endocrinology (Steve Franks), with their objectives somewhat scaled down.

Thus, as ESHRE approached its seventh annual meeting in association with the world congress in Paris the firmer basis which Cohen had aimed for four years earlier seemed now within ESHRE's sights. ESHRE was indeed taking on a life of its own. There is no doubt that the turnaround in *Human Reproduction's* fortunes played a major part, both as a source of revenue and as a flagship for ESHRE's place in the science of reproductive medicine. But Cohen and Crosignani had also introduced significant changes to ESHRE, and it was now clear throughout the world that ESHRE had an important role to play. In more practical terms the structures were in place to strengthen the society's financial reserves, to manage its business more efficiently, and to become more involved with its membership, both through training and the SIG programme. At the seventh AGM in Paris ESHRE's secretary Michelle Plachot would report a membership

of 1262 (though still many unpaid) with growth on an upward curve which showed no signs of stalling. The treasurer Gerard Zeilmaker would announce the first ever profit gleaned from the journal, and a consolidated programme of systematic sponsorship arrangements with Serono, Organon and Schering. The financial situation, said Zeilmaker, was “sound”. ESHRE had indeed struggled through its growing pains, and was now poised for further growth and challenges.

6

‘I HAVE A TASK FOR YOU.’ WORKSHOPS AND TRAINING 1985-1994

Although he had spent 12 months as a member of the temporary organizing committee and had in 1985 been elected to the Executive Committee (EC), Arne Sunde still felt a little out of place. He was, of course, modest enough to recognise that, as a young embryologist from Norway, he was there to represent science in the Nordic countries. But his nomination to the EC in Bonn - alongside the “names” of Edwards and Cohen and in preference to Hamberger or Wikland - was a real surprise. Sunde, in fact, was so surprised that, when the new EC assembled for the first AGM in Bonn and took its seat on the podium, he remained innocently in his chair on the floor, unaware that he too should join his new colleagues at the top table. But Jean Cohen had other ideas. He spotted Sunde in the crowd and hurried him along to the front. “Come on,” said Cohen. “I have a task for you.” Sunde duly took his seat alongside the rest of the EC, keen to find out what Cohen had in mind.

As he chased Sunde to the podium to be formally voted on to the EC, Cohen said that the task was “training”, but nothing more. “In fact,” Sunde recalls, “no-one ever really explained to me what the task involved. There was no clear idea of what it meant, just that training should be a part of ESHRE.” Nevertheless, even though there was no detailed aim in view, it

was clear already that ESHRE would take its educational role seriously. There were two good reasons to do so: first, as Edwards would insist, ESHRE as a “learned society” had a responsibility for education; and second, both in the emerging science of embryology and in the clinical techniques of IVF there was no formal practical training available anywhere. People - like Sunde himself - had to learn on the job.

For ESHRE to develop a formalised training structure for reproductive medicine in Europe would require both human and financial resources, neither of which were in abundance. A training programme was thus an ambition which in 1985 was simply beyond the society’s reach; however, with the ambition in place and Sunde installed as “special advisor on workshops”, Sunde had to make a start.

“I started canvassing,” he explains. “I couldn’t organise the workshops myself so I had to find the people who could. And having found the people, I then tried to find the funding. But the people came first. The most important thing was that the course was good. I thought it better for us to have a good course on a bad subject than to have a bad course on an important subject. So if I couldn’t find the right person for the course, I didn’t do it. I was looking for people I knew I could rely on. So I did think about the course, but really I had to think of who could do it. And if I couldn’t find the right person to do it, the course had to stay on the ideas list. In the beginning everything was dependent on who could do it.”

As the first ideas for courses were aired among the early ESHRE members in Bonn, three groups came forward with suggestions: Zeilmaker and Alberda from Rotterdam on the practical aspects of IVF; Brambati from Milan on prenatal diagnosis; and Van Steirteghem at the VUB on reproductive endocrinology. By the time of ESHRE’s second EC meeting in Brussels in August 1985 these three courses had all been approved, to be run by the three groups at their own centres but “under the auspices of ESHRE” in 1986. “Under the auspices of ESHRE” would in a short time become a stamp of ESHRE’s approval, a sign that the course had been facilitated by ESHRE but organised outside the society and funded independently (through registrations and educational grants).

The first, in February 1986, was Zeilmaker’s course in Rotterdam on IVF, which promised “lectures, discussions and practical work”. Although it was advertised in *Human Reproduction* from issue 1, and was restricted to just 27 participants (“12 clinicians and 15 laboratory workers”), it did not prove popular - or even encouraging as ESHRE’s opening throw in education. Only six registered, which was deemed too few for future

viability. The second workshop, on reproductive endocrinology, proved more popular and was planned by Van Steirteghem to precede the second annual meeting in Brussels; as such it would set an indelible pattern of pre-congress workshops which still thrives in ESHRE today - and a precedent too for the VUB in running ESHRE courses of enormous popularity and relevance.

Meanwhile, at around the same time another idea for a further workshop had been put to the EC by Pier Giorgio Crosignani. In Melbourne in November 1985 he had proposed to the EC, as an extra to the courses already planned by ESHRE, a workshop on infertility treatment with GnRH analogues. The workshop, he explained, had been conceived with the support of Schering Italy as a small invited discussion group intent on devising guidelines; indeed, such guideline meetings had already been arranged independently by Crosignani and Schering in Italy and had been highly successful. In July 1985, following Crosignani's first suggestion, Edwards had written to him: "I think your idea of an initial workshop producing guidelines on some aspects of gynaecological endocrinology would be wonderful. The Journal is the most suitable place to publish them and I like the idea very much." Thus, by the following EC meeting in Brussels, Crosignani's ideas had been worked up and presented as a provisional programme, which the EC accepted. The workshop, "Current treatments with LHRH and its analogues", would occupy a day in September 1986, and would be held on the island of Capri. Crosignani added that Schering Italy seemed prepared to sponsor the event each year.

"Capri was my original idea," says Crosignani, "but I was not too confident it would be successful. In Europe in 1986 it was actually very difficult to organise a small informal meeting dedicated to one issue and aiming to put some guidelines on paper and publish them. Capri was designed as an informal discussion meeting, with a few dedicated persons, and a few rules. I was the first to be surprised by its success." Crosignani, in fact, had found the sponsorship in his regular chats with Schering Italy and had raised the issue of producing simple guidelines in the many emerging disciplines of fertility treatment. For Schering it was indeed an intriguing exercise, and in time would become an association with experts in their fields which would prove valuable alike to sponsors, participants and the wider scientific community. At the time, neither Crosignani nor the most optimistic members of Schering Italy could ever have imagined that in 2004 a Capri workshop on "hormonal contraception without

The Capri workshops

The Capri workshops were originally devised by Pier Giorgio Crosignani, with sponsorship from Schering Italy. The formula for them, he later said, was “quite simple”: eight to ten lecturers discuss a clinical problem and a group of experts discuss the presentations, and these discussions form the basis for a “brief set of practical guidelines”. From 1996 two workshops were organised each year, with Ferring joining Schering Italy as sponsors of the event. All publications from these workshops can be found in Appendix C.

20th September 1986

Current treatments with LHRH and its analogues

18-19th September 1987

Risks and benefits of steroid replacement therapy

16-17th September 1988

Strategies for the treatment of hirsutism

18-19th September 1989

Dysfunctional uterine bleeding

9-11th September 1990

Recurrent spontaneous abortion

30th-31st August 1991

Sexually transmitted diseases

28-29th August 1992

Unexplained infertility

27-28th August 1993

Male sterility and sub-fertility: guidelines for management

26-27th August 1994

Anovulatory infertility

25-26th August 1995

Infertility revisited: the state of the art today and tomorrow

22nd-26th August 1996

Female infertility: treatment options for complicated cases

Cardiovascular effects of combined oral contraceptives and hormone replacement therapy

4-8th September 1997

Male infertility update

Oral contraceptives and hormonal replacement therapy: differential effects on coronary heart disease, deep vein thrombosis and stroke

27th-31st August 1998

Screening before and during the use of oral contraceptives and hormone replacement therapy

Optimal use of infertility diagnostic tests and treatments

25-30th August 1999

Multiple gestation pregnancy

Continuation rates for oral contraceptives and hormone replacement therapy

23rd-28th August 2000

Ovarian and endometrial function during hormonal contraception

Social determinants of human reproduction

30th August-3rd September 2001

Hormonal contraception: what is new?

Physiopathological determinants of human infertility

29th August-2nd September 2002

Hormonal contraception without estrogens

Mono-ovulatory cycles: a key goal in profertility programmes

3rd-7th September 2003

Hormones and breast cancer

Diagnosis and management of the infertile couple: missing information

1st-5th September 2004

Non-contraceptive health benefits of contraception

Fertility and aging

estrogens” would still be organised with Schering’s support - and an invitation to take part still be recognised as a real honour.

Crosignani later described the formula for the Capri workshops as “quite simple”. Around ten selected experts would make presentations on a specific clinical problem and discuss the problem with a further selected group of experts. Based on the discussions a paper would be prepared in co-operation with the full group in the form of a brief set of practical guidelines covering the biological and clinical aspects of the issue discussed. From the start all the papers were published in *Human Reproduction*, and many of them set standards of care and practice where otherwise there were none. While the first Capri workshop in 1986 did indeed discuss an emerging issue in infertility treatment, Crosignani’s hand of influence is clearly evident in the choice of subject for the second: “Risks and benefits of steroid replacement therapy”. Even if there were those who thought the menopause had no place in ESHRE’s range of interest, Crosignani was determined to keep it on the agenda. Thus, experts who might never have been introduced to ESHRE - epidemiologists like Carlo La Vecchia, or menopause specialists like John Studd and David McKay Hart, or endocrinologists like Herman Schneider - now found

themselves on the record and laying out guidelines on the menopause for ESHRE.

Over the years the Capri workshops would bring some of the world's (and not just Europe's) leading authorities to the ESHRE debating table and to the pages of *Human Reproduction*. The third workshop was "strategies for the treatment of hirsutism" and introduced Eli Adashi from the USA and Steve Franks from London, who would each recognise moderate hirsutism in many women as a symptom of polycystic ovary disease. That debate - symptomatology or cause in PCO - continues in *Human Reproduction* today, with publication in 2003 of a joint ESHRE/ASRM consensus on the diagnostic criteria and risks associated with the PCO syndrome. Egon Diczfalusy, who was elected an honorary member of ESHRE in 1991, and Tim Farley from the WHO would be regular participants, and occasional invitees would later include Ian Fraser from Australia (on dysfunctional uterine bleeding), Ian Cooke (on unexplained infertility), Howard Jones's former Norfolk colleague Anibal Acosta (on male subfertility), and Dan Mishell, editor of the journal *Contraception* (on anovulatory infertility and male infertility). In 1996 the format of the Capri workshops was extended to two events, a guidelines discussion in an area of hormonal therapy (HRT or contraception) sponsored by Schering, and one in infertility sponsored by Ferring.

The Capri workshops made two much cited contributions. The 1995 and three preceding guidelines were collated and updated under the auspices of the National Research Council of Italy, and published as "Guidelines to the prevalence, diagnosis, treatment and management of infertility" (*Hum Reprod* 1996; 11: 1775-1807). This substantial review and consensus was introduced by Diczfalusy and Crosignani and gave the stamp of the WHO's new definitions on reproductive health to the efforts of ESHRE. "Although infertility per se may not threaten physical health," wrote Diczfalusy and Crosignani, "it has a serious impact on the mental and social well-being of couples." Such a view would - and from such a source - help raise the low social and political priority of infertility treatment in most public health programmes of the world: "The ESHRE workshops hope to play a modest but definite role in the advancement and progress of reproductive health."

The second high profile issue addressed by the Capri workshops (and again one which reflects the influence of Crosignani) came first in 1996 when the subject for discussion was the effect of steroidal hormones on cardiovascular disease. The issue had erupted in late 1995 with the

publication in the *Lancet* and *British Medical Journal* of three epidemiological studies showing that “third generation” oral contraceptives (those containing the progestogens gestodene or desogestrel) were associated with a higher risk of venous thromboembolism (VTE) than earlier types. A second workshop followed in 1997, and a third - on screening for thrombophilias - in 1998. The 1995 epidemiological studies had been front page news in the lay press, and within hours a full blown Pill scare was evident throughout the world. The scientific debate would be heated and eventually bitter, with the manufacturers and many clinicians insistent that flaws in the design of the original studies would explain the results. After assessing the data the Capri workshop of 1996 concluded that women at higher risk of VTE (with thrombophilias and/or a close family history) should not use the Pill, but that those at no increased risk should not let the risk of VTE be a deterrent. Such views, however, although echoed by many expert groups throughout the world and eventually reflected in new epidemiological studies, carried little weight with regulatory authorities, which in Europe restricted the first-line use of third generation Pills. By the time the dispute spilled over into the courts in 2001, and a judge in London finally ruled that third generation Pills were not causally associated with any added risk of VTE, the public’s enthusiasm for brands containing desogestrel and gestodene had long since evaporated. But it had, nevertheless been a heated - and important - scientific debate, and one in which ESHRE had played a not insignificant part.

Fifteen years earlier, however, as he settled into his role as ESHRE’s first chairman, Robert Edwards was the driving force behind the first flurry of workshops. Along the corridors of the annual meeting in Bonn he was clearly canvassing for support and ideas, and passing these on in his encouraging way to Sunde. Workshops on the immunology of spontaneous abortion, follicle puncture, embryo freezing, transgenic animals, hormone receptors... all ideas for Sunde to pursue. Equally, Edwards incorporated an item on training into the agenda of every EC meeting, and no meeting would close without Sunde’s report and a discussion of forthcoming workshops or new proposals.

Thus, within two or three years workshops “under the auspices of ESHRE” were beginning to settle into a recognisable pattern: four or five workshops a year organised by experts in the field and financially self-supporting, with two or three pre-congress workshops in June. The structure would be similar - lectures in the morning and hands-on training in the afternoon. However, by 1987 a week-long basic workshop in

“reproductive medicine”, based loosely on the workshop organised by Van Steirteghem at the VUB before the 1986 congress, had also been incorporated into the training agenda to alternate as a regular January event between the VUB and Klaus Diedrich’s base in Bonn. The format would follow a pattern (management of an IVF programme, patient selection, ovarian stimulation protocols, endocrinology, oocyte retrieval, semen evaluation and preparation, in vitro culture and embryo replacement) and, to keep costs to a minimum and provide a location for practical training, the venue would be on the campuses of the VUB and University of Bonn. In 1989, following the successful organisation of a similar meeting in Thessaloniki, Basil Tarlatzis proposed to the EC that the Greek venue should join the VUB and Bonn as an alternating site for the January workshop.

Tarlatzis had returned to Greece from Yale in 1985 to open the country’s first IVF clinic in Thessaloniki. It was a hectic time, he recalls, before the introduction of GnRH agonists to programme the cycle and without fully trained colleagues. And Thessaloniki was a long way from Yale. “In the beginning I was doing everything,” he explained, “the lab, the clinical work, ovulation induction, everything. We had to do the pick-ups on Saturdays, Sundays, holidays...” So basic training in reproductive medicine in Greece was an important priority for Tarlatzis. Once settled in Thessaloniki he had joined ESHRE’s Advisory Committee (AC) in 1988 as elected representative for Greece and the following year Kjessler’s ethics committee in preparation of the first guidelines.

Thus, for 1990 ESHRE announced two basic reproductive medicine workshops, one in Brussels and one in Thessaloniki, and, at the 21st EC meeting in Malmo in June 1989, it was proposed that these would be organised as “part of the ESHRE Campus project”. The idea of “campus” workshops was a natural for ESHRE, because, in keeping with its low-cost student-friendly philosophy, the university campus was the obvious environment for ESHRE training.

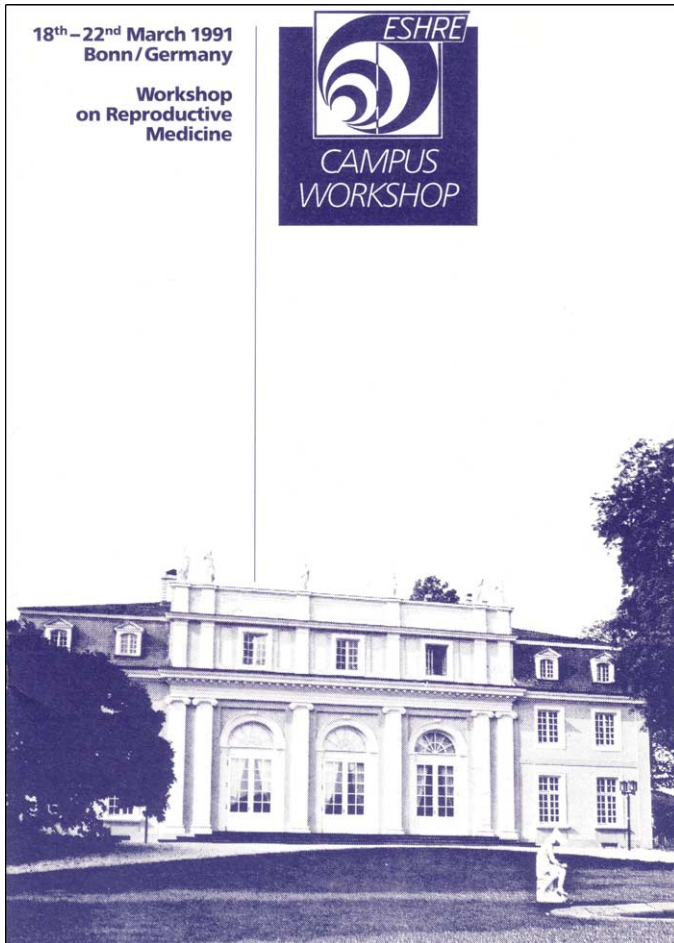
However, as Sunde’s reports to the EC reflect throughout 1989, there were signs at the time of a lack of co-ordination in the training events. In Malmo Sunde had complained that three workshops had been organised without sufficient recognition of ESHRE’s patronage, and the ESHRE logo was popping up too frequently on programmes which Sunde knew little about. The EC was intent on giving the workshops more definition but, as Sunde was all too well aware, there were no funds available for ESHRE’s own organisational input.

The funding problem had been raised informally by Crosignani, Cohen, Edwards and Van Steirteghem at the 6th World IVF Congress in Israel in April 1989 before a delegation from Serono which included Fabio Bertarelli from the company's founding family. Serono, of course, along with Organon and Schering, had been consistent supporters of ESHRE from the beginning and had already provided some ad hoc support for ESHRE workshops. Training, Serono would argue, was a reflection of the company's commitment to infertility which would be later (in 1998) formalised by charter in the founding of the Bertarelli Foundation, with a mission to "promote and improve the understanding" of infertility. But now, in June 1989, the proposal before the EC was that Serono would provide funding for four Campus workshops a year, with each workshop adopting the organisational framework established in Bonn and Brussels. That meeting with Serono in Israel, Cohen recalls, lasted no longer than 15 minutes before an agreement was reached, so sure were they of the Campus idea and its value to ESHRE and Serono.

However, with Serono as sole sponsor, it was not an easy proposal for the rest of the EC to accept. Sunde was anxious that any ESHRE-funded Campus workshops would take a higher profile than the many other local workshops now being organised. But the main grounds for unease - as ever - was ESHRE's independence and the risk of conflict of interest. Cohen, the chairman, Van Steirteghem, Zeilmaker and Hull all advised that ESHRE's freedom in devising the courses' content was an absolutely necessary prerequisite.

By December 1989 and following further discussions with Serono the EC had approved Campus workshops for 1990 in Brussels, Thessaloniki and Paris with a budget of \$12,000 for each workshop. At the same time, ESHRE was receiving a considerable number of requests to support or approve other local educational events. Antonio Pellicer, who sought ESHRE's approval for a meeting in Valencia on new technology in assisted reproduction, told the EC that ESHRE's involvement would be "an insurance of quality and scientific success". However, some organisers of local events under ESHRE's auspices were not happy with the society's contribution and Sunde suggested that ESHRE might offer more help in the selection and participation of speakers and in promotion of the events. Pellicer's Valencia meeting, for example, was not listed in the 1990 workshops in *Human Reproduction*.

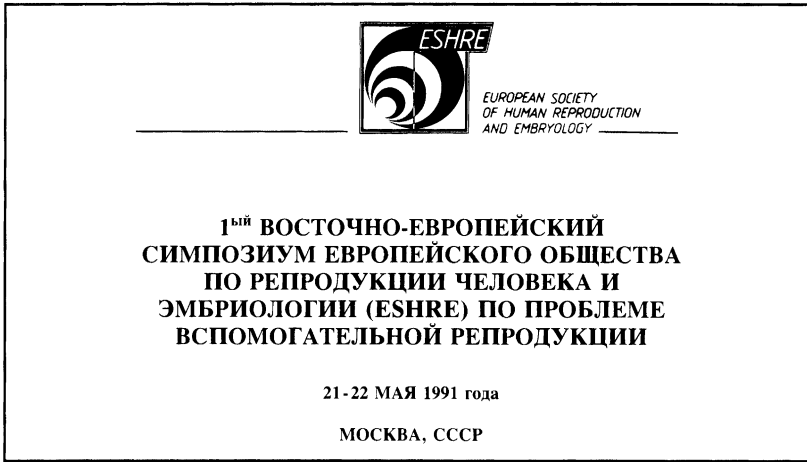
Other requests for ESHRE's involvement came from the Middle East, Russia and Latin America, all of which the EC agreed to with the financial



ESHRE's first Campus workshop of 1991 took place in Bonn. In 1989 ESHRE had concluded a deal with Serono for the funding of four Campus workshops a year, alternating mainly between Bonn, Brussels and Thessaloniki.

support of Organon. In the event ESHRE's first workshop outside Europe took place in Moscow in May 1991, a two-day event organised by Professors Kulakov and Leonov which was later described as "the real beginning of IVF in the USSR"; a second non-European Campus workshop followed later that year in September in Israel, and a third in Cairo in November with more than 500 in attendance; a similar meeting planned in Saudi Arabia was cancelled at a late stage. Meanwhile, for 1990 plans were in hand for ten possible workshops in Europe, three or which would be organised as part of the new Campus initiative - and for the first time with centralised funding courtesy of Serono.

However, outside the Campus framework, proposals and training events were popping up with increasing frequency and without any obvious



ESHRE's first workshop in Eastern Europe took place in Moscow in May 1991, a two-day event organised by Professors Kulakov and Leonov which attracted more than 100 participants. Although the event was later described as "the real beginning of IVF in the USSR", many participants described the "serious financial and organisational difficulties" in setting up an IVF clinic in the USSR.

pattern. "We were trying to give some definition to the courses," says Sunde, "so a workshop usually involved some hands-on training, and symposia were usually oral. Some of the courses were successful, but some weren't, and overall I felt there was quite a gap between our ambitions and what we actually did." It was clearly a situation which couldn't continue so haphazardly, and one in which ESHRE's role had to be more clearly defined, both for the society itself and for those groups who sought its patronage. Finally, at its 24th meeting in Brussels in February 1990, the EC decided that groups seeking ESHRE's approval should pay a small fee (\$250) for the right to describe their event as organised "under the auspices of ESHRE" and that the programme should be submitted in advance for approval. Van Steirteghem stressed that such moves were to maintain standards and avoid the kind of complaints Sunde had raised.

Sunde was therefore asked to provide guidelines for organisers of workshops to be held under ESHRE's auspices. These set out the definitions (Campus, Specialized, Certifying and Symposium), how the meetings should be organised, and ESHRE's own responsibilities (to assist with finding speakers, promote the meeting, issue attendance/education certification, but not provide direct financial support).

The workshops were also on the agenda of the business consultant William Metcalf, whom Crosignani had hired to develop ESHRE's business basis. Metcalf, in his report to the EC in 1990, had described the workshops as "one of the strongest selling points for membership" but "much underplayed". And, in line with his advice in other areas of ESHRE's activities, he recommended that the workshops should fall under the direction of a sub-committee and the programme reviewed with an eye to geography and specialty. Sunde would chair the committee, supported by Pellicer, Jean-René Zorn, Mike Hull and Anita Sjogren representing the Paramedical Group. In its efforts to rationalise its scope the committee simply split training into two - workshops and symposia organised centrally by ESHRE (which would include the Campus workshops) and those organised under the auspices of ESHRE. Members could present their ideas to the training committee for inclusion in the central programme, while for the \$250 fee applicants for ESHRE patronage could expect ESHRE's help in the choice of participants, promotion of the meeting, and "the right to use the ESHRE logo".

The new order worked, and for two or three years a plethora of symposia and workshops - Campus or under the auspices - appeared under the ESHRE banner. In 1991, for example, the Campus workshop on the basics of assisted reproduction was staged in Bonn and Tel-Aviv, with additional courses on reproductive biology (Tours), operative laser endoscopy (Leuven and Heidelberg), laparoscopy and hysteroscopy (Brussels), embryology (Palermo), and a further basic ART course in Cairo. The following year planning began for a workshop on preimplantation genetic diagnosis under the auspices of ESHRE at the Hammersmith Hospital in London (where Handyside and colleagues had achieved the first live birth following PGD), and a two-day symposium on preimplantation genetics at the VUB. With a SIG now in place under the chairmanship of Alan Handyside, PGD was clearly high on ESHRE's agenda.

However, despite the proliferation of courses, Sunde was still not happy with their organisational structure. The two-tier framework of centrally organised activities and those under ESHRE's patronage had still not given ESHRE any clear direction in its educational efforts. The centrally organised meetings, argued Sunde, including the Campus workshops, set the role model. They were of excellent quality, they properly promoted ESHRE's scientific seriousness, and they produced some income for the reserves. By contrast, Sunde described activities under ESHRE's auspices as ranging from "excellent to poor", with many organisers now not even

Pre-congress courses

Pre-congress courses have been a feature of every ESHRE annual meeting since 1987 in Cambridge. There, two courses were offered, both at Bourn Hall:

- * The Cryopreservation of Human Embryos, organised by Ashwood-Smith and Van Steirteghem
- * Ultrasound, organised by Rajat Goswamy

The following year, in Barcelona, three pre-congress courses were on offer:

- * Prenatal Diagnosis, organised by Egozcue and Barri
- * GnRH and its Analogues in Reproductive Medicine, again organised by Egozcue and Barri
- * Chromosomes from Oocytes, Zygotes and Human Spermatozoa, organised by Benet, Genesca and Santalo.

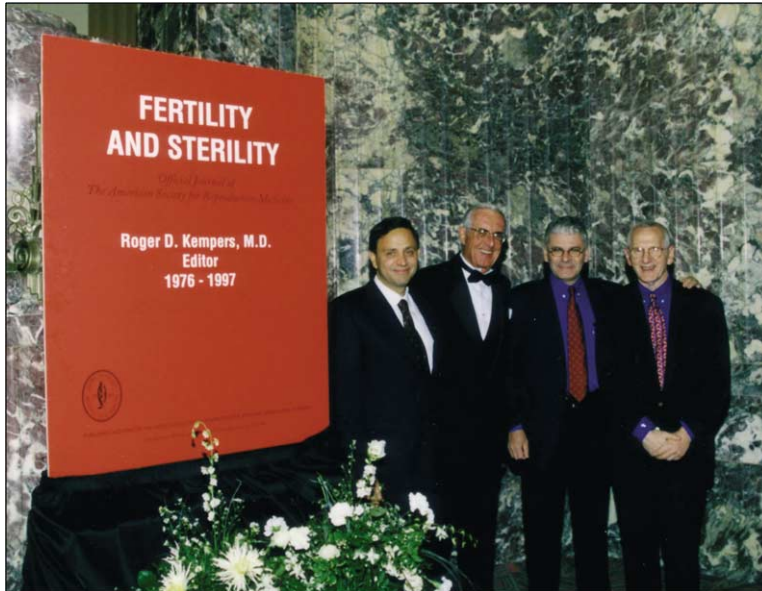
From 1993 in Thessaloniki responsibility for the organisation of pre-congress courses was put mainly in the hands of the Special Interest Groups. In 1994 in Brussels there were six pre-congress courses organised (including the joint ESHRE/AFS course), which by Bologna in 2000 had grown to nine - on reproductive endocrinology (joint ASRM/ESHRE), embryology, early pregnancy, endometriosis, reproductive surgery, contraception, law and ethics ("an ethical approach to medical practice and advertising"), and laboratory practice.

bothering to pay the \$250 fee. In some cases, the EC heard, the ESHRE logo was still being used in course announcements without ESHRE's approval.

The EC's first initiative, proposed by Tarlatzis, was to pass responsibility for the pre-congress courses to the Special Interest Groups; the SIGs, it was reasoned, could better select appealing topics and bring together those who would be most interested. Moreover, some pre-congress workshops (particularly in The Hague in 1992) had been poorly attended. Thus, in the first year of the new initiative - in Thessaloniki in 1993 - the SIG in endoscopic surgery organised one course, the SIG in reproductive endocrinology two courses, and the SIG in reproductive biology one course. "It was all part of our efforts to structure training and co-ordinate our activities better," said Basil Tarlatzis, chairman of the Thessaloniki congress.

Another important pre-congress development also emerged at this time. Back at the joint ESHRE/World Congress in Paris in 1991 Leon Speroff, the new chairman of the AFS, had made it clear to members of the EC that the AFS wished to develop and encourage its relationship with ESHRE. It was a time when the idea of an exchange lecture award with the Pacific Coast Fertility Society was also developing, and the EC was encouraged by these

collaborative initiatives in the USA. Subsequently, ESHRE agreed with the AFS to exchange scientific sessions at their respective annual meetings and to promote each other's activities. It was for ESHRE a comfortable relationship, and one which - unlike that with ESCO or even the contraception organisations - posed little conflict of interest. Indeed, at the EC meeting in Brussels at the close of 1992 the new chairman André Van Steirteghem named the AFS as the model for ESHRE's future. Van Steirteghem saw "a well structured society with centralised activities, publishing its own journal and organising its own congresses". He told the EC that "this is the direction in which ESHRE should be heading". So it was no surprise to hear that, when the EC returned from the AFS's 1992 meeting in New Orleans, its determination to collaborate even further with the AFS was clear. The first exchange session with the AFS took place at ESHRE's 1993 annual meeting in Thessaloniki, and was reciprocated later that year at the 49th AFS meeting in Montreal. The following year there was a further exchange event in a two-day pre-congress workshop



ESHRE's relationship with the American Fertility Society (after 1994 the American Society of Reproductive Medicine) was founded on training and exchange sessions at annual meetings. In 1997 at the ASRM's annual meeting in Cincinnati an ESHRE delegation of Basil Tarlatzis, Paul Devroey and André Van Steirteghem acknowledged the 21-year *Fertility and Sterility* editorship of Roger Kempers (second from left).

organised by the AFS before ESHRE's annual meeting in Brussels. The course was heavily publicised by the AFS and designed for CME accreditation. Among the instructors was a fair split of AFS and ESHRE experts - Joe Leigh Simpson and Alan DeCherney from the USA, and Mike Hull, Hans Evers and Van Steirteghem from Europe. The AFS/ESHRE pre-congress course would become a regular feature of the annual meetings, regularly attracting around 100 participants and maintaining ESHRE's amicable relationship with colleagues in the USA.

However, while the SIGs tried to raise the profile of the pre-congress courses, other training activities throughout the rest of the year stumbled along still without any obvious direction. Not until the end of 1993 did the EC finally agree to a simplified but clearly defined structure of "workshops" (with some hands-on training), "symposia" (purely theoretical) and "certified courses" (at which a certificate was issued at the end). But there was still no agreement on funding or on how groups might apply for patronage or financial support. Once again, Sunde told the EC, an endoscopy course was being advertised under the ESHRE logo without any permission given, and elsewhere applications were queuing up for Campus or logo approval without any efficient system in place to deal with them. "Despite our intentions," says Sunde, "training still seemed an haphazard activity. It didn't seem good enough to me that the workshops were just one of several activities of ESHRE, and unco-ordinated. It was OK to be like this in the beginning, but ESHRE had grown. I felt it was no longer acceptable and - in the circumstances - I didn't feel able to do the job which needed doing."

At the 41st EC meeting in Lübeck in March 1994 Sunde resigned from his post as special advisor on training. He had in fact been a member of ESHRE's temporary and full executive since its origins in 1984, when he wandered aimlessly into Hall B at the Finlandia Hall in Helsinki. But it would be wrong to infer that now, as Sunde offered his resignation to EC, his commitment to ESHRE's educational responsibilities as a learned society had waned. Far from it. "Some of the courses, we organised - and still organise - are exemplary and in some instances have provided the only opportunities for learning new techniques. I attended one of the ICSI workshops in Brussels and it was outstanding. But that wasn't the point. Some of the courses were extremely good, but there wasn't a grand plan, the courses didn't fill the whole picture. And in terms of strategy our training efforts hadn't progressed since 1985. That's what I found frustrating."

What Sunde was looking for was more co-ordination, more centralised planning, and more investment by the EC in the training programme and in resources to meet those objectives. He was not alone in such views, and in particular - as a new generation of members slowly began to supersede the first - the opinion of new EC members hardened that ESHRE had to take a long look at its training objectives and apply them to a longer-term more transparent strategy.

Sunde's contribution, however, as the EC acknowledged, had been huge throughout the past ten years. As he himself recognised, ESHRE workshops were for most European clinicians and reproductive scientists the only training opportunities they had; proficiency in new treatment techniques like ICSI or PGD depended on a learning curve, and ESHRE workshops in these emerging techniques were crucial in gaining that experience. The practical expertise offered in the workshops literally allowed the pupil to learn at the elbow of a master, and in this respect ESHRE stood alone. But there was more that could be done, and this Sunde recognised. What training needed, he felt, was incorporation into a clearer long-term strategy for ESHRE, and this is what he would later address with one of the new generation of ESHRE members, Hans Evers.

7

TOWARDS THE LONG-TERM VIEW: 1991-95

E SHRE's joint meeting in Paris with the 7th World Congress of IVF was an enormous success. ESHRE's sessions, following an opening ceremony on the Friday evening, had occupied two full days of the weekend, before the world congress took over for three further days. On the Sunday both organisations had hosted a joint session on the ethics of reproduction in the Grand Auditorium of the Palais des Congrès, moderated by Anne McLaren, Claude Sureau and Jacques Testart. Issues under discussion were the "progress" of assisted reproduction, its risks, and PGD. It was a heated session, and for the first time brought into open debate public challenges to the place of ART as a viable treatment for infertile couples.

In December 1989 a review had appeared in the *Lancet* (1989; 2: 1327-1329) asking if IVF and embryo transfer were "of benefit to all". The first of the two authors of the review, Marsden Wagner and Patricia St Clair, was from the European Regional Office of the WHO in Copenhagen, and their draconian views appeared to put the WHO's stamp of doubt on IVF. They reviewed the efficacy, safety, costs and benefits of IVF and concluded that it was of benefit to just a small proportion of infertile women, was expensive, and - most alarmingly - carried "serious health risks". Policies and resources for the management of infertility, the reviewers argued, would be better directed at preventing infertility than at treating it.



ESHRE's joint event with the world IVF congress in Paris in 1991 was staged at the Palais des Congrès, the first time an annual meeting was held in a major convention centre. Not until Madrid in 2003 would ESHRE abandon its smaller low-cost locations for the bigger congress cities able to accommodate more than 5000 participants.

The review caused a storm in newspapers throughout Europe (the headline in *The Times* was "Test-tube technique 'has health risk' for mothers and babies") and consternation among the ART establishment, including ESHRE, especially as at the time IVF was finally making huge strides forward and becoming a routine procedure. While there had been visible progress in success rates, the technique had in the late 1980s also become simpler and more efficient - for the clinic and patient alike. First, the advocacy of ultrasound-guided follicle puncture by Wikland, Enk and Hamberger in 1985 (Ann NY Acad Sci 1985; 442: 182-194) and the possibility of transvaginal oocyte collection had made the IVF procedure much easier and, by removing the need for laparoscopy, far less invasive. Moreover, ultrasonic ovarian scanning during the follicular phase of stimulated cycles removed much of the guesswork from optimal oocyte retrieval - now oocytes could be aspirated according to an accurate visualisation of their size.

But what brought even more efficiency to the IVF clinic was the introduction of GnRH agonists in the mid-1980s. Following the

Nobel-prize winning isolation of LHRH by Schalley and Guillemin a decade earlier, Howard Jacobs and colleagues in London had shown that by slowly suppressing the pituitary with an agonist of LHRH the naturally occurring oestrogen-mediated positive feedback could be prevented - and thereby any risk of a spontaneous surge of LH during the IVF cycle (Porter RN, Smith W, Craft IL, et al. *Lancet* 1984; 2: 1284-1285). Thus, once downregulation had been achieved with the agonist and release of reproductive hormones from the pituitary suppressed, the clinician could take control of the cycle and stimulate the ovary according to his own schedule, with minimal risk of a spontaneous LH surge and a lost cycle. Even more important from the everyday practicalities of the clinic, the timing of when hCG should be given to trigger ovulation was no longer considered critical in downregulated cycles; oocyte collections could thus be avoided at weekends, holidays and unsocial hours. Not only would the introduction of GnRH agonists revolutionise the everyday practice of IVF but in time a huge series of results from Jacobs' own base at the Hallam Medical Centre in London (involving 7863 consecutive cycles of IVF) would show after statistical adjustments that agonist cycles appeared to increase pregnancy rates, reduce miscarriage rates, and increase the chances of a live birth (Tan SL, Kingsland C, Campbell S, et al. *Fertil Steril* 1992; 57: 810-814).

IVF was on a roll: simpler, more efficient, friendlier. More and more infertile couples were seeking treatment, results were slowly improving and, as embryologists tinkered with techniques of "micromanipulation", it seemed too that the indications for ART were set to broaden into male factor infertility. Yet here was Wagner and the WHO branding IVF as an irrelevant procedure denied to the majority and fraught with risk. The review had already been discussed by ESHRE's Executive Committee (EC) and the idea floated that Wagner might be invited to defend his claims in Paris in 1991. Not all the EC were in favour: Wagner did not represent the WHO, some said, while others - notably Edwards, Sunde, Franks and McLaren - thought that open discussion would clear the air and lay out unequivocally the data on IVF's safety and efficacy.

Jean Cohen was thus charged with the task of defending IVF in debate with Wagner in Paris - but there was not too much data at his disposal. One or two follow-up studies of babies born after IVF had been published, perhaps the most important in the first report from what would be a huge cohort from Australia assembled by Paul Lancaster. Cohen could also draw on the data from FIVNAT, France's own IVF register, which already



Jean Cohen, who had organised ESHRE's meeting in Paris in 1991 and was a member of the world congress's executive committee, defended IVF in a packed joint session on ethics.

offered some reassurance. Even though this early FIVNAT data found some prematurity among babies born after IVF, the treatment itself was not deemed a direct cause, but more an influence on outcome - mainly in its association with multiple pregnancies. The technique itself, FIVNAT and Cohen would argue, was safe.

The jointly organised session on ethics was one of the highlights of Paris. Overall, there were more than 2500 registrants at the congress, with almost a half taking part in both events. Moreover, the final balance sheet would show a surplus for ESHRE's reserves of more than \$100,000, a triumph for programme planning which exceeded all expectations. Never before had an ESHRE meeting attracted such numbers nor generated such a surplus, and as such Paris now set a benchmark for all future congress organisation. Never again, said the new chairman André Van Steirteghem, would a joint meeting be organised without the kind of involvement enjoyed by Cohen and Michelle Plachot on the congress's executive committee. This was evident the following year when ESHRE turned down opportunities to collaborate with the 1995 IFFS congress in Montpellier and with the World Congress on IVF organised by Feichtinger in Vienna. The EC considered the latter congress as "a personal initiative" and a source of "discredit" to ESHRE if collaboration were pursued. Indeed, it was at this time, says Basil Tarlatzis, that ESHRE first showed a

visible degree of self-confidence and finally realised that it could shape its own future without the necessary co-operation of other associations.

In fact, the seeds of change in how ESHRE organised its annual meetings had been sown before Van Steirteghem's chairmanship began in Paris. Barcelona, Malmo, Milan and Paris had all made surpluses but had all been staged with the help of a professional congress organiser. In every case, and especially in Milan, the PCO had taken a sizeable slice from that surplus, which had left Cohen and Crosignani shaking their heads. Metcalf in his business consultancy report had recommended more centralisation for ESHRE, more involvement for the Central Office, more responsibility for sub-committees. Thus, there was a view already evident in the EC that there should be a clear set of rules for the organisation of an annual meeting, that the format should follow a recognisable pattern, and that the scientific sessions should be determined not by local politics or jobs for the boys but by objectively applied criteria from an independent and international scientific committee (whose members could not be invited speakers). As a result, from 1991 onwards all groups applying to ESHRE to host an annual meeting would have to recognise ESHRE's own organisational guidelines and agree in their submission to follow them.

Thus, when André Van Steirteghem replaced Pier Giorgio Crosignani as chairman in June 1991 there was already some evidence that ESHRE was moving from a random collection of "enthusiastic volunteers whose main concern was science and medicine" (as Metcalf called them) to a more centralised organisation committed to quality and identifiable homogeneity in its many activities. "ESHRE is now on the verge of a new era," Van Steirteghem wrote in *Focus on Reproduction* in mid-1992, anticipating the developments which lay ahead.

This advance of ESHRE, however, and the changes now evident in the society's structure were not without problems. At the AGM in Paris Hans Evers from the floor had urged ESHRE not to lose sight of its first principles of low registration fees, academic environments, and a balance of scientific and clinical interests. Evers would later that year describe ESHRE as at a crossroads: "Should we strive for large meetings with high quality presentations which make attendance rewarding," he asked, "or should we go back to the roots of Bonn", with basic science and affordable fees for young scientists. Yet the fact remained, as Van Steirteghem told his first EC meeting, that the annual meeting was now irrevocably "a large scale event"; university campuses simply couldn't cope with more than

1000 delegates or a substantial commercial exhibition. The future, as Crosignani advised, was not so much in taking this or that position, but in recognising the applicability of basic science to progressive clinical medicine. Speakers should be chosen because they had new data to report in developments which were of genuine scientific and clinical interest - and this choice lay with the scientific committee. In the end, said Van Steirteghem, ESHRE's future - as its past - lay with the scientific quality of its activities. And in the end that too was where Evers' conclusions lay, in an annual meeting of high quality papers from original work.

ESHRE's evolution at this time was also evident in changes to the EC ratified by the AGM in Paris. Stepping down from the EC were Cohen (as past chairman), Hamberger, McLaren and Zeilmaker, to be replaced by Kjessler, Carlo La Vecchia and Tarlatzis. Tarlatzis would take over as treasurer from Zeilmaker, while Klaus Diedrich, who had been replaced as secretary by Michelle Plachot in 1990, was now voted in as chairman elect. Also remaining in place alongside Plachot were Pedro Barri, Henning Beier and Steve Franks. This was now a much different EC from that which had pioneered ESHRE's progress in Bonn and Brussels. The new

Fourth Executive Committee 1991-1993

Chairman

André Van Steirteghem

Chairman elect

Klaus Diedrich

Past chairman

Pier Giorgio Crosignani

Secretary

Michelle Plachot

Treasurer

Basil Tarlatzis

Members

Pedro Barri

Henning Beier

Steve Franks

Berndt Kjessler

Carlo La Vecchia

Arne Sunde (special advisor training)

Hilde Olbrechts (paramedical)

generation were all active in ESHRE's Special Interest Groups (SIGs), had lectured on training courses and were all involved in clinical or basic research programmes - and what's more they were relatively young (and almost eligible - under 35 - for the newly instituted "Most promising young scientist" award to be made at each annual meeting starting with The Hague). La Vecchia, an epidemiologist, also represented a diversion of interest for ESHRE, away from the old guard of the infertility establishment.

"Because the society was growing very fast and so many different activities were being developed, it needed doers," explains Tarlatzis, "and not just prominent people who might be there but, because of other commitments, would not be able to contribute. So ESHRE tried to recruit those who had already served the society in some capacity - either in the Advisory Committee or in the Special Interest Groups - so that they were familiar with ESHRE and had shown that they were active."

Bruno Van den Eede's guidelines for the organisation of annual meetings appeared in the fourth 1991 issue of the restyled and invigorated ESHRE newsletter *Focus on Reproduction*. The guidelines committed the EC to supervising the "overall organization" of the annual meeting, with rights to approve (or not) the scientific programme and keep a running view on the balance sheet. The guidelines also described the day-by-day format of the meeting, identifying plenary sessions, invited lectures and free communication sessions in their various parallel slots. The same format, said the guidelines, would now be used for each ESHRE congress. General organisation was deemed the responsibility of ESHRE's Central Office in co-operation with the local organising committee for practical arrangements (though in later years more and more of the everyday practicalities would become the responsibility of Central Office and Bruno Van den Eede). "Both aspects of our annual meeting," wrote Van Steirteghem, "- keeping a standardised and easily recognisable framework together with a constant re-evaluation of what is scientifically important at the time of the meeting - will form the major challenges for our future congresses."

The EC had agreed in principle in Milan in June 1990 that the 1993 annual meeting would go ahead as an experiment in centralised self-organisation, with Basil Tarlatzis agreeing to take up the challenge in Thessaloniki. In Paris a year later Tarlatzis had confirmed that the programme would indeed be determined by an international scientific committee (as had been proposed in November 1990 at the EC in Brussels) and pre-congress workshops selected by the SIGs. Thessaloniki, therefore,

would be ESHRE's first independent congress run according to its own guidelines, without the support of a PCO, and under the eye of an international scientific committee whose only brief was quality and originality. Applications for sponsorship would now be made from Central Office and to companies' international headquarters. Again, Tarlatzis would also confirm that an exhibitors' kit would be produced for sponsors in Thessaloniki to ensure efficient organisation and a consistent policy.

"It was a gigantic job," recalls Tarlatzis, because at the time the management structures advised by William Metcalf were not yet fully in place. "It meant that Bruno was supervising in general, but all the day-to-day activity took place locally." Tarlatzis and his local colleagues (two secretaries) would be responsible for all registrations, social events and satellite activities, while Central Office took care of abstracts and exhibition space. "Looking back our decision to organise the 1993 meeting independently reflected a very important phase for ESHRE," says Tarlatzis, "and the 1993 congress proved a turning point. There was a big increase in participation, and we had strict financial management. It gave us confidence that we were moving in the right direction."

But for Tarlatzis the one development in planning for Thessaloniki of lasting importance to ESHRE was the introduction of an independent scientific committee to assess submitted abstracts and plan the meeting's content. "This put down the roots for a high quality scientific programme," says Tarlatzis. "It was very evident in Thessaloniki and has been in every congress thereafter." One important rule for this committee was that members could not be invited speakers at the annual meeting, thereby ensuring that scientific quality was the only criterion for selection. In later years, when a more structured form of weighted abstract review was introduced, the non-invited speaker rule for scientific committee members would be maintained.

While planning for 1993 went ahead in Thessaloniki and at Central Office, Van Steirteghem's first specific initiative as chairman was to review the activity and election of the Advisory Committee (AC). The composition of the AC was determined by article 15 of the by-laws, and according to an AGM decision of 1985 allowed two representatives from European countries with more than 20 million inhabitants and 15 ESHRE members, and one representative from countries with fewer inhabitants but more than 15 members. Van Steirteghem now proposed that the election procedure should be made more transparent and that each

member should now be asked to nominate candidates for election and then vote by ballot. Thus, the full membership of ESHRE would be allowed to nominate and vote for its AC representatives - and, at the AGM in The Hague in July 1992, the first ballot results were announced and the new membership of the AC ratified.

The Hague was yet again judged a successful meeting. Almost 1000 took part and more than 350 abstracts were accepted. This was in fact the first annual meeting at which a blind scoring system was applied to each abstract. The abstracts were marked out of 5 for study design, clear statement of results, significance, originality and relevance. "No abstract was perfect," congress chairman Frans Helmerhorst later reported, "since there were no scores above 4.4, but, with a minimum score of 2, only 27 were rejected by the committee." Helmerhorst also addressed the charge that there was bias in favour of Dutch abstracts: a paired t-test of scores given to the 68 Dutch abstracts by two Dutch and two non-Dutch referees showed unequivocally that bias did not occur. It might also be said that at this time IVF in The Netherlands was proving an increasingly popular option for infertile couples, such that by the mid-1990s there were reports that around 1 per cent of all babies born there were conceived by IVF; "transport" IVF (as well as the cryopreservation of embryos) had been pioneered in Rotterdam; and Dutch membership of ESHRE ranked third at the end of 1992 (behind only the UK and Belgium). In his round-up of The Hague Helmerhorst warned that never again would an ESHRE annual meeting attract fewer than 1000 delegates.

Indeed, in his planning for the independent 1993 meeting in Thessaloniki, Tarlatzis could already report a multitude of pre-congress and mid-congress activities guaranteed to generate interest and attendance. Tarlatzis also insisted that the lead of the SIGs in determining the pre-congress courses would be crucial; Michelle Plachot would co-ordinate a course on embryology, John Newton on contraception, Paul Devroey on endoscopic surgery, and Steve Franks on endocrinology. The fact that all new members would now declare their own "special interest" on their application forms would hopefully increase the pool for attendance. By March 1993 Tarlatzis would report that 529 abstracts had been received, 150 more than the previous year, 90 per cent of the commercial exhibition space allocated, and numerous ancillary activities confirmed: Edwards himself would stage a self-financing satellite symposium on the "Physiological aspects on new forms of contraception", the newly formed Middle East Fertility Society would hold its inaugural meeting, and

Organon would unveil at a pre-congress symposium new clinical and in vitro data on its recombinant FSH Puregon. "It was all a sign," says Tarlatzis, "of the increased recognition of ESHRE." Incidentally, the first live births following ovarian stimulation with two preparations of recombinant FSH had been reported in the *Lancet* in 1992, and interest (as well as competition) was inevitably intense.

But, as in Paris, there were still fires to be fought in Thessaloniki. At the close of 1992 the American epidemiologist Alice Whittemore and colleagues proposed in an *American Journal of Epidemiology* report (1992; 136: 1184-1203) that "fertility drugs" increased the relative risk of ovarian cancer (RR = 2.8). The study was based on an analysis of 12 case-control studies of ovarian cancer undertaken between 1956 and 1986 but, as Whittemore herself admitted, the finding was "based on very small numbers and is really very tenuous". Nevertheless, the results were splashed in the lay press, and once again there was the hint of a crisis of confidence in infertility treatment. Few professional groups accepted the Whittemore findings. ESHRE itself, the IFFS and the AFS all issued statements rejecting any causal association and explaining why the study



At ESHRE's ninth annual meeting in Thessaloniki a session on the safety of ovarian hyperstimulation was hastily organised following publication of a report suggesting a raised risk of ovarian cancer from "fertility drugs". There was standing room only long before the session began.

was flawed. Their arguments were essentially that the recorded cases of ovarian cancer and its known latency were incompatible with a relative risk of 2.8. The paper was discussed at ESHRE's 37th EC meeting in March 1993 and it was agreed that "a small session" should cover it in Thessaloniki. Already, Jean Cohen had convened an IFFS group to produce a critical statement, which would be published in *Human Reproduction* alongside a debate on the issue (1993; 8: 990). However, the "small session" in Thessaloniki (chaired by Cohen, Bruno Lunenfeld and Tarlatzis) in the end became a joint IFFS and ESHRE marathon involving epidemiologist Susan Harlap from the USA, Jacques de Mouzon from FIVNAT in France and Allan Templeton representing Britain's HFEA. De Mouzon argued that IVF's relative risk of 2.8 would explain 15 per cent of all ovarian cancer cases, yet cancer registry figures did not reflect this. Moreover, as Templeton said, the NIH's surveillance of 3100 IVF patients in the USA recorded no cases of ovarian cancer. It was a high-energy session, with standing-room only - even though Whittemore herself later described the event as "tedious, petty and unproductive haggling".

However, the hottest presentation in Thessaloniki came not from the epidemiologists but from ESHRE's own chairman in a paper which would have lasting worldwide consequences both for the treatment of infertility and for ESHRE itself. Its repercussions would be felt in a surge of citation ranking for *Human Reproduction*, in the escalating profile of ESHRE's scientific reputation, and indeed in the place of Europe as the leading force of progress in reproductive medicine. For it was here in Thessaloniki that André Van Steirteghem reported to a packed and spellbound audience the outcome of injecting single sperm cells into the ooplasm of 3000 oocytes; intracytoplasmic sperm injection, or ICSI, said Van Steirteghem, would finally give us a treatment for almost all kinds of male infertility.

The story of ICSI is a story of Brussels. There were, of course, other groups around the world working in micromanipulation, and many of these experimental techniques had already been tried and proved in cattle. In humans the first initiatives in micromanipulation (reporting in 1988) had attempted to improve the efficiency of fertilisation in vitro by "drilling" the outer zona pellucida of an aspirated oocyte to form a minute gap. However, following such zona drilling, rates of polyspermy were found to be high (50 per cent in one study), as was oocyte damage (33 per cent). An alternative technique of partial zona dissection (PZD) developed in the USA by Jacques Cohen and colleagues in Atlanta and later at Cornell had some success in reducing polyspermy rates, but rates

of oocyte damage remained high, and some reports would later describe decreased pregnancy rates.

The big breakthrough in micromanipulation - especially in treating couples in whom the male partner had low sperm counts - came with a technique known as sub-zonal insemination, or SUZI. This was the first microinjection procedure to show that several sperm cells, when pretreated to induce their acrosome reaction, could achieve fertilisation when placed beneath the zona pellucida of the oocyte. The first human pregnancy following SUZI was reported in 1988 by Soon-Chye Ng and Ariff Bongso in Singapore (*Lancet* 1988; 2: 790). The implications of the report, and of SUZI, were enormous, for here, for the first time, was a technique which held the promise of actually circumventing a sperm defect and treating male infertility. So far, men with poor sperm quality or azoospermia had few options for fatherhood but donor insemination or adoption; now, SUZI was a procedure which offered a glimmer of hope from just a few sperm cells, and the possibility for men with sperm abnormalities to father their own children.

Not surprisingly, at a meeting on Micromanipulation in Human Reproduction in Rome in 1991 (and later that year at the joint congress in Paris) at least ten groups were already reporting data from their work with SUZI, the largest series from Simon Fishel (working in Rome and Nottingham) describing 82 embryo transfers from 225 SUZI cycles and a clinical pregnancy rate of 15 per cent. Also reporting data in Rome were groups from Monash (112 cycles) and the VUB (44 cycles).

And it was at the VUB that a young Italian gynaecologist found himself working on SUZI oocytes one afternoon in October 1990. Gianpiero Palermo, peering into a microscope in a room no bigger than a kitchen and hidden from daylight by dark-room blinds, had penetrated the zona pellucida of an oocyte with an injection needle, but the injection had gone too far and inadvertently damaged the membrane between the zona and the inner cytoplasm of the egg, allowing the injected sperm to enter freely. Palermo didn't think too much about it and left the oocyte with his other SUZI oocytes overnight in the incubator. By next day, the damaged oocyte had fertilised, to become the first fertilisation from direct intracytoplasmic injection, albeit an accident.

More (deliberate) ICSI fertilisations followed at the VUB, and with them the even more difficult decision of whether to transfer these ICSI embryos or not. Finally, after experiments in mouse models and many further human fertilisations, with ethical approval secured and pre-conditions in

place (karyotyping, prenatal diagnosis), the VUB's first ICSI embryo was transferred in the spring of 1991, and the first baby born in January 1992.

By the time Arjoko Wisanto took the podium at the 8th World Congress of Human Reproduction in Bali in early 1993, the superiority of ICSI over SUZI was already beyond dispute - at least in Brussels. Wisanto reported that from its second comparative series 51 per cent of ICSI oocytes reached the two pronuclei stage of their development, but only 17 per cent of SUZI oocytes. And it was from this second series, Van Steirteghem would subsequently report in Thessaloniki, that the real clinical potential of ICSI would emerge. Indeed, even a separate series of just 16 ICSI cycles in patients "with no sperms observed at the initial assessment" showed a 69 per cent fertilisation rate using the few sperms salvaged from ejaculate samples. Embryo transfer was possible in 14 of these 16 cycles and a pregnancy rate of 43 per cent per transfer was recorded. More than 50 per cent of the 3000 ICSI injections described by Van Steirteghem in Thessaloniki achieved fertilisation to the 2PN stage - against just 17 per cent of the SUZIs. Brussels abandoned SUZI in favour of ICSI in August 1992.

The VUB's extraordinary success now meant that male factor infertility, which had so far proved one of reproductive medicine's greatest



Thessaloniki 1993. It was here that André Van Steirteghem reported the outcome of injecting sperm cells into the cytoplasm of 3000 oocytes; ICSI, he said, would finally offer a treatment for almost all kinds of male infertility.

challenges, was now amenable to treatment. Formerly, semen which contained fewer than a half million sperms was beyond the scope of conventional IVF; now, just a single sperm cell - and even one which appeared at first analysis immotile - was enough to achieve fertilisation, pregnancy and the chance of fatherhood for men who formerly had little hope. The whole miracle of reproduction now lay - quite literally - in the hands of the embryologist. In an editorial in *Human Reproduction* in July following the Thessaloniki meeting (1993; 8: 988) Edwards and Van Steirteghem rather cautiously proposed that "ICSI now seems to be the most beneficial approach to obtain fertilisation and live births in cases of severe male infertility".

The VUB's remarkable advance left most other groups around the world gasping for breath, and there were some who just couldn't believe it. "There was a lot of scepticism about ICSI," Van Steirteghem later said. "It was only after the first workshops we did in 1993, when all the big groups came to watch and see if it was real, that interest really took off." ESHRE's first Campus workshop on ICSI - Advanced Training Course in Assisted Fertilization by Intracytoplasmic Sperm Injection - took place over two days in April 1993 with 100 participants. Registrants would follow the procedures of sperm preparation and selection, cumulus and corona cell removal, microinjection, evaluation of fertilisation, and preparation of tools. The last procedure was crucial, for each injection needle had at the time to be ground and forged to a diameter more than ten times finer than a human hair. A second similar course followed in November that year, and two more in 1994, by which time pressure from pupils was such that a practical session (arranged in co-operation with Nikon) was arranged so that all 48 registrants would have hands-on experience. With infertility centres throughout the world now anxious to add ICSI to their treatments - and early experiences showing that successful fertilisation seemed dependent on the skills of the embryologist - the ICSI workshops were always oversubscribed.

Although the VUB's first announcement of a pregnancy following ICSI was published as a short report to the *Lancet* (1992; 340: 17-18), data from all subsequent patient series appeared in *Human Reproduction*, notably details of the second series described in Thessaloniki (1993; 8: 1055-1060). This would have an inevitable repercussion on impact factors for the journal at this time and help strengthen ESHRE's position in negotiations with OUP for a new contract.

André Van Steirteghem

ESHRE's fourth chairman 1991-1993

André Van Steirteghem is Scientific and Laboratory Director of the Clinical Centre for Reproductive Medicine and the Research Centre Reproduction and Genetics of the Dutch-speaking Brussels Free University (VUB). His group was responsible in 1991 for the introduction of ICSI into clinical practice and, since 1993, has carried out a prospective follow-up study of all pregnancies and births after IVF and ICSI.

Van Steirteghem qualified at the VUB in 1969, and obtained his PhD ten years later. After qualifying he took up a five-year residency at the VUB in paediatrics before moving to the USA as a visiting scientist for the NIH. He returned to Brussels and the VUB in 1977 as assistant professor and two years later became Director of the Department of Radioimmunology and Reproductive Biology and Scientific Director of the Centre for Reproductive Medicine. He was elected Dean of the VUB's Medical School from 2000 to 2004.

André Van Steirteghem was a member of ESHRE's original temporary committee and of its first Executive Committee as treasurer. He was a member of the organising committee of the first annual meeting in Bonn and chairman of the second meeting in Brussels. Van Steirteghem was chairman of ESHRE from 1991 to 1993 and in 1995 was made Executive Director. He is currently an associate editor of *Human Reproduction* and on the editorial boards of many other journals. He is an author of more than 600 papers in peer-reviewed journals.

In Belgium Van Steirteghem is chairman of the College of Physicians in Reproductive Medicine, a member of the Royal Academy of Medicine and a member of the National Advisory Committee on Bioethics.

Van Steirteghem's presentation to the annual meeting in Thessaloniki had also mentioned paediatric follow-up of 75 babies born after ICSI. One malformation and one developmental abnormality had been found, rates, said Van Steirteghem, which were comparable with those of normal childbirth. The follow-up study would continue at the VUB, with Van Steirteghem and Devroey insistent that, despite its success and apparent safety, ICSI would remain an experimental procedure. "We are in a similar position to IVF in the late 1970s," Van Steirteghem said at the time. "We have to collect the data and be sure of the long-term safety." A second report on the VUB follow-up study presented by Maryse Bonduelle at ESHRE's tenth annual meeting in Brussels in 1994 won the congress's general prize. Now, data on 130 ICSI children and 130 matched IVF controls showed five major malformations in the ICSI group and six in the matched IVF group. Again, the VUB reported no differences between the ICSI births and the controls. In later years, when concerns arose from anecdotal reports and small studies over ICSI's safety, the VUB follow-up data would prove an important source of reassurance.

It was with these future considerations in mind that Van Steirteghem also proposed in March 1994 that ESHRE should form a task force to collect

worldwide data on ICSI. Members of the task force would be Van Steirteghem as chairman, Bonduelle, Lars Hamberger and Basil Tarlatzis. However, the task force's first objective to survey ICSI experience up to December 1993 would never be easily met. There was an initial problem of identifying those centres using ICSI - and from 350 groups contacted only 35 reported results. In some countries - the UK and France, for example - national registries for data collection were already in place, so there were known gaps in the numbers; however, the first report did include three groups from Australia (but not Monash) and three from the USA (including Cornell). All but one group (unidentified but presumably the VUB) had completed fewer than 150 cycles, and most fewer than 50; the VUB reported data on 1403 cycles. From a total of 345 children born at the 35 centres, three major congenital malformations were recorded. By the time the task force next gathered for its second meeting in July 1995 in Hamburg there were now more than 50 groups reporting ICSI data for 1994, with the possibility of collaboration with national registries in Germany and France. The ICSI task force published three reports in all, presenting data from 1993 to 1996 (Focus on Reproduction 1995; 3: 9-12, Hum Reprod 1998; 13: 1737-1746, Hum Reprod 1998; 13 (Suppl 1): 165-177).

Although ICSI was the scientific highlight of Thessaloniki, the 1993 meeting was also a triumph for ESHRE's independent centralised organisation and programme planning by the scientific committee. No other meeting before had been staged without contractual support, and Tarlatzis rounded up friends and family to fill the roles. "Thessaloniki was a huge success," Tarlatzis recalls, "with 1600 people attending. We had a bus system operating from the hotels to the congress centre and this was set up through friends. The congress posters were changed at the end of each day and this was organised by André Van Sterteghem's two sons and my daughter. My daughter was also responsible for all announcements from the microphone - she was only ten years old, but fortunately she was bilingual and she could do it. We also introduced keynote lectures on broader subjects on the first day. Everyone enjoyed Thessaloniki, and it was a big success both in terms of participation, organisation and financial benefit to the society." Two keynote lectures - on a variety of broad-interest topics - have continued to open the scientific sessions of every annual meeting since.

Ironically, it was only through good fortune and not good planning that the Thessaloniki meeting went ahead at all. Just one month before, in May 1993, Tarlatzis and Van Steirteghem were guest speakers at a conference on ART organised by Timur Guban in Cappadocia, the ancient region of



ESHRE's ninth annual meeting in Thessaloniki was the first to be organised without the help of a professional congress organiser. Local chairman Basil Tarlatzis and Bruno Van den Eede from ESHRE's Central Office are flanked by some of the family, friends and colleagues who helped behind the scenes.

central Turkey. While there, they were both taken by jeep to view the historic sites of Asia Minor. "Our guide was a good man but a bad driver," says Tarlatzis, "and on the way back from our tour we swerved to avoid a car coming the other way. The jeep left the road and rolled down a slope. We finally stopped upside down with gasoline pouring out, broken glass everywhere." The two explorers crawled from the jeep, dusted themselves down and inspected the damage. "Luckily, there were only minor injuries - and the congress could go ahead," smiles Tarlatzis.

There were, of course, changes to the EC ratified in Thessaloniki by the AGM and it was here that Van Steirteghem stood down as chairman to be replaced by Klaus Diedrich. Also completing their terms on the EC were Barri, Beier, Franks, Plachot and Kjessler, as well as Crosignani, whose two-year term as past chairman was now over. Tarlatzis was elected for a further term of two years as treasurer, to be joined on the EC by José Egozcue, Paul Devroey, Hans Evers, Matts Wikland, Jean-René Zorn and Lynn Fraser. Both La Vecchia and Sunde remained in place. Egozcue, a geneticist, had been active in ESHRE from its beginnings ten years earlier



Robert Edwards was made an honorary member of ESHRE at the annual meeting in 1993. He is here seen receiving his award from the society's outgoing chairman André Van Steirteghem and congress chairman Basil Tarlatzis.

and had served on the temporary committee and EC from 1984 to 1988. He would also be active in the formation of the SIG on preimplantation genetics in 1994, but now, in the tradition of a scientist replacing a clinician, he was confirmed as chairman elect to succeed Klaus Diedrich in 1995.

The ESHRE which welcomed Diedrich in 1993 had continued to progress in the two years of Van Steirteghem's chairmanship. By the end of the year membership had passed 2000 (though there were still around 300 unpaid), reserves at the bank were such that there was now - for the first time - some discussion as to how the money should be constructively spent, and at least five workshops were planned for 1994, as well as a host of pre-congress courses and other symposia. The London biologist Lynn Fraser was keen to start a new workshop in semen analysis, and Michelle Plachot in embryology. ESHRE was clearly in a phase of major growth.

"I felt it was my task as chairman," says Diedrich, "to make sure the growth continued and that the society did not become a victim of its own success." That success, Diedrich reasoned, was now reflected in the sheer scale and volume of ESHRE's activities, "an indication of how much more complicated and more difficult it has become to manage this growing organisation. One of the challenges for the future, therefore, will be in finding a more efficient structure that can deal with the complexities of

Membership of the Advisory Committee 1992-1994

The Advisory Committee formed in 1992 was the first to be elected by nomination and full membership ballot.

Safaa Al-Hasani (Germany)	Peter Kemeter (Austria)
Anders Nyboe Andersen (Denmark)	Heribert Kentenich (Germany)
John Bontis (Greece)	Jacques Lansac (France)
Antonio Cano (Spain)	Jacqueline Mandelbaum (France)
Paul Devroey (Belgium)	Shlomo Mashiach (Israel)
Leonardo Formigli (Italy)	Anne McLaren (UK)
Marc Germond (Switzerland)	Guido Ragni (Italy)
Timur Gurgan (Turkey)	Markku Saaranen (Finland)
Cees Jansen (Netherlands)	Josep Santalo (Spain)
Jarl Kahn (Norway)	Allan Templeton (UK)
A Kalelioglu (Turkey)	Matts Wikland (Sweden)

organising our own meetings, of publishing our own newsletter and journal, of working out an administrative body and of establishing sound financial management.” It was a tough call.

Diedrich’s first administrative task was to find a replacement for Pedro Barri as co-ordinator of the SIGs. Since their inception following Metcalf’s business consultancy report in 1990, the SIGs had stumbled along, some more active than others, and some more welcome than others. Their subjects and titles had been reshuffled and shuffled again, and finally their roles scrubbed up and polished as a basic resource for pre-congress workshops. Four had been organised through the SIGs in Thessaloniki and six would be planned for the tenth annual meeting in Brussels in 1994. Immediately after the Brussels congress the SIG in reproductive biology chaired by Michelle Plachot ran its first “summer school” in embryology which, over its five days, combined theory with practical sessions in various laboratories throughout Belgium. In Brussels too Egozcue had teamed up with Alan Handyside to set up a new SIG in preimplantation genetics, while Lynn Fraser, chair of a new SIG in andrology, had staged her first course in semen analysis with Chris Barrat to raise standards in European labs in line with the WHO’s 1992 Laboratory Manual. This course, held in Sheffield in April 1994 in association with the British Andrology Society, was run as a blueprint for other ESHRE-accredited semen assessment training centres.

With seven SIGs now available to members and all active - in ART (now chaired by Wikland), reproductive endocrinology, andrology,

Fifth Executive Committee 1993-1995

Chairman

Klaus Diedrich

Chairman elect

José Egozcue

Past chairman

André Van Steirteghem

Treasurer

Basil Tarlatzis

Members

Paul Devroey

Hans Evers

Lynn Fraser

Matts Wikland

Carlo La Vecchia

Jean-René Zorn

Arne Sunde (special advisor training)

Frederike Wegener (paramedical)

reproductive surgery, reproductive biology, psychology and counselling, and reproductive genetics - the EC turned to Hans Evers to take over their co-ordination from Pedro Barri. Evers by now was Professor of O&G and Director of Reproductive Endocrinology and Fertility at the Academic Hospital of Maastricht. He had been involved with ESHRE for several years before joining the EC, first as a member of the international scientific committee for ESHRE's eighth meeting in The Hague and later as a faculty member of numerous ESHRE courses. In Thessaloniki he had chaired the poster award committee and - in his characteristically constructive way - had offered suggestions to reduce the number of posters at future meetings (there were 374 in Thessaloniki), ease the running of the poster committee, and improve the post-poster discussion. Now, in December 1993 at the 40th meeting of the EC, Evers was handed responsibility for the SIGs.

Evers, in a report he compiled for the next EC meeting in Lübeck in March 1994, took a view that the SIGs represented a huge source of expertise and influence for ESHRE. Here, he would argue, were the foundations and the leading edge of scientific and clinical disciplines at the heart of ESHRE, and as such he supported those SIG co-ordinators who wished for more involvement in the scientific sessions of the annual meeting.

Klaus Diedrich

ESHRE's fifth chairman 1993-95

Klaus Diedrich studied medicine at the University of Hamburg, qualifying in 1972. Following military service he took up a post as senior house officer in obstetrics and gynaecology at the University Hospital in Hamburg. In 1979 he was appointed consultant in ob/gyn at the university women's clinic of Lübeck under Dieter Krebs and in 1981 was awarded his PhD (in immunological sterility in rabbits). A residency with Alex Lopata in Melbourne secured his foundation in IVF. Lübeck's IVF programme was approved in 1981 and achieved its first live birth the following year - just a few months after Siegfried Trotnow's group in Erlangen reported the birth of Germany's first IVF baby. In 1984 Diedrich moved to Bonn as first consultant in ob/gyn and Professor at the University Hospital. He remained in Bonn until 1993, when he returned to Lübeck as head of the Department of Obstetrics and Gynecology.

Klaus Diedrich, along with Edwards, Cohen, Van Steirteghem, Sunde and Crosignani, was a founding member of ESHRE and a member of the temporary and first executive committees. It was also Diedrich who, with his German colleagues Al Hasani, Beier, Krebs and Van der Ven, organised ESHRE's first annual meeting in Bonn. Diedrich became chairman of ESHRE in 1993.

Klaus Diedrich has published extensively in reproductive medicine and, through ESHRE's Campus workshop programme, established both Bonn and Lübeck as important training centres. In 1994 he was made secretary of the German Society of Obstetrics and Gynecology (DGGG), and in 2002 president.

However, it was also at this same EC meeting in Lübeck that Arne Sunde, after almost a decade, resigned from his position as co-ordinator for workshops. Sunde, as noted in chapter 6, felt he didn't have the resources to run ESHRE's training programme as efficiently as he thought it should be done. Sunde's surprise resignation left Diedrich and the rest of the EC in a quandary, for they all felt that training should be streamlined, standardised, centralised, and even harmonised with other ESHRE activities. And so Hans Evers was yet again asked to consider the co-ordination of both training and the SIGs, such that the SIGs might form the basis of a revised and simplified training programme. It was a major commitment for Evers; however, before that Lübeck EC meeting was over, ESHRE had much more in store for him.

From the beginning of ESHRE's history the EC had always had in hand several proposals from members to host the annual meeting. As the popularity of the meeting grew, the choice of venue became more difficult - both for political reasons of fair geographical representation and for practical reasons of access and accommodation. At the same time, while major European congress cities like Berlin, Brussels or Barcelona could easily stage enormous congresses, their costs were also high and likely to

upset ESHRE's low-fee policy. So from the beginning the ESHRE annual meeting was always considered by many countries large and small an attractive event to stage, of high scientific quality and, for its hosts, a prestigious occasion. The EC was never short of suggestions. At the end of 1990, for example, the EC was sitting on proposals from Helsinki, Lisbon, Belgrade, Jerusalem and Istanbul.

By 1991 all applicants for staging an annual meeting would receive ESHRE's congress guidelines and, in their formal submissions, agree to abide by them. Once these congress guidelines had been published, interest in hosting the annual meeting escalated yet again, such that by December 1991 applications from ten cities were before the EC for discussion. One of them, possibly for 1996, was from Birmingham in the UK. Against two other competitors, and following the usual detailed discussion, Birmingham won its bid to stage the 1996 annual meeting at the 33rd EC meeting in March 1992, and John Newton, chairman of the provisional local committee, was informed. Newton, a senior figure in Britain's and the international O&G establishment, had been recruited by Pedro Barri to head the newly formed but uneasy SIG in contraception in 1991, and he now rallied support from sponsors, the British Fertility Society and the City of Birmingham authorities. He also retained a PCO to help with local practicalities, arguing that organisation without a PCO "would put too great a strain on both the local committee and the office in Brussels".

As was by now customary, all chairmen of forthcoming annual meetings were invited to each EC meeting to report on progress and to join the international scientific committee of preceding annual meetings. Thus, at the 36th EC meeting Newton reviewed his initial budget and outlined costs at the newly constructed ICC conference centre in Birmingham. But for the 37th EC meeting he sent apologies, nor was he present at the 40th, in December 1993, or 41st the following March in Lübeck. By now, only two years before the event, this was a critical meeting for the EC, for by this time they hoped that all the major planning details for Birmingham would be in place, that the international scientific committee would be formed, and that the text for the first announcement would be ready. But Newton was nowhere to be seen, and none of the deadlines appeared to have been met. It was a difficult decision for Diedrich and the EC, but there appeared few alternatives. There was little time, said Diedrich, and an urgent decision had to be made - so the EC finally agreed that the annual meeting in Birmingham would be "postponed to a later date".

It was a disagreeable episode for everyone. Newton, of course, was angry and offended, but the EC, albeit reluctantly, felt justified in its decision. In his defence Newton would cite poor communication from the EC and too short notice to attend meetings. But the records show that Newton was conspicuous by his absence from crucial EC meetings, that many letters from ESHRE's Central Office went unanswered, and that few progress reports were received by the EC. Diedrich, in his letter confirming the decision to Newton, said that the EC's position was supported by other British representatives, who agreed that "the organisation of the meeting in Birmingham was not heading in the way we expected".

The decision, of course, was not taken lightly, and didn't solve all the EC's problems. For now, with a little more than two years to go, there was not even the hint of a venue for the 1996 annual meeting, let alone a first announcement ready for press. Once again, quick decisions had to be made, and once again the EC turned to Hans Evers for a solution. Maastricht, Evers proposed, could be a possible substitute for Birmingham - although The Hague, the Dutch capital, had been ESHRE's venue in 1992. But with so few alternatives and time running out, such considerations were now hardly relevant - and the EC expediently agreed that the 1996 meeting would indeed be held in Maastricht, with Evers as congress chairman.

Lübeck had been a momentous EC meeting for Evers, and when he boarded the plane in Hamburg back to Amsterdam he carried in his baggage ESHRE portfolios for the SIGs, for training and now for the 1996 annual meeting. It was a huge responsibility, but one with which Evers slowly began to impose the discipline of a long-term view on ESHRE and the EC, and urge protection from the kind of vulnerability reflected in the Birmingham episode. "When I was just a member," he recalls, "I would look at the executive committee and think that these were very shrewd politicians, manoeuvring ESHRE through all kinds of dangerous situations. But when I joined the EC it didn't turn out like that at all. I just found people meeting a few times a year and brainstorming, raising ideas, discarding ideas. What I missed was the long-term view. I'm sure there was a long-term view in the beginning, when ESHRE was a small group of friends developing the same set of plans. But now we were in a real phase of growth. We were on the EC not because we were friends but because we were representatives of our fields and of our countries. We had to agree on a common path to follow, because we didn't have the guide of common ideas which the guys in Helsinki had."

It was thus Evers' view that, while the inspiration, integrity and energy of the early days had indeed generated ESHRE's success, that success was also vulnerable without a strong foundation or a forward-looking plan. "Many of the pioneers had now left the EC," says Evers, "and their replacements were there because of their abilities and what they could offer to ESHRE. Many were quite new to the society. If we had to wait, say, a year before they got to know each other and how to interact, that would be a hopeless situation. So we needed a common plan that we'd all agree to follow."

However, if Birmingham 1996 had proved a salutary reminder of ESHRE's vulnerability, Brussels 1994 was yet another testimony to its strengths and near exponential growth. The commercial exhibition space was totally booked, more than 600 abstracts were reviewed, and more than 1700 attended, three times more than in Bonn in 1985. Indeed, such was ESHRE's confidence in the 1994 event, and its concern to maintain scientific quality, that Evers' recommendation to restrict the number of posters to 200 was applied; moreover, in the selection of abstracts for free or poster communication, the EC opted to follow the AFS's system of "weighted" abstract scoring (by which an assessor's individual scoring trend is adjusted to the overall measure). Thus, all abstracts received for assessment would not only be assessed blind by the referees, but also weighted to remove personal bias. With posters restricted to 200, Tarlatzis calculated that the rejection rate for an ESHRE annual meeting would now be around 50 per cent.

By Brussels too collaboration with the AFS had matured with the first European joint pre-congress course in assisted reproduction, and there were now seven awards available to participants: the Promising Young Scientist Award (worth \$3000 and sponsored by Serono), the General Prize Winning Award (worth \$3000 and sponsored by Organon), the Pacific Coast Fertility Society Award (with which the winning paper would be presented at the PCFS's 1995 meeting in California), The Poster Award (worth \$1000 and sponsored by Abbott), the Ferring Analogue Award (worth Ecu 2000 and sponsored by Ferring), the BioMérieux Award for Reproductive Endocrinology (worth BeF75,000 and sponsored by BioMérieux) and the Paramedical Award (worth \$1500 and sponsored by Organon). None of the pre-congress courses attracted fewer than 20 participants, and Michelle Plachot's post-congress course in reproductive biology had 26. Overall, Brussels brought in a surplus of \$300,000 for ESHRE's reserves, assuaging somewhat the spectre of "vulnerability" raised by the Birmingham fiasco. Thus, in the treasurer's final report for

1994 ESHRE's reserves stood at more than \$500,000, a sum which, the EC agreed, now required serious management.

However, despite the runaway success of the annual meeting, no small part of the contribution to ESHRE's funds was now coming from *Human Reproduction*, which in 1995 was set for the biggest lift in its ten-year history. By the end of the year the EC had signed its new five-year contract with OUP, two new titles - *Human Reproduction Update* and *Molecular Human Reproduction* - were in production, and total sales of the main title had reached 2500 per issue. Gross profit on the journal was now almost £100,000 per year, and by the following year, under the terms of the new contract, would almost double.

Thus, when José Egozcue took over from Klaus Diedrich as ESHRE chairman in June 1995 he would chair a society whose financial basis was soundly underpinned by substantial secure investment, whose membership was increasing year on year, whose journal was generating high impact factors (and appreciable profit), and whose self-organised annual meeting was rapidly becoming the most attractive in the field outside the USA. Moreover, in the election to the EC of members like Evers and Tarlatzis a longer-term, more structured view of the society was slowly taking shape, which would now gather momentum with the appointment of ESHRE's first Executive Director and culminate in December 2001 with Evers' strategy report for ESHRE. However, in the meantime, there was still plenty to keep the EC immediately occupied and, in 2000, the biggest test yet of its strength and determination.

8

THE PARAMEDICAL GROUP

When Klaus Diedrich stepped down from the chairmanship of ESHRE in June 1995, around one tenth of the society's 2500+ membership were involved in the paramedical field of reproductive medicine. These were mainly people who had settled down into the more clearly defined nursing and laboratory roles of an IVF clinic or infertility unit. The part of the IVF nurse co-ordinator had by now become a specialist role among support personnel in infertility and the unit's success dependent upon an interdisciplinary team of clinicians, embryologists, laboratory technicians and nursing staff.

Recognising their emerging role - as well as the requirements for specialist knowledge - and taking a cue from developments in the USA, a self-appointed delegation of nurses and lab technicians working in IVF had asked the Executive Committee (EC) for permission to organise a half-day assembly (with a leaflet in the congress bag) at ESHRE's third annual meeting in Cambridge in June 1987. Some were specialist co-ordinators, sometimes involved in ultrasound scanning, assistance in the operating theatre, counselling and recording of data. However, there were many others with less clearly defined roles, perhaps attached to gynaecology or andrology departments, to day-care or outpatients, in big centres and small. What was needed, they claimed, was some identification as infertility support staff whereby their roles might be recognised and their knowledge more coherently updated. Their learning, so far, was entirely on the job.

The idea of a paramedical group within ESHRE had actually been raised before Cambridge, initially during the EC's first discussions of workshops, and as early as the fifth EC meeting (in Brussels in March 1986) any developments for the paramedics were put in the hands of André Van Steirteghem. Subsequently, during ESHRE's annual meeting in Brussels in 1986, two of the delegation, nurse co-ordinator Peter Erard and lab technician Ronny Janssens, both from Van Steirteghem's centre at the VUB, had organised a "foundation reunion" to explore the possibilities of an ESHRE paramedical group and set out objectives. "There was no communication possibility for paramedical workers in a programme of human reproduction," said Erard at the time. "Such communication should be on our own level and about our own interests, and an ESHRE paramedical group was to provide that means of communication."

The Cambridge meeting was the first organised activity of the group, and it elected Hilde Olbrechts, a nurse co-ordinator at the VUB, as chairman. Thus, although initially envisaged as a workshop event, the outcome of the Cambridge gathering was to give the paramedical group formal recognition within ESHRE and to make plans for its first proper workshop, which would be held at the VUB the following January. The Paramedical Group (PMG) thus formally emerged from Cambridge in response to an agreed "need for a separate but closely linked group whose aim was (and remains) to offer all paramedics involved in scientific and medical IVF programmes a well structured and authoritative platform for discussion and exchange of information". At the AGM in Cambridge Olbrechts had announced the formation of the PMG, noting that support staff working in IVF had been given so few opportunities to raise their concerns and express their views.

That first workshop of January 1988 was organised by the VUB technologist Ronny Janssens, who in Cambridge had been elected as secretary of the group. The two-day workshop was planned to cover IVF laboratory techniques, cryopreservation, hormone analysis, operating theatre support, and counselling. More than 60 took part - in lectures and practical sessions. At the time, following a mailing announcing the PMG, its membership had risen to 117, and it was already clear to chairman Jean Cohen and his colleagues on the EC that this would be an important development for ESHRE. By the 15th meeting of the EC - in the smoke-filled offices of Gyn.Obs in Paris in May 1988 - membership of the PMG had risen to 135, thanks largely to the success of the VUB workshop. Clearly, as Van Steirteghem reported in Paris, the PMG would have to be

taken seriously and its presence acknowledged as an important component of ESHRE's membership.

The group now planned two more activities, each of which would lift its profile, expand its membership base, and clarify its role within the society. First, members of the PMG were asked to take part in the organisation of a three-day international conference for IVF nurses and support personnel in Jerusalem in March-April 1989 (prior to the sixth World Congress on IVF). This was the first time that an international meeting had been designed for paramedics, and it featured as speakers both local experts (Mashiach, Schenker, Ben-Rafael and Laufer) and many of the PMG's own members, including Olbrechts and the PMG newsletter editor Josephine Mitchell (then working in Bristol with Mike Hull). Many of these presentations were reproduced in the PMG's newsletter, which had begun to take shape during 1988 and in 1989 was running as a 50-page publication (with some industry support from Hybritech); the newsletter, reduced to just a page or so, would be absorbed into *Focus on Reproduction* in 1990.

However, the PMG's other activity after Cambridge - in June 1988 - would prove even more significant in its own history and that of ESHRE. As a pre-congress event before the fourth annual meeting in Barcelona the PMG organised its first annual assembly with an additional workshop on semen analysis. Other topics covered by the meeting included patient counselling, laboratory techniques, post-operative nursing and psychological support. This again proved an attractive and valuable event, such that the officers of the PMG now comprised members representing 15 countries, and total membership had climbed to more than 150. Thus, the EC determined that from now on (beginning in Malmo in 1989) the PMG's annual assembly and dedicated scientific sessions would become an integral part of the annual meeting's programme, with presentations on offer from both the PMG's own members and from outside experts.

With such progress, there had already been informal proposals that the PMG should be represented on the EC - and the EC had already agreed in principle; thus, at the AGM in Barcelona Cohen sought approval from the floor for one PMG representative (without voting power) to be nominated to the EC, and all members voted in favour. In Barcelona the EC made it unequivocally clear that the PMG would be part of ESHRE and not a self-contained satellite group. The organisation of workshops, therefore, would fall under the same rules as those for any other group - and from Barcelona onwards the chairman of the PMG would be an active

participant in the meetings of the EC. Thus, in June 1988 Hilde Olbrechts joined Arne Sunde and Berndt Kjessler as special advisors to the society and non-voting members of the EC.

The EC made it clear to Olbrechts that, while the PMG was an integrated part of the society, its activities should be self-financing, and to this end she had tentatively sought the support of Serono. Following the success of the first PMG meeting in Barcelona, a follow-up was now planned within the scientific programme of the following year's annual meeting in Malmo - which around 50 PMG members attended. Malmo would also stage the second meeting of national representatives from the PMG, at which concerns over membership eligibility were raised. Some German biologists and lab technicians were unsure whether their membership was with ESHRE itself or the PMG. This was not an isolated concern and it was subsequently left to the PMG's executive to decide on appropriate membership. However, the EC continued to reaffirm that within ESHRE's membership - or its principles - there was no distinction between scientists, clinicians or paramedics; ESHRE would bring them all together as equals, even though the membership fee for the PMG was set at 50 per cent of the full fee (and the same as student membership). This policy of discounted membership fees for students and paramedics continues today.

A second international conference for IVF nurse co-ordinators and support personnel - as a follow-up to Jerusalem - had also been organised in parallel with the 1991 joint ESHRE and world congress in Paris in June 1991. The initiative had begun when the PMG's treasurer, Peter Erard (who would later join ESHRE's permanent staff at Central Office), had attended the second US national conferences for IVF nurse co-ordinators in 1987 in Norfolk. Now, with the support of Serono Symposia USA, and with two PMG members on the organising committee, an ambitious programme of workshops and oral and poster presentations was planned for Paris. Of course, as chapter 5 records, Paris was a huge success for ESHRE, and it was equally so for the PMG. More than 200 delegates from within and outside Europe attended the event, which was described as "a logical consequence" of the joint organisation between the PMG and the US nurses. Organisation of the Paris meeting was largely in the hands of Joan Jack of Serono Symposia, and in time her support of the PMG and its activities would be remembered in the eponymous exchange lecture between ESHRE's PMG and the annual International Conference for Nurses and Support Personnel in Reproductive Medicine in the USA.

The PMG award for the best paramedical presentation at the annual meeting first became available in The Hague in 1992.

Olbrechts stood down from her chairmanship of the PMG in Thessaloniki in 1993, where the PMG board elected the Amsterdam nurse co-ordinator Frederike Wegener to the post. Wegener, already a member of the PMG board, had also been a member of the local organising committee of the 1992 annual meeting in The Hague. However, her election was the beginning of what would be a sometimes frustrating period of chairmanship, when support for the PMG and PMG abstract submissions to the annual meeting were not always as abundant as board members would have wished. "It was difficult to find the people who were willing and able to give up their time to the PMG board," says Wegener, "and that's why so many of the executive tasks were taken on for several years by the same individuals. It was also difficult for us to generate new ideas and get new information from our members. We tried on several occasions by questionnaire, but the response was never very fruitful."

For example, at the 40th meeting of the EC following the 1993 meeting in Thessaloniki Wegener expressed concern at a decline in PMG membership and several notices in *Focus on Reproduction* during 1994 and 95 made appeals for papers for PMG sessions at the annual meeting. PMG attendance at the annual meeting, however, remained buoyant; more than 9 per cent of participants in Brussels in 1994 registered as paramedics - and there was a strong interest from clinicians in some of the PMG sessions. However, in Hamburg in 1995 only 11 paramedical abstracts were submitted, prompting the PMG board to question its members about their apparent lukewarm involvement.

The 1996 PMG programme for the annual meeting in Maastricht was a new kick-start for the PMG, a rejuvenated mix of invited lectures (Edwards on the physiology of fertilisation, Liebaers on PGD), the Joan Jack exchange lectureship, and members' own contributions. Among the latter was a roundtable discussion on the place of ideology in ART counseling, with members presenting Catholic, humanist, Protestant, Jewish and Islamic interests. It was also in Maastricht that Wegener announced her decision to stand down from the chairmanship of the PMG board, to be replaced following an election at the PMG assembly by Ronny Janssens, who was formerly secretary of the group. "I'd been a member of the PMG board for nearly ten years," says Wegener, "and I thought it was time for new ideas and younger people." However, it was under Wegener's chairmanship that a network of contacts among paramedics



Ronny Janssens, who in 1996 would become chairman of the Paramedical Group, won the 1994 award for the best paramedic presentation at the annual meeting in Brussels. He here receives his award from ESHRE's chairman Klaus Diedrich.

in different European Countries had been developed and that the paramedic's role within an IVF programme became properly recognised.

The PMG's first activity under Janssens' chairmanship was a pre-congress course in Edinburgh in 1997 on the manufacture of tools for micromanipulation, which at the time were still individually ground and calibrated. It was in Edinburgh too that Serono Symposia offered further support for PMG activities - and that Liz Corrigan, an IVF nurse from Bristol, was elected to the PMG board. Five year later, in 2002, Corrigan would take over as chairman of the PMG.

The Serono initiative, as well as information coming from the USA on the role of infertility nurses and their requirements for registration and continuing education, prompted Janssens and the PMG's secretary Hubert Joris to assemble an advisory committee briefed to explore the role of infertility nurses in the USA and the support and co-ordination provided by Serono. The committee met with a delegation from Serono Symposia in

November 1997 and heard that, while American nurses were required to gain 20 “continuing education units” every two years to maintain their registration with the ASRM, no such requirements were made in Europe (except for registration in the UK). Yet the committee was agreed that demands on nurse education were growing so rapidly as a result of new treatments and the broader responsibility of the nurse, that some form of “minimum standard” accreditation was desirable. The first step was the organisation of a pre-congress course for nurses at Gothenburg in 1998 in which training would become a central part. The aim, insisted Janssens, was not that nurses should become a focal point on the fringe of ESHRE’s interests but, like the SIGs, would become a forum for specialist information.

The following year, in Tours in 1999, a more specialist educational programme with a stream of paramedical presentations (from management skills to dealing with grief) would be planned in collaboration with the SIG in psychology and counselling. Also in the plans was the establishment of local associations for infertility nurses in each of the main countries represented. The PMG board hoped that Serono Symposia would give its financial and organisational support to the project, and bring the stamp of homogeneity to nurse education and practice in Europe in much the same way as it had done in the USA. The collaboration with Serono Symposia was formalised in a one-year agreement made in November 1998, and central to this agreement was a commitment by the PMG board to produce and publish *ESHRE IVF Nursing Standards* with the support of an unrestricted educational grant.

In the event, the guidelines were a long time coming, but this was more the result of language difficulties and variable standards across Europe than inertia on the PMG’s part. Liz Corrigan, who was a member of the working group, explains: “Each member of the group began by describing her own role in her own country - and even then we realised that our individual roles were so diverse that there was no way we could draft guidelines which would be applicable to all the different countries. The standards of nursing care and the qualifications which nurses needed - as well as their roles - were simply too diverse. Responsibilities in the north European countries were far more advanced, the UK most of all. In the UK, for example, nurses were already doing ultrasound scanning and embryo transfer, and in some centres even egg collection and testicular biopsies. Some of the nurses said this would not be feasible in their countries.”

In the end, the guidelines, which were eventually posted on ESHRE's website for evaluation, did little more than set out ideas on how nurses could promote in-service and certified training, staffing levels, equipment and patient information - all areas which the working group deemed within its control.

Both the pre-congress courses in Gothenburg and Tours had been well attended, with more the 70 at the former and 85 at the latter (including 45 nurses), and this flurry of PMG activity saw a rise in the group's membership as well as a rationalisation in its administrative structure. In Tours the PMG board was defined as comprising eight members, including a chairman, chairman elect, secretary and five members. Any member of the PMG would be eligible for membership of the board.

For Bologna in 2000 two pre-congress courses were planned: a "reproductive medicine team" course for nurses and a workshop on microscopy for technicians. The latter was a hands-on course which reviewed the use of optics in clinical and research ART, and presented updates on micromanipulation, fluorescence microscopy and imaging. It was also in Bologna that Ronny Janssens stepped down from the chairmanship of the PMG board to be replaced by Marc Van den Bergh, a technician from the IVF laboratory at the Erasmus Hospital in Brussels. The three-year chairmanship of Janssens had seen a rise in the PMG's profile, the first efforts to establish pan-European standards in IVF nursing, consolidated support from Serono Symposia, and a rise in the participation of PMG members in the programme of the annual meeting. In Bologna, for example, there were eight nursing abstracts approved, as against just two in 1997, and 13 from laboratory technicians.

However, the microscopy workshop in Bologna, though well organised, had not been well attended. There were also concerns among PMG board members, expressed in a letter Van den Bergh wrote to ESHRE's chairman Lynn Fraser, that Serono Symposia appeared not to be honouring their agreement in terms of the nurse guidelines and a coherent training policy. As a result, Van den Bergh told the 72nd EC meeting at Central office in December 2000 that the planning of future pre-congress courses had been somewhat disrupted. However, a joint pre-congress course with the SIG in psychology and counselling was planned for 2001 in Lausanne (which 81 attended) and 2003 in Madrid (which 88 attended), and a pre-congress course on pain relief during oocyte pick-up attracted 47 nurses in Vienna in 2002. Meanwhile, the exchange Joan Jack lectureship continued within the main scientific programme alongside a range of hot-topic high-quality

invited PMG lectures - for example, in Madrid Anna Veiga on single blastocyst transfer and Catherine Staessen on setting up an aneuploidy screening programme. In view of the part played by the paramedic sessions within the scientific programme, the EC agreed in 2000 that a member of the PMG board should have a place on each international scientific committee for each annual meeting.

Marc Van den Bergh relinquished his paramedical status in 2002 and his place as chairman of the PMG was taken over by Liz Corrigan. She had already been an active member of the group, and had recently been involved in the organisation of the PMG's pre-congress courses for Madrid in 2003 (with the psychology SIG) and Berlin in 2004. However, at the 81st meeting of the EC in April 2003, following her request for additional travel funding, she was challenged on the mission of the PMG and the quality of the abstracts submitted. There had been further discomfort for the group just months before when the draft nursing guidelines in IVF had been assessed by *Human Reproduction* as "premature and incomplete".

When Corrigan took over the chairmanship of the PMG board it was evident that interest in PMG activities at the annual meeting - particularly the pre-congress courses - was high, but at other times it proved difficult to generate active involvement. Similarly, although membership of the PMG had remained fairly static overall, it was also characterised by a flurry of memberships before the annual meeting and lapsed memberships soon after. "It was obvious over the years," says Corrigan, "that membership of the PMG would go up and down, but overall remain at around the same level. People would join before an annual meeting in the hope that they can attend or join the courses. But we found that, once they'd had their turn at the meeting, they wouldn't get another chance for two or three years, so they let their membership lapse. Only those who had the luxury of attending on a regular basis would renew their memberships. And I could see this at the meetings. Some people I see every year, but there are those I see once and never again."

Another reason, of course, for the lapsed membership was that many members, particularly those employed in hospital laboratories, would exclude themselves from PMG eligibility by gaining new qualifications and added responsibilities. The PMG's original definition of "paramedic" described a member "with no medical degree but working closely with the medical profession". And indeed, in the early days members of the PMG did not hold a first degree; it was up to them to decide whether or not they met the eligibility requirement. However, since then many members of the

group have gained university degrees - and their status today must be confirmed before they can be accepted as PMG members.

The future for the PMG, therefore, may well lie in a greater representation of nurses and a clearer definition of junior service laboratory staff (as distinct from qualified senior embryologists). Corrigan herself sees the PMG taking on a role similar to that of the SIGs, where nursing standards and laboratory support are a recognisable centre of expertise to be drawn upon in the planning of training events and the PMG programme at the annual meeting. However, in her response to the EC on the PMG's mission, she was insistent that the aims of the PMG remain much today as they were back in 1987: to encourage the exchange of information and best practice across national boundaries, to present their work before their own peers, and to develop training programmes which recognised the real interests of members - basic and more advanced nursing courses, and training opportunities for those whose interests also lay in research.

9

GROWING PAINS: 1995-1997

Following the two-year rotation principle of scientist and clinician, the Barcelona geneticist José Egozcue was elected chairman of ESHRE at the 1995 annual meeting in Hamburg to succeed Klaus Diedrich. While many of the Executive Committee's (EC) new members were also new faces to ESHRE, Egozcue had been active with ESHRE since the formation of the temporary committee in Helsinki and had served as a member of the first EC alongside Edwards, Cohen, Diedrich, Van Steirteghem, Crosignani and Sunde. In 1987 he had been elected to a second two-year term. Egozcue had also served on the scientific advisory committees of all the early annual meetings, and - with Pedro Barri - was co-chairman of the scientific committee for the fourth annual meeting in Barcelona in 1988.

Egozcue, who was then Professor of Cell Biology at the Universitat Autònoma de Barcelona, had huge international experience as an advisor to the WHO, NIH and UNESCO, and was a member of the Council of Europe's Working Group on Human Embryos and Research. After being nominated as chairman elect in 1993 Egozcue had - with the London embryologist Alan Handyside - chaired a small group briefed to explore the possibilities of forming a new Special Interest Group (SIG) in reproductive genetics. A steering committee comprising Egozcue, Handyside, Inge Liebaers and Math Pieters had been formed at the 1994 annual meeting in Brussels and had agreed to develop its interests as an ESHRE SIG in close collaboration with the International Working Group on Preimplantation Genetics. Around 30 attended the first Brussels meeting

José Egozcue

ESHRE's sixth chairman 1995-1997



José Egozcue's record with ESHRE dates back to the founding of the society when, alongside the pioneers Edwards, Cohen, Crosignani, Diedrich, Sunde and Van Steirteghem, he represented Spain on the temporary committee and became a full member of the first Executive Committee in 1985. Since then his commitments and contributions to ESHRE have remained constant: joint chairman of the international scientific committee for the fourth annual meeting in Barcelona in 1988, a member of the editorial board of *Human Reproduction*, a founder of the Special Interest Group in reproductive genetics in 1994, and chairman of ESHRE in 1995. He was made an honorary member of ESHRE in 2003.

José Egozcue is today Professor of Cell Biology at the Universitat Autònoma de Barcelona in Spain and has held numerous consultative roles in bioethics for the Spanish Parliament, Government of Catalonia, Council of Europe, European Commission, Ministry of Health of the Spanish Government, and European Association of Centers on Medical Ethics. He has formerly acted as consultant to the National Institutes of Health in the USA, the Ford Foundation, UNESCO and the WHO.

José Egozcue is also Head of the Cytogenetics Laboratory of the Institut de Biotecnologia i Biomedicina, Head of the Research Group on Preimplantation Human Embryos, a Member of the Institut d'Estudis Catalans (Catalan Academy; Biology), a member of the Royal Academy of Science, Barcelona, and was made an honorary member of the Asociación Española de Biología de la Reproducción in 2001.

in 1994, representing most of the eight centres worldwide then known to be active in this specialist field.

The SIG in reproductive genetics was formed to stimulate communication among the groups, raise laboratory standards, and encourage appropriate research in this highly experimental technique. PGD was the subject of a full plenary session at the annual meeting in 1995, and, by November that year, was included in a Campus workshop organised by Tarlatzis in Thessaloniki and, a few weeks later, in an exclusively dedicated two-day Campus workshop in Maastricht, where Santiago Munné spoke on the application of FISH techniques and on the relevance of aneuploidy, polyploidy and mosaicism in human embryos.

Another important ESHRE symposium, this time organised in collaboration with the National Institute of Child Health of the NIH, had also

From genetic diagnosis to genetic screening

While Handyside's original work in preimplantation genetic diagnosis at the Hammersmith Hospital in London had used polymerase chain reaction (PCR) to determine the gender of an embryo - and thereby exclude sex-linked genetic disease in the transferred embryo - more recent techniques had by 1994 introduced fluorescent in situ hybridisation (FISH) to detect structural chromosomal disorders in the blastomere and would eventually, as the number of specific genetic probes was extended, pave the way for preimplantation genetic screening. In time, in experimental work within the groups of Munné in New Jersey, Barri in Barcelona, Gianaroli in Bologna and Van Steirteghem in Brussels, women at risk of IVF failure (through advanced reproductive age or previous failed cycles) appeared to improve their chance of live birth through the detection of embryonic aneuploidy before implantation.

Subsequent definitions would recognise a distinction between preimplantation genetic *diagnosis* and preimplantation genetic *screening*. The former would be defined as a treatment for patients at high risk of transmitting a genetic or chromosomal abnormality to their children (which would include single gene defects), while the latter ("low risk PGD") could be applied to all infertile patients with the objective of increasing IVF pregnancy rates.

taken place just a few days earlier (on 9th December 1995) at the VUB in Brussels on the outcomes of ART, and particularly of ICSI. It was here that David Page of the Massachusetts Institute of Technology described his findings that a significant proportion of men with azoospermia also had deletions on the long arm of the Y chromosome (thus raising the likelihood of an inherited component to male infertility), and also here where Maryse Bonduelle reported data from the VUB's follow-up study of children born after ICSI.

By March 1995 the VUB had accumulated data on 1160 pregnancies following ICSI, with 491 prenatal karyotypes. Ongoing analysis now showed that of these 479 were normal (46,XX or 46,XY), six had structural aberrations inherited from one parent, and six were abnormal. In addition, 460 children had been followed-up for at least two months and the incidence of pre-term delivery, low birth weight and neonatal morbidity were all found to be within the normal range. The incidence of major malformations (2.7 per cent) was also found to be no different from that of the general population.

The VUB follow-up results were enormously important, for just two months before their presentation at the Brussels symposium a letter to the *Lancet* (1995; 345: 770) from the group of In't Veld in Rotterdam had reported sex chromosomal abnormalities in five of 15 pregnancies

achieved after ICSI. Although the findings were based on a small sample (just 15 prenatal karyotypes) the letter once again caused public alarm over the safety of an ART procedure - not least because a *Lancet* press release had, in advance of publication, splashed the letter under the headline "Bad news for 'test-tube' babies". Now, not only would the December symposium in Brussels address the scare with the VUB's own data, but it would also hear the first report from ESHRE's task force on ICSI formed the previous year under the chairmanship of Van Steirteghem.

The task force had set itself the difficult job of assembling all past data in a European ICSI registry but, by the time of the task force's second meeting in July 1995 in Hamburg, there were more than 50 groups reporting and an accurate record seemed impossible. Nevertheless, announcing the task force's findings to the Brussels symposium Basil Tarlatzis insisted that such accurate and substantial numbers were necessary to evaluate the safety and success of ICSI and lay to rest many of the anxieties raised by the apparently invasive nature of the technique and by the *Lancet* letter.

In the event Tarlatzis presented data from 65 centres performing ICSI in 1993 and '94, which reflected a total of more than 15,000 cycles, 100,000 oocytes injected, 50,000 oocytes fertilised and 40,000 embryo transfers. Of the 8313 couples having ICSI with ejaculated sperm at these centres in 1994, 93 per cent reached embryo transfer, and 21 per cent a viable ongoing pregnancy. Results were no less impressive with sperm cells aspirated from the epididymis (31 per cent ongoing pregnancy) or retrieved from

Reporting ICSI follow-up results from Brussels

Proceedings from the 1995 Brussels ESHRE/NIH symposium on the outcomes of ART were published as a supplement to *Human Reproduction* in December 1996 (11; Suppl 4) and Bonduelle's comparative study of 130 ICSI and IVF children published in the journal itself in December 1995 (*Hum Reprod* 1995; 10: 3327-3331). Subsequently, all reports from the VUB's ICSI follow-up programme were published in *Human Reproduction*; by July 1996 (1996; 11: 1558-1564) data were published on 423 children, who by February 2003, when results on developmental outcome at two years were reported, were part of an ICSI cohort in Brussels of more than 3600 (2003; 18: 342-350).

That 2003 report, incidentally, found no indication that ICSI children have a lower psychomotor development than IVF children or that paternal risk factors associated with male factor infertility were associated with developmental outcome. Proceedings of the ICSI task force appeared on the CD-rom version of *Human Reproduction Update* in 1995 and in three journal reports, presenting data from 1993 to 1996 (*Focus on Reproduction* 1995; 3: 9-12, *Hum Reprod* 1998; 13: 1737-1746, *Hum Reprod* 1998; 13 (Suppl 1): 165-177).

testicular biopsies (22 per cent). Follow-up data presented from the VUB programme by Ari Wisanto once again confirmed that 97.6 per cent of prenatal diagnoses from 900 + ICSI pregnancies were normal. However, the task force registry data would additionally show that only 71 per cent of the babies born were singletons and that all neonatal risks, whether after ICSI or conventional IVF, seemed to increase with multiplicity. Safety concerns, as always, appeared more related to higher order pregnancy than to the procedure itself. Thus, as far as ICSI was concerned, Brussels would prove an important and reassuring meeting, but not yet the grounds for complacency. "It is still too early to stop the studies," said Bonduelle at the time. "We should continue follow-up - with karyotyping, ultrasound, amniocentesis or CVS, and developmentally at birth. But we can reassure our patients that almost all babies born after ICSI will be quite normal and healthy."

Another SIG making great strides of progress by the time of the 1995 annual meeting in Hamburg was that in andrology. Under the impetus of Lynn Fraser the andrology SIG had been running its basic semen analysis course in several European countries and had now bought its own equipment for the hands-on sessions. According to Fraser and in its development of a single syllabus, the SIG had the ultimate aim of standardising semen assessment throughout Europe in line with the WHO's 1992 manual. During the Hamburg annual meeting the group held a pre-congress workshop to reach a common position on computer assisted semen analysis, acrosome reaction tests, zona-free hamster egg penetration tests and sperm-zona binding tests. The workshop's findings and conclusions - that a clear definition of the role of diagnostic andrology in male infertility should now be a priority of the SIG to set common standards and strategies - were published in *Human Reproduction* in July 1996 (11: 1463-1479).

That Hamburg annual meeting's honorary president was Dieter Krebs, whose DM10,000 "loan" in 1985 had helped Klaus Diedrich secure Bonn as the venue for the society's first event. Now, a decade later and despite competition from the World Congress of IVF in Vienna and the IFFS congress in Montpellier, ESHRE would attract more than 1400 participants and almost 400 oral presentations. Once again, the event was a huge success, and testimony if necessary to ESHRE's committed policy of centralised self-organisation.

This was also the first congress to advertise its scientific programme on the Internet and the first to give congress space to the infertility patient.

The International Federation of Infertility Patient Associations (IFIPA) had been formed in 1993 around 12 national societies. Now, its first president, Sandra Dill from Australia, spoke at the opening ceremony in Hamburg of IFIPA's aims to support the recognition of infertility as a medical condition worthy of healthcare funding and the rightful place of the patient in all discussions on infertility policy. In Australia, said Sandra, patient representation within the Fertility Society of Australia had culminated in a 1990 decision to rebate the costs of ART within the national health scheme.

Two days later, at the 11th AGM, Egozcue was confirmed as the new chairman of ESHRE, with Tarlatzis, then treasurer, now nominated and approved as chairman elect. Paul Devroey would succeed him as treasurer, while Evers, Wikland and Lynn Fraser would continue their membership of the EC. Stepping down were Van Steirteghem, La Vecchia and Zorn, to be replaced by Eberhard Nieschlag, Dominique Royère and Paulo Vercellini. Frederike Wegener would also continue her non-voting seat on the EC as the PMG representative.

The nomination and approval of EC officers had caused a momentary stir at the AGM on a procedural matter, and there was criticism from the floor that no notice of the nominations had been given. The episode was

Sixth Executive Committee 1995-1997

Chairman

José Egozcue

Chairman elect

Basil Tarlatzis

Past chairman

Klaus Diedrich

Treasurer

Paul Devroey

Members

Hans Evers

Lynn Fraser

Eberhard Nieschlag

Dominique Royere

Matts Wikland

Paulo Vercellini

Frederike Wegener (paramedical)

The Advisory Committee 1996-1998

In a move designed to increase the representative function of the Advisory Committee, the 1995 AGM approved an amendment whereby countries with more than 200 members were entitled to two representatives on the AC. The former agreements of the 1985 AGM remained in place - that countries with more than 20 million inhabitants and 15 ESHRE members could elect two members to the AC, and countries with fewer than 20 million inhabitants but more than 15 members one. The amendment resulted in an increased membership of the Advisory Committee, which now made possible double representation from Russia, Poland and The Netherlands. Members elected in 1996 were:

Safaa Al-Hasani (Germany)	Longin Marianowski (Poland)
Silvia Alvarez (France)	Karl Nygren (Sweden)
Margarita Anshina (Russia)	Kasten Petersen (Denmark)
Peter Brinsden (UK)	Jose Remohi (Spain)
Carlos Calhaz-Jorge (Portugal)	Bernard Sèle (France)
Brian Dale (Italy)	Ernst Siebzehrubl (Germany)
John Dumoulin (Netherlands)	Johan Smitz (Belgium)
Marc Germond (Switzerland)	Marian Szamatowicz (Poland)
Luca Gianaroli (Italy)	Aila Tiitinen (Finland)
Roy Homburg (Israel)	Herman Tournaye (Belgium)
Cees Jansen (Netherlands)	Turan Cetin (Turkey)
Jarl Kahn (Norway)	Cihat Unlü (Turkey)
Achilles Kalogeropoulos (Greece)	Janos Urbancsek (Hungary)
Henry Leese (UK)	Wolfgang Urdl (Austria)
Boris Leonov (Russia)	Francesca Vidal (Spain)

uncomfortable for the EC and once more emphasised a need for greater transparency - and the importance to the society of the Advisory Committee (AC), whose members *were* nominated and voted for by ballot. As a prelude to EC appointments due for ratification in two years' time in Edinburgh, the EC resolved to publish details of all the nominees well in advance, and explain the by-laws by which they are appointed.

However, the Hamburg AGM would take an even more far-reaching decision in ESHRE's administrative affairs, by approving the position of an executive director to ensure management continuity and supervision of the Central Office. The AGM was told that the post, along with a job profile, would be advertised in the newsletter. The following day the EC agreed that the executive director should be "easily available" to offer advice on the everyday affairs of the society, would have a legal mandate to represent the society, and would make a "personal commitment which excludes any form of payment or salary". The post was formally

advertised in the second 1995 issue of *Focus on Reproduction*, with a nine-point job description and stated objective "to safeguard a continuity in the management of the Society, which has become more complex over the past years". Applications for the job were invited before 31st November 1995.

Not surprisingly, for a post which offered no remuneration and which required easy access to ESHRE's Central Office, there were few applicants - and only one obviously eligible. Thus, at the 48th meeting of the EC in Brussels André Van Steirteghem, who in July had stepped down from the EC after ten years of membership, was confirmed as ESHRE's first executive director and once again took his seat at the table as a non-voting member of the EC. "There was a detailed description of the job," Van Steirteghem recalls, "but we really wanted someone who could assist the Central Office, assist in the meetings of the EC and, if questions were asked, be ready with answers. For instance, if there was a legal problem, I would make contacts with the lawyers. So it was really to ensure that the decisions of the Executive Committee were fulfilled - and that's an easy job for me to do because I know the society and I'm available to assist."

The appointment of an executive director was a reflection of how the society was now growing in size and complexity. Growing pains for the Central Office were already evident almost two years before when a second full-time member of staff was taken on to assist Bruno Van den Eede. Peter Erard, who had been a nurse member of the PMG, joined ESHRE as assistant administrative co-ordinator, while Van den Eede himself became administrative co-ordinator. At the time the Central Office was run from above the blood transfusion service at the VUB - though not since 1993 in rent-free accommodation. With Central Office now committed to organising the annual meeting, processing applications for workshop attendance, production of the newsletter as well as maintaining membership payments, there was continuing pressure on the staff - and on office space. It thus became one of Van Steirteghem's first jobs as executive director to consider the whole question of staffing and accommodation, and to steer ESHRE to more appropriate headquarters.

New offices were eventually found in the small suburban town of Grimbergen, just outside the Brussels ring road and a ten-minute drive from the VUB, traffic permitting. The EC had considered buying office space - primarily as an appropriate investment for its not inconsiderable reserves (of which by 1996 more than \$1 million was deposited in two investment schemes). However, prudence won that debate and the EC opted for rented premises. ESHRE moved into its new Central Office,

which had considerably more floor space than the VUB accommodation, in early 1996, and remained there until 2004. "We simply needed more space than we had at the VUB," says Van den Eede. "And there was so much more to do. Organisation of the annual meeting was an enormous job, and we had to learn as we went along. Just processing the abstracts and organising the published programme was a big responsibility. But all these new activities were ESHRE initiatives, and we felt that they could be better done - and done with more continuity and efficiency - if they were done in house." The new office had meeting space on the ground and first floors, and the first meeting of the EC from its own offices (its 50th in total) took place on 8th June 1996.

Also moving to new premises in 1996 was the editorial staff of *Human Reproduction*, which now totalled 12 including secretaries. Since its launch the journal had been edited (and pages produced) from Bourn Hall, but now, with space there under pressure (the journal's offices needed a new roof) and ESHRE's new contract with OUP on a firm business footing, offices outside Cambridge had been found in the converted buildings of Moor Barns Farm. The journal was now on-line and the third title, *Molecular Human Reproduction*, had been launched as a monthly stand-alone title at the beginning of the year - with around ten papers per issue planned. Though the two new titles were struggling to show any sign of profit, *Human Reproduction* and its supplements continued to do well, attracting huge numbers of manuscripts, which Edwards was rarely inclined to reject. Edwards not surprisingly came under renewed pressure to increase the rejection rate for submitted papers and keep page numbers to an agreed budgeted limit. Edwards, as bullish as ever, was more disposed to maximise income than minimise costs, but agreed to maintain a rejection rate of around 45 per cent. It was of course a question of balance; there were those (like Hans Evers and Lynn Fraser) who saw the addition of extra pages to accommodate more and more papers as a dilution of quality (like printing more bank notes), and those (like Basil Tarlatzis) who feared that an increase in rejection rate would lower the volume of clinical papers relative to scientific.

The first major task for the relocated Central Office was the hastily rescheduled annual meeting from Birmingham to Maastricht. Hans Evers had quickly won the support of his ever enthusiastic Dutch colleagues and the deadlines of first and second announcements had all been met. Evers, always the moderniser, had introduced several innovations for the 1996 meeting, including a series of "clinical tutorials" designed to help

everyday practice and decision-making, and a final-day session on “late-breaking research”. Progress, Evers reasoned, was now quicker than the programme book could keep up with. It was also to raise the profile of research that Evers elevated the poster discussions to a plenary session, “to allow poster presenters maximum exposure of their work”, with moderators as “senior clinicians and scientists”. The clinical tutorials, explained Evers, would be evidence-based, and would thereby raise for the first time within ESHRE a concept which had so far gained little ground in reproductive medicine. As subsequent meta-analyses would show, many of the studies on which consensus had been based in reproduction were of minimal quality when their “evidence” came to be graded. Maastricht also formalised and extended the catalogue of awards, and there were now fully judged prizes for the most “promising young scientist” as well as the “established scientist”, for the “most promising young clinician” as well as the “established clinician”, plus a range of other sponsored awards and ongoing exchange lectureship with the Pacific Coast Fertility Society.

Maastricht was also a big event for ESHRE’s commercial sponsors and it was here that Organon’s recombinant FSH, Puregon, was fully introduced at a pre-congress symposium. Competition between the manufacturers of gonadotrophins had always been high, but now the launch of Puregon and Gonal-F brought that competition to a new level of intensity - and the forum of ESHRE’s annual meeting was a natural battle-ground. The exhibition stands grew bigger, more colourful, more embracing, and, with the age of IT about to dawn, more animated. The study on which Organon built the introduction of Puregon would, incidentally, have met Evers’ demand for evidence-based medicine in reproduction. This comparative multicentre trial, which was published in *Human Reproduction* (Out HJ, Mannaerts BMJL, Driessen SGAJ, et al. 1995; 10: 2534-2540), was billed as the biggest randomised trial yet in IVF, involving almost 1000 couples at 18 centres across Europe. As such, the study would set a benchmark for all future late-phase trials supporting the introduction of new preparations in ART, including the GnRH antagonists a few years later.

The manufacturers’ commitment to their products also brought in more sponsored delegates to the Maastricht congress, and once again ESHRE found itself bursting at the seams - in the exhibition hall at the Maastricht Exhibition and Congress Centre and in the city hotels. Around one-third of the 2178 registrations were sponsored. Social events were fully booked and



By the mid 1990s commercial interest in ESHRE's annual meetings - especially after the introductions of Gonal-F and Puregon - had seen the exhibition stands become bigger, more colourful and more interactive. Equally, with more and more sponsored delegates, attendance at the meetings rose at a rapid rate, such that by Edinburgh in 1997 many of the meeting halls were filled beyond capacity.



The Australian reproductive biologist Roger Short was made an honorary member of ESHRE in 1996 in Maastricht. To his left are ESHRE's chairman José Egozcue, congress chairman Hans Evers, 1999 chairman Lynn Fraser, and 1997 chairman Basil Tarlatzis.

a new bussing system had to be introduced to bring in delegates from outlying hotels. "It was," said Evers, "an overwhelming success."

And success had its own attraction - not least for the other national societies around the world who also now wished to form some alliance with ESHRE. "Relationships with other societies" suddenly became a recurring item on the EC agenda. The exchange lecture scheme with the Pacific Coast Fertility Society had continued happily and informally since its inception in Paris in 1991 (when Ricardo Asch spoke on ART options for the woman over 40). Similarly, the pre-congress courses organised jointly by ESHRE and the AFS on a broad range of infertility investigation and treatment had proved popular since their introduction in Brussels in 1994. And this relationship with the AFS was now poised to develop.

In 1991 the AFS had adopted a new sub-title - The American Society of Reproductive Medicine - in recognition of its broadening range of interest, and, at the society's 50th annual meeting in San Antonio, Texas, in 1994 the new sub-title became the new official name of the AFS. Basil Tarlatzis, who had been ESHRE's main contact with the AFS, met with his new ASRM

colleagues in Hamburg the following year and they made it clear that they wished the collaboration with ESHRE to continue and develop. Thus, at the ASRM's 1995 annual meeting in Seattle Tarlatzis helped organise a further joint pre-congress course, which thereafter continued each year as a two-day event along with an exchange scientific session in the main programme. It was thus no surprise to the EC that in the AGM's report of 1996 ESHRE members from the USA totalled 168, ranking the USA fifth behind The Netherlands (274), UK (249), Belgium (237), and Germany (190). Meanwhile, total membership of the society now stood at 2700, and was still growing.

"ESHRE certainly caught the attention of our American colleagues," says Tarlatzis. "The annual meeting and the journal were both very successful and I think the society was becoming more self-confident and more extroverted - and this was seen in our collaboration with the ASRM. It was also fortunate at this time that Alan DeCherney and Joe Leigh Simpson were key figures in the ASRM and they played an important role in promoting their collaboration with ESHRE. But ESHRE was certainly becoming more confident and more international. We were finally gaining respect from our American colleagues, so this was a very important phase in ESHRE's history."

Also during 1995 ESHRE was approached by David Healey representing the Fertility Society of Australia with a request to explore the possibility of an exchange lecture scheme like that with the Pacific Coast Fertility Society. A similar request had also been favourably received from the Canadian Fertility and Andrology Society, and exchange lecture schemes were incorporated into the annual meeting's scientific programme with both societies.

However, ESHRE's relationships with other associations remained selective during this time of growth and popularity. The society had become - as Tarlatzis had said - self-confident and self-contained, and continued to turn down offers for joint events or for projects which might compromise its reputation and independence. The EC, for instance, declined an offer from Frans Helmerhorst to jointly organise a World Congress of IVF, and was initially doubtful about involvement in Fertinet, the first large-scale infertility website, because of its exclusive funding by Serono. In early 1996, however, ESHRE's website did appear for the first time via the Fertinet facility. The first ESHRE home page allowed on-line application for membership and on-line registration and abstract submission for the 1997 annual meeting in Edinburgh.

Andrology on the road in the Ukraine

In 1996 six four-day semen analysis courses had been organised in Europe by the andrology SIG and had proved so popular that they attracted attention from the Ukraine - would Lynn Fraser and her colleagues take the show to Kharkov?

The EC agreed to Fraser's request for funding for four members of the andrology SIG to travel to Kharkov, and the SIG's own equipment and several loaned Olympus microscopes were duly dispatched to the Ukraine. When the ESHRE delegation of Fraser, Chris Barratt, Lars Bjorndahl and David Mortimer arrived at the airport in Kiev on a cold April afternoon, they were told by the welcoming party from Kharkov that the equipment was still in customs and would not be released without payment of around \$11,000. Welcome to the Ukraine.

The delegation climbed into a car and, without microscopes or other equipment, set off on the 500 kilometre journey to Kharkov. Next day, after fumbling with extension leads and distant sockets, the group made some attempt at lectures, while the mayor of Kharkov exercised his authority in the customs shed at Kiev. By the end of the day the equipment arrived, and with it the chance to run the course properly. In the end all 22 students passed the written examination, and 20 the practical. However, they were, according to Fraser's polite understatement, "less than ideal circumstances" and the SIG resolved not to return until they improved.

There were several other landmarks for ESHRE during the Maastricht annual meeting, not least the ongoing involvement of the SIGs in the planning of pre-congress courses and the continuing clarification of the SIGs' role. Lynn Fraser had produced formal guidelines for running the SIGs, which included a job description for co-ordinators and a definition of how group activities might be conducted. "If the members are unwilling to become involved," said Fraser, "then the Special Interest Group will not survive" - which is what had happened to the SIGs in contraception or even in ART (which disbanded in March 1996). However, the SIGs in reproductive surgery (co-ordinated by Paul Devroey), andrology (Fraser), reproductive genetics (Handyside), reproductive endocrinology (Bart Fauser) and psychology and counselling (Heribert Kantenich) were all strongly supported and behind a catalogue of training, guideline and information activities.

In Maastricht a further SIG was added to the list when proposals from Exalto, Hustin and Jauniaux (with the endorsement of Edwards) were accepted for the formation of a new group with an interest in early pregnancy. In 1990 around 20 scientists had formed a loose association known as Euro-Team Early Pregnancy to encourage exchange of information and training. The group had already organised a session at ESHRE's 1994 annual meeting in Brussels and now planned a follow-up pre-congress course in Maastricht on early pregnancy failure and a session

in the scientific programme. It was in the course of this planning that proposals were made for the group to become a SIG of ESHRE. The place of the SIG, said its co-ordinator Niek Exalto, would serve as a link between infertility, fertility and obstetrics, with all disciplines involved. Just a few weeks later the SIG in embryology, which had been dormant for several years, was revived by Luca Gianaroli. By the time of the 1997 annual meeting in Edinburgh four of the SIGs would be responsible for all four pre-congress courses, including the joint ASRM course in reproductive surgery.

Hans Evers, who was now co-ordinator for the SIGs and training, would also report in Maastricht a substantial programme of Campus workshops and courses throughout the year, as well as a newly instituted ongoing programme of evidence-based reproductive medicine. The annual meeting in Maastricht had set the precedent with the introduction of clinical tutorials, and now a further evidence-based course was planned for Lisbon in November, with two further clinical tutorials at the annual meeting in Edinburgh in 1997, one on ectopic pregnancy and the other on semen analysis. Semen analysis courses were scheduled for Rotterdam, Leuven, Pisa and Bregenz in Austria. Taken together, the 1996 training events totalled 20, with a similar number scheduled for 1997.

The Edinburgh annual meeting was planned largely on the Maastricht format with pre-congress courses, invited lectures, free communications, and poster sessions with discussion. However, there was disquiet among some of the EC about the role of sponsors in the planning of satellite symposia. There had been comments from members that the satellite sessions were becoming too overtly promotional and compromised the scientific quality of the meeting. For 1997, therefore, the international scientific committee, which still maintained responsibility for the programme, had been asked to define the contents of each satellite event and submit them for approval to the respective sponsoring companies. Not surprisingly, the sponsors were not pleased, and felt that the move reflected a scant disregard for their huge investment in ESHRE - which in Maastricht would total almost \$500,000. The clash was, of course, the resurrection of a long-standing dilemma for the EC - how to strike a balance between ESHRE's independent scientific integrity and the necessary income which commercial sponsorship brought in. Thus, at the 51st EC meeting in Maastricht Egozcue diplomatically asked if the Edinburgh policy - with which all the EC at the time agreed - would remain ESHRE's policy. A compromise was clearly needed, and some

constructive discussion with the sponsors. There was no doubt that, if the sponsors were faced with a centrally determined symposium programme, they would simply walk away.

When the international scientific committee met at Central Office in November 1996 to finalise the programme for Gothenburg in 1998, there was apparently little change to the policy. Five sessions were identified as available for sponsorship - on GnRH antagonists, on the structure and function of FSH, on laboratory quality control, on endometriosis, and on the health of children born after ART. However, there was some compromise by the EC in their selection of companies likely to favour sponsorship and in matching symposium content with commercial interest. In Gothenburg the sponsors grudgingly accepted the situation but the issue once more raised its head a year later when the programme for Tours '99 came under discussion at the EC's 58th meeting in Brussels. After Edinburgh the EC had received letters from ASTA, Ferring, Organon and Serono complaining about the symposium policy, and making it clear that they were opposed to the preselection of content by the scientific committee. The EC finally accepted the point, and there were none who now disagreed, provided that the sponsored symposia were clearly identified in the programme book and kept separate from the rest of the scientific programme. The EC also agreed - by unanimous vote - that the second congress announcement would identify the sponsored symposium by title but would not name the papers, and abstracts would not be included in the final abstract book. Sponsors were thus left to carry out their own planning and their own promotion.

"There's no doubt that the companies were unhappy about our control over sponsorship," Tarlatzis now says. "And I think we were right to change the policy and leave the content of satellite symposia up to them. Now, they have total responsibility for the content, speakers, abstracts, and we have nothing to do with it. This was a big improvement, and we're no longer chasing them for speakers and abstracts. It's now a separate activity performed during the congress, but there's no confusion about what's happening. That's been a big step forward for the companies and for ESHRE." The closer working relationship with sponsors was developed even further under the chairmanship of Tarlatzis when business meetings with companies were scheduled. "They've helped make our relationships with sponsors more open," says Tarlatzis, "and allowed us to discuss their expectations alongside ours."

Sponsor activity in the mid 1990s - as was evident in Maastricht - put renewed pressure on accommodation and subsequent venue plans for the annual meeting. It was not easy for the EC to assess applications, not least because choices were made at least three years before the event and, with participants increasing so dramatically in number, forecasting size was not an exact science. Following Maastricht it was agreed that Bruno Van den Eede would pay site visits to all proposed venues in future, to ensure at least that four essential requirements could be met - international access, adequate meeting rooms and exhibition facilities, and enough hotel accommodation. Throughout the latter months of 1995 Van den Eede paid visits to Bologna, Bordeaux, Budapest, Tours and Valencia - but found only Tours and Bologna suitable.

But even with the policy of site visits in place, there was still unrelenting pressure on accommodation. The 13th annual meeting in Edinburgh in 1997 saw a "spectacular" increase in delegate numbers, with more than 2800 taking part in total, an increase of around 1000 in just two years. So once again, an ESHRE congress found itself stretched to the limit, with delegates at the new ICC in Edinburgh denied access to some sessions merely because the room was full. Van den Eede later explained that the decision to take the meeting to Edinburgh was based on 1500 anticipated participants, which construction plans for the new ICC were well able to accommodate. "More thought will need to be given to the selection of venues," wrote Tarlatzis in his *Focus on Reproduction* editorial - but what it meant was that the era of low-cost academic environments for the annual meeting was slowly coming to an end. By 1997 decisions had already been made for Tours in 1999, Bologna in 2000 and Lausanne in 2001 - and all three events would see some delegates commuting in from Paris by TGV, by bus from the rural hotels around Bologna, and by train from Geneva. Subsequent plans for Vienna in 2002, Madrid in 2003 (where more than 5000 took part in total) and Berlin in 2004 would all ensure that every delegate could be easily accommodated within the city and in easy reach of the congress centre. "Lausanne was the end of the era in which we could run congresses in small centres," says Tarlatzis. "It was a hard decision, but something we had to do."

By now, the scientific programme of the annual meeting had fallen into a reliable pattern of management, but, with around 500 abstracts submitted for consideration, it remained a substantial logistical challenge for the Central Office. The international scientific committee, under the

chairmanship of the society's past chairman, remained the starting point for devising the programme (with the continuing proviso that members of the committee could not be nominated as speakers). Once abstracts began arriving they were categorised into subject sections (andrology, ART, embryology, endocrinology, general programme, genetics, psychology and reproductive surgery) scanned into the computer network, and distributed to three or four members of a panel of experts for blind, weighted scoring. By the time of Edinburgh more than 150 names made up these expert groups, and co-ordination of the abstracts and of their scores was a heavy responsibility for Van den Eede and his colleagues. Successful abstracts would be slotted into the programme and transmitted to *Human Reproduction's* editorial offices outside Cambridge for publication in the abstract book.

At the 53rd meeting of the EC at Central Office in November 1996 such dramatic growth in the society had been formally recognised and plans introduced to cope with its added size and "complications". Egozcue's proposal to the EC was the formation of two new sub-committees, one to deal with the society's finances and the other to oversee ESHRE's publications. The former was to be chaired by the chairman of the society and would include the treasurer (at the time Paul Devroey), local organisers of current meetings (Wikland for Gothenburg and Royère for Tours), the co-ordinator for training (Evers) and as ex officio members the executive director (Van Steirteghem) and Van den Eede. The finance committee, said Egozcue, would discuss and formulate proposals on budgeting and accounting for the operational budget (which included Central Office, annual meetings, training and publications), investment policy, and strategies for funding scientific activities.

The publications sub-committee would be chaired by the chairman elect of the society (Tarlatis), and would include the journal editor (Edwards), the deputy editor (Helen Beard) as well as Lynn Fraser, Crosignani, Nieschlag and as ex officio members the executive director and Van den Eede. The responsibilities of this committee - which would within a few years be extended beyond all imagination - were expected to be ethical issues, the composition of the editorial board, editorial policy (which included page numbers, rejection rates, style and the organisation of supplements) and contracts with the publisher.

In addition, Egozcue proposed that ESHRE's activities in training and in the SIGs, which had since Lübeck in March 1994 both been in the sole care

of Hans Evers, be reorganised under the umbrellas of two new sub-committees, that for training chaired by Evers and for the SIGs chaired by Paul Devroey. All committee members, it was agreed, should serve for a term of two years. Thus, both SIG and training activities would from now on be dealt with in sub-committee, whose outcomes would be reported to the EC by the respective chairmen.

Egozcue's term as ESHRE chairman would come to an end six months later in Edinburgh, when Tarlatzis would take over. However, by November 1996 there had been no formal decision made on a replacement for Tarlatzis as chairman in 1999. The protocol of alternating scientist and clinician demanded that the next chairman be a scientist. There had, of course, been informal discussions, notably in Hamburg at the 1996 annual meeting, and in Capri, where past chairmen would meet at Crosignani's consensus workshops. The view was that women had not been well represented in ESHRE, with only Anne McLaren, Michelle Plachot and Lynn Fraser having full voting membership of the EC since the society's foundation in 1984. Even the AGM in Hamburg had heard from the floor that the next chairman should be female - and the obvious choice of a scientist who was also a "doer" in ESHRE was Lynn Fraser. Thus, during the autumn of 1996 Fraser was summoned from a practical biology class in her laboratories at King's College in London to take a call

Anne McLaren, the Cambridge reproductive biologist was made an honorary member of ESHRE in 1997. She was the first woman to serve on the Executive Committee (from 1987 to 1991); she was a member of Edwards's first editorial board of *Human Reproduction* and of the second ethics committee formed in 1988.



Seventh Executive Committee 1997-1999

Chairman

Basil Tarlatzis

Chairman elect

Lynn Fraser

Past chairman

José Egozcue

Treasurer

Johan Smitz

Members

Anders Nyboe Andersen

Maas Jan Heineman

Eberhard Nieschlag

Karl Nygren

Antonio Pellicer

Dominique Royère

Paulo Vercellini

Hans Evers (co-ordinator training)

Paul Devroey (co-ordinator SIGs)

Ronny Janssens (paramedical)

from Egozcue, who asked if she might consider nomination as chairman elect to succeed Tarlatzis - which was confirmed at the November EC meeting later that year.

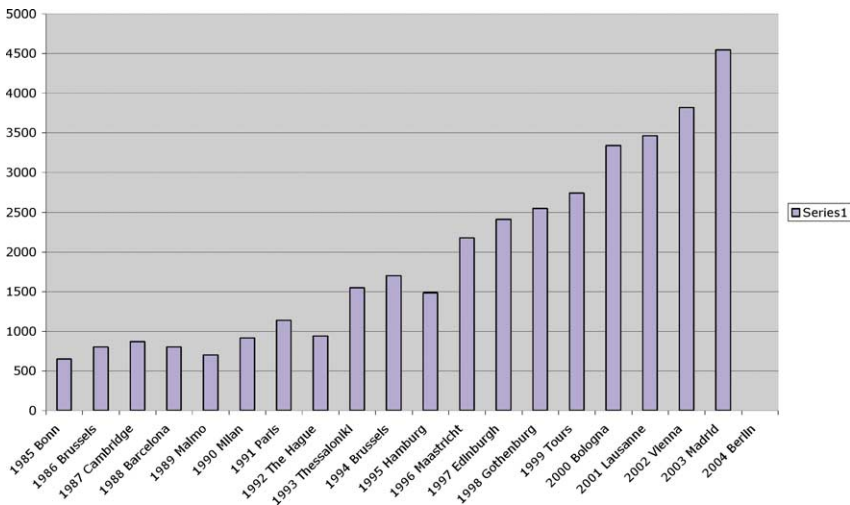
“I felt it was a great honour to be asked,” Fraser recalls, “especially to be the first woman chairman. But I still think ESHRE could have done more to develop female representation in the executive committee. If you look at those attending an annual meeting, there are many women there, but many of them come from backgrounds where it’s men who usually get to the top. There aren’t many women professors of O&G. I’ve spoken with female clinicians in various countries and I think it’s easy to rise to a certain level, but after that . . . it does sound as if there’s a glass ceiling. I was not happy when I saw this room full of men at my first committee meeting for ESHRE. Sometimes women see things differently, and it’s nice to have a variety of views.”

But Fraser’s qualifications for the chairmanship were not just that she was a woman, or a scientist - for there was no doubting her dedication and inclination for activity. She had already served ESHRE as a UK member of

the AC, and more recently, after heading up the andrology SIG, had devised guidelines on how the SIGs should be run. The andrology group itself had taken a lead in the organisation of pre-congress workshops and its basic semen analysis course had been implemented in numerous centres with a single syllabus designed to standardise qualification and procedures.

ESHRE’s seven SIGs continued to flourish, with the reproductive surgery group under Devroey hosting the joint ASRM-ESHRE pre-congress course in Edinburgh, and others - particularly in reproductive endocrinology under Bart Fauser - active in a wide range of courses. The reproductive surgery SIG had also in 1996 developed guidelines for training, accreditation and monitoring in gynaecological endoscopy, which were published in *Focus on Reproduction* (2/96) and *Human Reproduction* (1997; 12: 867-868). The guidelines, said Devroey, recognised the shift in surgical procedure from laparotomy or transvaginal access to laparoscopy or hysteroscopy, and such new techniques required evaluation and training. The SIG in reproductive surgery took on this challenge.

For his part Evers had now simplified the style of ESHRE training and had finally dropped the “under the auspices” designation in November 1996. Thereafter, courses would be “endorsed”, or not, by ESHRE at the co-ordinator’s discretion; other Campus events would be either “courses” (lectures) or “workshops” (practical). More than 20 were scheduled for 1997, many with the involvement of the SIGs.



Egozcue's chairmanship of ESHRE thus closed with an abundance of workshop activity at the society's roots and an escalating membership which, before the annual meeting in Edinburgh, finally reached 3000. The finance sub-committee was now in place to manage ESHRE's reserves, and its first decision, made at the 54th EC meeting in March 1997, was to allocate 5 per cent of the society's total surplus to the organisation of member activities, which would be financed from a dedicated fund.

It had in fact been a phase of huge growth for ESHRE, reflected in the remarkable fact that registrations at the annual meeting in Edinburgh in 1997 had risen from 1484 to almost 2500 in just two years. Such growth, not surprisingly, had had its growing pains, but the EC had tried to adapt and introduce changes to accommodate - if not anticipate - that growth. What now lay in store was not just adjustment necessary from within the society, but recognition of ESHRE's place within the world at large. It was a time to recognise ESHRE's public role, a time when the ethical issues of assisted reproduction were no longer the preserve of the initiated behind closed doors. It was a time for big decisions.

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THE END OF AN ERA: 1997-2000

In February 1997 the journal *Nature* carried a report from scientists at the Roslin Institute in Edinburgh that a live offspring had been born from an embryo created not by fertilisation but from the nucleus of an adult mammalian cell. During 1996 the Roslin scientists had transferred the nuclei from several types of sheep cells into unfertilised sheep oocytes from which their own genetic material had been removed. The renucleated oocytes were then activated to cause cell cleavage, cultured and transferred to a surrogate mother ewe. One of these transferred oocytes implanted, and was carried to term by the surrogate. The resulting lamb - known throughout the world as Dolly - thus carried the exact genetic material of the adult ewe who provided the cell (from her mammary gland), not of the sheep who provided the egg.

What everyone saw on news bulletins and front pages across the world was a chirpy well grown lamb whose life had been derived not from fertilisation but from the genetic material of a single adult cell. To this extent, Dolly was a clone of the six-year-old ewe who provided the mammary cell whose nucleus was transferred and activated in the donor enucleated oocyte. Thus, to the public at large it was now apparent that adult cells do have within their structure the genetic material necessary for the production of living organisms. Despite the Roslin's protests that "nuclear transfer" was not cloning, in the public's perception the age of the clone had dawned.

For ESHRE the birth of Dolly would have both direct and indirect lasting consequences. First among them was that now the ethics of reproduction by any “assisted” method had become a matter of enormous public debate. The public, of course, was not asked to understand the techniques of nuclear transfer, nor the mysteries of DNA technology, but it did have a crude understanding that life was now possible without fertilisation and that mammals could be “replicated” from a single adult cell.

What made the ethical impact of Dolly that much more intense was also that science and medicine - like everything else in public life - were now subject to so much more public scrutiny. The information technology revolution was moving so rapidly that science was no longer the preserve of scientists, medicine no longer the preserve of doctors. Accountability was now an item on the agenda of all news organisations, controversy a matter not just for experts but now for the public at large.

Of course, ESHRE was no stranger to the ethical debates of reproductive science and medicine. Jean Cohen had defended the safety of IVF against Marsden Wagner’s complaints in 1991 and against claims of an added risk of ovarian cancer in 1993, the ICSI task force had been formed partly to provide the numbers necessary to underpin its success and its safety, and numerous annual meetings had called for restraint in the number of embryos transferred in IVF and a reduction in the incidence of multiple pregnancies. Indeed, with ESHRE’s pioneers acutely aware that any progress in their discipline would inevitably attract discussion, the first AGM in Bonn in 1985 had even then approved the formation of an ethics committee, with Cohen as its chairman. By 1989 that committee, after hosting several sessions at annual meetings and taking part in congress and regulatory discussions, had set about the huge task of issuing guidelines on ART and prenatal diagnosis. These first appeared in the third newsletter of 1991 and were subsequently updated for publication in 1995 (*Hum Reprod* 1995; 10: 1246-1271).

Two years later, in March 1997, the Executive Committee (EC) had received a request from the legally qualified London physician Françoise Shenfield that the ethics committee, whose activities since 1995 had been no more than modest, should be reformed as a Special Interest Group (SIG) in ethics and law. The EC agreed and, by the time of the first meeting of the newly established SIGs sub-committee in November that year, heard from Shenfield that the group would be officially formed the following year (1998) and attempt to assemble its ideas and positions at a pre-congress course in Tours in 1999.

But the birth of Dolly brought a new intensity to the ethical debates in reproduction for which the SIG was not yet prepared but which ESHRE could not ignore. At the 54th meeting of the EC at Central Office, just a few weeks after the Roslin announcement, two items under “any other business” both gave an indication of the public responsibility now felt by the EC to take a lead in the reproduction debates. The first came from the new EC member Karl Nygren, who tentatively proposed that ESHRE should support a long-term programme of IVF data collection in Europe. However, on the second and more immediate item of “cloning”, the EC felt “that ESHRE should take a position”, and asked Van Steirteghem to produce a statement in which ESHRE expressed its support for the procedure in research but its objection when applied for reproductive purposes in humans. The statement, which called for a “five-year moratorium” on reproductive cloning in humans, was approved at the 58th EC meeting in November, and published in *Focus on Reproduction* later that year (3/97). The main ethical objections, said the report, were that the efficiency of embryonic development after nuclear transfer is so low (Dolly was the only success from a series of 277 nuclear transfers) and the chance of abnormal offspring so high that experimentation in humans was deemed “unsafe” and “reprehensible”. The statement added that a voluntary moratorium “is an effective means of preventing procedures that are potentially harmful”.

The ESHRE statement was one small voice in what was now a gigantic world debate, even involving government leaders and government-funded research programmes. In the USA President Clinton called for more information on the issues, and in the meantime federal funding for embryo research in the USA looked even less likely. In Europe the EU itself (through its biotechnology advisory body), the Council of Europe (for an amendment to its Bioethics Convention), the UK’s Human Fertilisation and Embryology Authority and France’s Comité Consultatif National d’Ethique were all involved in consultations as a prelude to their own declarations and legislation - which were somewhat pre-empted by UNESCO’s amendment to its Declaration on the Human Genome and Human Rights, adopted in November 1997, which forbade the replication of identical human beings.

It was a sign of the times that ESHRE’s approval of its statement on human cloning took place alongside a further discussion of how its contents might be communicated to the press and European Parliament. And it was here for the first time that the Executive Committee discussed

the possibility of hiring a professional public relations company - to give shape to ESHRE's public responsibilities and ensure that its views were heard. By the end of 1998 a British communications agency (led by Margaret Willson, a former head of PR for the Imperial Cancer Research Fund in London) had been hired to organise an ESHRE press office at the annual meeting within a structured media plan. It would be ESHRE's first exercise in media relations since Edwards assigned a press office to his arrangements for the Cambridge annual meeting in 1987. At a pre-congress media workshop in Tours Edwards himself not surprisingly addressed the assembled press on future issues for reproductive medicine and guided them through the ethical conundrums. The ultimate idea, said ESHRE's new chairman Lynn Fraser, "is that ESHRE becomes an obvious source for informed comment on all matters relating to assisted reproduction".

The Swedish gynaecologist Karl Nygren, along with his Danish colleague Anders Nyboe Andersen, had joined the EC at the 1997 AGM in Edinburgh. It was here where José Egozcue stepped down from the chairmanship to be replaced by Basil Tarlatzis, with Fraser standing by as chairman elect. Also joining the EC were the Spanish gynaecologist Antonio Pellicer, the Dutch gynaecologist Maas Jan Heineman, and the Belgian reproductive endocrinologist Johan Smits as treasurer. (Because ESHRE remained registered as a charity in Belgium, local law insisted that at least one voting member of the EC should be Belgian). Leaving the committee were Matts Wikland, Hans Evers and Paul Devroey. However, both Evers and Devroey would remain as ex-officio members of the EC as co-ordinators of training and the SIGs, while Nieschlag, Royère and Vercellini would retain their places under the consecutive two-year terms allowed in the by-laws.

The question of an IVF registry run under the auspices of ESHRE was not a new concept. Back in 1993 at the 37th EC meeting Tarlatzis had reported on the recent formation of an International Working Group for Registers on Assisted Reproduction and it was hoped that ESHRE might be involved in establishing a framework for data collection for Europe. However, even then there were anxieties over the practicalities of such a venture, and warnings from the epidemiologist Carlo La Vecchia that 100 per cent compliance would be necessary for the numbers to have any scientific value. Meetings with the French epidemiologist Jacques de Mouzon (who organised France's IVF data collection for FIVNAT and was a leading member of the IWGRAP) took place at the annual meeting in Thessaloniki

but there was no agreement on how progress might be made. Arne Sunde thought the IWGRAP survey forms were too complicated (certainly for Norway), while Tarlatzis remained convinced that the only way forward was indeed with the IWGRAP.

In December 1994 De Mouzon and his French clinical colleague Jean-René Zorn submitted a proposal to the EC for a European registry for IVF. ESHRE, they said, “appears to be the best organisation to set up such a European register” (“the most developed organisation in the reproductive technology field in the world”), and proposed that the working group running the register through the Central Office should be put together as a SIG. The project, they insisted, needed big numbers to demonstrate improvement in success rates, to evaluate new procedures, and to reaffirm the methods’ safety. Europe, they added, was now responsible for around half the world’s total IVF cycles.

However, despite the strong case for the proposal, the EC remained unconvinced that water-tight data collection was possible, and finally, after consultations with La Vecchia and the Australian epidemiologist Paul Lancaster then working on data collection for IFFS, appeared to abandon any notion of developing its own registry. Tarlatzis thus proposed that ESHRE should join forces with the IFFS’s programme and try to extrapolate from its world data a “simple” report for Europe.

While data collection through ESHRE’s ICSI task force continued without interruption (the third report was published in a *Human Reproduction* supplement in early 1998 (Suppl 1: 165-177)) there seemed little enthusiasm for any broader ambitions, and the whole question of an IVF registry for Europe lay neglected and unaddressed until 1998 when, at the 59th meeting of the EC in March, Nygren and Nyboe Andersen submitted a formal proposal for the establishment of a European IVF monitoring (EIM) committee. It was noteworthy that the two Scandinavians spoke of data “monitoring” and not data “collection”, although in their proposal “collecting” and auditing data (from national registries) were essential activities. European monitoring, they said, was needed to prevent IVF activities in any country from “derailing” as a result of negative publicity. It was also noteworthy that spreading the findings of the EIM committee each year to the public and medical profession was deemed an essential priority.

As was by now ESHRE’s usual way, a small committee was formed to take the Scandinavian proposal forward, and this group met at the next annual meeting in Gothenburg in June 1998. Nygren there informed the

EC that the aim of the EIM committee's annual report would be to cover the number of cycles, the characteristics of patients (age, indications), efficacy, cost and risks. By the next meeting of the EC at Central Office in November 1998 the EIM committee had moved on yet again and now had for approval various survey forms on which a summary of national registry data might be returned. Thus, with the EC now more reassured than ever before of the project's feasibility, the EC finally agreed to go ahead. The EIM was formally established at the annual meeting in Tours in 1999, and attracted representatives from 19 European countries, who each provided an overview of national data collection registries. Just six of the 19 countries had compulsory requirements to report data to a national register (Denmark, The Netherlands, Norway, Sweden, Turkey, and UK), while the remainder ran voluntary systems which only rarely included every clinic in the country.

It was a long time coming, but the EC's decision to encourage the EIM consortium would have important and far-reaching consequences. At a Campus workshop on data collection in Bologna in November 2003 Hans Evers, by now an immediate past chairman of ESHRE, would say that the EIM committee in initiating data monitoring in Europe "has played a pivotal role in drawing our attention to the many great advantages of recording accurately what we are doing in our daily clinics. We now all agree that monitoring systems are mandatory for clinical science to progress." By then, the EIM committee had produced three annual reports and found in its first survey of 1997 a clinical pregnancy



Karl Nygren, along with his Scandinavian colleague Anders Nyboe Andersen, in 1989 made a formal proposal to the Executive Committee for the formation of a European IVF Monitoring committee. By the close of 2004 the committee had published four reports, its work recognised as one of ESHRE's most important activities.

rate per transfer of 26.1 per cent after IVF, which by 2000 had increased to 28.4 per cent (Hum Reprod 2000; 16: 384-391, Hum Reprod 2004; 19: 490-503). However, while a steady increase in pregnancy rates was encouraging, the EIM committee still found in 2000 a similar rate of multiple pregnancies to 1997 (26.4 per cent), and huge differences between countries in the number of embryos transferred and in the rate of triplets. More than 60 per cent of cycles in Russia, Spain, Ukraine, Hungary and Greece had three or more embryos transferred, while in Denmark, Finland and Sweden the figure was well under 10 per cent. Thus, in their analysis and conclusions Nygren and Nyboe Andersen suggested that only one “parameter of excellence” would eventually be relevant, the number of embryos transferred in order to achieve a singleton delivery.

Also intent on data collection at this time was the SIG in reproductive genetics under the chairmanship of Alan Handyside. At its business meeting in Edinburgh in 1997 the SIG had broadened its scope to include the self-styled PGD Consortium as a “sub-activity”. Handyside had set out the group’s objectives as drawing up guidelines to promote what was then deemed best practice and to collect data from the 20+ centres then performing PGD (who by then had loosely identified themselves as the PGD Consortium). One important objective of collecting the data was to provide a basis for the follow-up of pregnancies, which had so far not been done.

By now, with Paul Devroey as co-ordinator, the SIGs had finally begun to take on a consistent shape within ESHRE - as a reference source for training, guidelines, speakers and papers for the annual meeting, referees and expertise within the field - but there was some disquiet among the EC that the genetics SIG was stepping onto new ground with its expert business meetings and ambitious programme of data collection. However, there was a successful precedent in the activities of the ICSI task force and a recognition that activity in PGD should indeed be monitored centrally. The SIG’s aim was to survey the availability of PGD for different conditions, to collect prospectively and retrospectively data on the accuracy, reliability and efficacy of PGD, initiate follow-up of pregnancies, produce guidelines of best practice and formulate a consensus on the use of PGD. The idea was that each centre registering with the programme and submitting an initial response (by fax) would provide a basis of data for a preliminary report. The SIG had also planned a pre-congress course for June 1999 in Tours and two hands-on workshops in Brussels and London.

Reporting progress in PGD

The reproductive genetics SIG's first report, which appeared in *Human Reproduction* in December 1999 (1999; 14: 3138-3148) and covered activity from January 1997 to September 1998, presented data on 323 couples referred for a variety of monogenic and chromosomal disorders. Investigations had led to 392 PGD cycles, resulting in 302 embryo transfers and 66 clinical pregnancies. However, the group also reported that, with biopsy, FISH and PCR protocols all being used, clearly "no consensus exists on technical aspects".

By the SIG's second report reviewing activity from October 1998 to May 2000 (Hum Reprod 2000; 15: 2673-2683) cumulative data on PGD was now "considerable": over a period of seven years (the oldest PGD cycle reported was from 1994), referral data on 886 couples, 1318 PGD cycles, 163 pregnancies and 162 babies had been collected. To the SIG, these were encouraging figures, showing first "that the practice of PGD is becoming more and more established, and an increasing number of different applications is emerging", and second, "that collecting these data is worthwhile". Already, by the end of 1997, the SIG was aware that more than 20 diseases were amenable to diagnosis by PCR, while an ever-increasing number of FISH assays were potentially applicable to sex determination, recurrent abortion, and the diagnosis of some translocations, deletions and aneuploidy.

However, by the time of the group's third report covering results into 2001 (Hum Reprod 2002; 17: 248-249) it was now evident that the "striking" feature of PGD was its emerging use for gender screening "for social reasons"; 78 cycles from 675 new referrals added to the database were for "social sexing", and this, said the report, was a matter for discussion. Not surprisingly, PGD would also be specifically addressed by the ethics and law SIG a year or two later, and its findings published in *Human Reproduction* (2003; 18: 649-651). Certainly, gender selection, like cloning and the source of therapeutic stem cells, were hot issues of debate and would test the ethical judgements of ESHRE throughout the last few years of the 1990s.

Another group making progress under the re-organised structure of the SIG sub-committee was that in embryology, which had been revived in Maastricht in 1996 under the new chairmanship of Luca Gianaroli. The group had planned a pre-congress course for Gothenburg in June 1998 featuring sessions on quality control within an ART programme, embryo culture, structural abnormalities in the embryo, ICSI and visual assessment. However, quality control in laboratories remained an ongoing concern of the group, which had begun in 1990 when *Focus on Reproduction* (1/90) published the first guidelines on good laboratory practice. Five years later these were updated, with the addition of newer procedures and agreements (Hum Reprod 1995; 10: 1246-1271). The SIG in embryology now planned to revise the guidelines yet again, this time to take account of further developments (such as blastocyst culture and transfer) but also to implement a common quality control system for all embryologists associated with ESHRE. This necessity, said the group, arose from an "increasing awareness that embryologists have a duty to prevent

unintentional incidents that might result from poor practice in the laboratory”.

The third ESHRE guidelines on good laboratory practice appeared in *Human Reproduction* in October 2000 (15; 2241-2246) and included paragraphs on insemination by ICSI (including the use of surgically retrieved sperm cells and preparation of oocytes), embryo scoring, the use of sequential culture media, and the recommendation “as a general rule” that no more than two embryos or blastocysts should be transferred. “In cases where more than two embryos are replaced, the couple has to be extensively informed on the risks of multiple gestations,” the guidelines added.

The Finance and Publications Committees - like the SIGs sub-committee - had been formed in November 1996 in response to the burgeoning attention these subjects now required in the society’s administration. It was, indeed, a measure of their importance that the EC had agreed that the Finance Committee should always be chaired by the current ESHRE chairman and the Publications Committee by the chairman elect. It was envisaged at this time that the main tasks of the Publications Committee would involve ethical issues (plagiarism in the journal, for example), the composition of the editorial board (limited to a maximum of 40 for *Human Reproduction*, 15 for *Human Reproduction Update*, and 20 for *Molecular Human Reproduction*) and the ever present questions of budget, page numbers, manuscript quality and rejection rate.

However, by the third meeting of the Publications Committee chaired by Basil Tarlatzis in June 1997 (his last as chairman elect), there were issues of a more contentious nature to be considered. While *Human Reproduction Update* had been introduced following an agreed decision by ESHRE and OUP to absorb two other review titles and free some of *Human Reproduction’s* pages for original papers, there was concern in the committee that *Molecular Human Reproduction* had developed as of its own volition as a bound-in sub-section of the main journal. When *Molecular Human Reproduction* a year later (1996) was rolled out as a separate title, there were even more unexpected headaches for the committee, with no clear view of its profitability or loss, nor of its rating for impact factor as determined by the Institute for Scientific Information. In 1996 *Human Reproduction* had scored highly in the impact factor categories of O&G (second of 50 behind *Fertility and Sterility*) and second in reproductive biology. *Molecular Human Reproduction*,

however, enjoyed no such visible success, and from day one was a loss-maker for OUP and ESHRE - and a sensitive problem for the EC and Publications Committee.

However, the other two titles continued their inexorable progress, with Edwards introducing web publication of papers in 1998 and thereby allowing the fast-track publication of Debates, original papers and abstracts. By the following year *Human Reproduction* and *Update* had reached numbers one and two in the O&G category rankings. Lead-time to publication in the main journal, incidentally, was now running at around eight months, a delay which Edwards calculated as considerably less than that at many competing journals. In 1997 *Human Reproduction* received more than 1200 submitted manuscripts, with standards “very high”, according to Edwards. The rejection rate was maintained at around 40 per cent.

And for the Finance Committee the annual meeting continued to return healthy surpluses. The 13th annual meeting in Edinburgh in 1997 had once again broken all records, attracting more than 2800 participants in total and generating a 15 per cent return on turnover for the society. The 14th



At the opening ceremony of ESHRE's 14th annual meeting in Gothenburg congress chairman Lars Hamberger introduced a brand new Volvo as the glittering prize for the best poster.

annual meeting in Gothenburg was planned along the same familiar lines as Edinburgh, with now more than 700 abstracts submitted for oral or poster presentation. Following blind weighted scoring, 193 were retained for oral presentation, and 280 by poster - once again a reflection of the high scientific regard in which the annual meeting was now held. In addition to 176 free communications, Gothenburg scheduled 12 plenary sessions, five sponsored symposia, one session on evidence-based medicine, and one session on late-breaking research. Again, numbers of participants continued to climb - with almost 3000 in attendance - and again there



Both Howard and his wife Geogeanna Jones were made honorary members of ESHRE in 1998 in Gothenburg. In his acceptance speech Howard recounted how he had heard the news of Louise Brown's birth while moving from Johns Hopkins in Baltimore to a new division of reproductive endocrinology at the Eastern Virginia Medical School in Norfolk, Virginia. A local reporter had asked what it would take to have an IVF baby in the USA, to which Jones replied: "Just a little money." Next day, following the local press report, an anonymous donation was made, and the Joneses were up and running in Norfolk.

was pressure on hotel rooms and meeting space within the Gothenburg congress centre. Venue selection, Tarlatzis once again reminded the EC, would continue to be “difficult”.

However, Gothenburg - like Maastricht and Edinburgh - generated a welcome surplus and a much needed injection to the society’s reserves. ESHRE, as executive director Van Steirteghem would report to the 63rd EC meeting in November 1998, was actually spending more than it was earning, and capital reserves were rather shakily standing at around €800,000. This, said Van Steirteghem, “should serve as a warning sign for future policy” and as a call for tighter budgetary control.

By now, with Tarlatzis beginning his two-year term as ESHRE chairman, Lynn Fraser as chairman elect had become chairman of the Publications Committee and, at its routine meeting that November, had raised for the first time the prospect of the 1995 journal contract with OUP coming to an end in December 2000. All at that meeting - including Fraser, Crosignani, Heineman, Mandelbaum, Nieschlag, Tarlatzis, Van Steirteghem and Edwards himself - agreed that a new contract was necessary, mainly because there had been so much change since 1995: there were now three titles (as well as a regular output of supplements), not one, *Human Reproduction* and *Update* were both extremely successful (with the highest impact factors), and both were now generating appreciable profits. And there was also the question of *Molecular Human Reproduction* struggling along, draining some profit from ESHRE and some high impact manuscripts from *Human Reproduction*.

While editorial quality was the ultimate objective for the journals, the immediate concern for the Publications Committee was the financial return they could generate for the society. “We couldn’t keep the journals going if they didn’t make any money,” Fraser explains, “because the two consistent sources of income for ESHRE are subscriptions from the members and profits from the journals. We could never be certain about the annual meeting - that will always be a risky event, and that’s why it has always been our financial aim to have sufficient reserves to overcome just one catastrophic meeting.”

The 1995 publication contract with OUP required at least 12 months’ notice of any change, so the Publications Committee and EC had little more than a year to reach a clear view of their intentions. To help them along, Fraser - as chairman of the committee - had lined up an independent consultant to assess ESHRE’s position, as well as the contract proposals due to be made by various publishers. OUP had already asked to make an

Basil Tarlatzis

ESHRE's seventh chairman 1997-1999

Basil Tarlatzis has had a long and hugely influential history with ESHRE. He became editor of the revived ESHRE newsletter *Focus on Reproduction* in 1991 and treasurer of the society that same year, he was chairman of the first independent annual meeting in Thessaloniki in 1993, became chairman of the society in 1997, and as past chairman steered some of the most difficult ESHRE committees during negotiations for *Human Reproduction's* new publishing contract in 2000.

Basil Tarlatzis qualified in medicine at the National University of Athens in 1974. After military service in the Greek Navy he became a resident in surgery at the Naval Hospital in Piraeus and, in 1977, resident in obstetrics and gynaecology at the Aristotle University of Thessaloniki; in 1982 he obtained his PhD in the Medical Faculty of the Aristotle University of Thessaloniki, Greece. In 1982 also, after a short visiting fellowship at Wayne State University in the USA, he took up a three-year postdoctoral fellowship in O&G at Yale.

Tarlatzis returned to Thessaloniki in 1986, becoming Assistant Professor in Obstetrics, Gynecology and Reproductive Medicine in 1992, Associate Professor in 1998 and Professor in 2004. Since 1985 he has also been director of the Geniki Kliniki IVF Centre in Thessaloniki.

Tarlatzis has been a tireless committee man for ESHRE, as chairman of the Special Interest Group in reproductive endocrinology, as a member of the ethics committee and in the ICSI task force, as well as in Publications and Finance Committees. In 2007 Tarlatzis will become president of the International Federation of Fertility Societies (IFFS).

offer, and several others had expressed an interest; the EC was committed to finding the best commercial deal, and one which the AGM would accept at its next meeting in 1999 in Tours.

Tarlatzis told the EC in November 98 that there seemed three contractual options: first, to continue with a fixed profit-share agreement as in the current contract with OUP; second, to raise the stakes and require a fixed guaranteed income each year (assuming agreement on production costs and circulation); and third, the biggest gamble, to grasp the nettle of self-publication as Edwards had urged five years ago and run the journals as an ESHRE enterprise. The EC saw virtue and risk in all options, and made no firm conclusions other than to hire Fraser's nominated consultant and form a small task force dedicated exclusively to a new publications contract. Central to that contract, the EC insisted, would be the structure and responsibilities of the editorial office, as well as financial arrangements. The task force would be chaired by Tarlatzis and would also include Fraser as chairman of the Publications Committee, Egozcue as past chairman, and Van Steirteghem as executive director.

By March 1999 ESHRE had formally requested and received tenders from six publishers, including OUP. Following assessment by the consultant Sally Morris, who was by now retained by ESHRE, four were rejected, leaving two front-runners to be further considered when the task force next met in April, OUP and Cambridge University Press. But also on the table for consideration, following last-minute telephone calls to Tarlatzis at home, was yet another proposal for self-publication from Edwards and the journals' deputy editor Helen Beard; Edwards would personally present his case on the first day of the two-day taskforce meeting at Central Office.

In the event, Edwards's case for self-publication was not much different from what the EC had heard in 1994 - that OUP offered little editorial support but still exacted overheads which were "disproportionally high". Edwards's argument, therefore, rested on the assumption that self-publication would allow greater editorial independence for ESHRE and, by removing OUP's overheads and profit-share, greater financial return.

For the veterans of the EC and those on the Publications Committee it was a familiar argument, but one no less intensely felt by Edwards or passionately expressed. Sally Morris looked in detail at the proposal, and applied to it the same criteria as she had to the commercial bids. She felt less confident that the journals' huge recent profitability would be maintained under self-publication, particularly as production costs would not benefit from the economies of scale found in a professional publishing house.

Once again, it was a difficult time for the EC, which found itself yet again forced into a commercial decision which had enormous personal implications. But as a commercial decision it was one which effectively came down to a matter of principle - either the safe option of guaranteed returns from a professional contract, or the high-risk route of independent enterprise. And once again, there were no simple solutions. Some societies did well out of self-publication, while others - like the ASRM, which had abandoned the self-publication of *Fertility and Sterility* in favour of a commercial contract with Elsevier in 1997 - had fared less well.

Discussion among the EC was intense, but it was the view of Lynn Fraser, as chairman of the Publications Committee, which finally swayed a decision - that ESHRE's aims for its journals were to ensure high scientific standards in their editorial content and *guarantee* a minimum income for its members. Now, as five years ago, was not a time to risk that income.

“The feeling in the EC,” Fraser recalls, “was always that we were simply looking for a professional publisher. None of us felt we had the time or expertise to be directly involved in publishing the journal. That was basically our position.” Thus, the EC rejected as a principle the self-publication option and agreed to present to the AGM in June the commercial tender option.

Edwards was again disappointed, but this time he felt bitterly frustrated too. He had been editor of *Human Reproduction* since its launch in January 1986, and in that time had seen it grow to become the world’s leading title in obstetrics and gynaecology, with more than 50 papers published per issue, more than 3000 subscribers and a gross annual profit of more than £200,000. Moreover, in 1994 production of the pages for *Human Reproduction* had passed from OUP to the editorial offices at Moor Barns Farmhouse, such that from then on responsibility for the journal’s entire activity - except advertising, marketing, finances and web publishing - had been achieved under Edwards’s direction and control.

Although Edwards had been allowed time at the April task force meeting to present his bid in person, he was especially frustrated that his proposal for self-publication was not given the consideration he thought it deserved. For their part, Tarlatzis and his task force colleagues had several queries about the proposal’s business planning and financial forecasts (as they had of OUP and CUP) and were never comfortable with Edwards’s initial bid. “There were lots of questions about the costings,” says Fraser. “So we quickly decided to stay with our original short list, and that was immediately communicated to Bob.” Nevertheless, although the EC had rejected the principle of self-publication and the task force had now formally rejected Edwards’s own proposal, the matter was not yet closed - at least not to Edwards, and he returned to Cambridge intent on reviving his bid and persuading the task force.

In May Edwards submitted an updated proposal which appeared to address the business-plan questions raised by the task force. But, to turn up the heat, he also drafted a motion for inclusion at the AGM in which he and other members would seek the membership’s support for self-publication. “We believe that this step (self-publication) would be beneficial to the stature and development of the Journals to increase the business flexibility and financial return to ESHRE and to provide a progressive working environment for the dedicated team of journal staff,” the draft proposal read. Among those supplying written support for the motion ahead of the AGM were Jean Cohen, Jacques Cohen, Colin Howles

from Serono, Howard Jacobs, Roger Gosden and former colleague Botros Rizk, then at the University of South Alabama. "Being involved with academic medicine and publishers for over two decades, I cannot overexpress my strong support for the motion to make the ESHRE journals independent of all publishers," wrote Rizk.

It had been the EC's hope and intention that the AGM in June would merely have to approve the task force's decision to pursue contractual negotiations with two publishers to safeguard the best editorial and commercial interests of ESHRE. It was a motion likely to be approved unanimously and without fuss. But now, as Edwards upped the stakes in a further (and maybe final) bid for independence, here was a much more contentious issue for the AGM, and one that was likely to drive an acrimonious divide into the ESHRE membership. "Most of us in the EC thought Bob's motion for the AGM was divisive," says Fraser, "and felt we should avoid it at all costs. We didn't want some catastrophe at the AGM. The bottom line was that the society would not benefit from having a public bust-up with Bob. It was disagreeable all round. So it was decided that his revised proposal would be considered once again - not just by the four members of the task force but now by a new committee which included all the past chairmen."

Discussions with Edwards about his AGM motion were held first in Cambridge with Fraser herself, and subsequently with Tarlatzis and Van Steirteghem. The outcome of these often heated talks was that, on the condition that Edwards withdrew his AGM proposal, the EC would table a new motion for the AGM which would allow a full business proposal from Edwards alongside those of OUP and CUP. The three proposals would now be considered by a re-formed task force, which comprised the new chairman (Fraser), the new chairman elect (Evers), and all past chairmen. This new task force, under the chairmanship of Tarlatzis, would first meet at Crosignani's consensus workshop in Capri in August and subsequently in November, when a final recommendation would be made to the EC. "It is imperative," Tarlatzis wrote to Edwards, "that we all agree in advance that we will accept the final decision of this Task Force and Executive Committee."

Edwards's new proposal, signed by himself and Helen Beard, was submitted by fax on 15th June. As requested, it provided a detailed financial summary and the outline of a legal framework within which ESHRE could run a commercial operation in the UK. "We do not foresee any financial

risk once the new structures have been functioning for one to two years," the proposal read. "By then, income and profits could be considerable."

As before, the task force sought advice on the bids, from publishing consultant Sally Morris and from ESHRE's own legal and accounting advisors in Brussels. Edwards would again be offered the chance to present his proposal personally in Capri, and answer any questions; however, as an interested party, he was asked not to join his past chairmen colleagues in the task force deliberations or voting. The AGM in Tours in June duly accepted the EC's plans for the journal, and thereby left the task force to assess Edwards's bid for self-publication alongside the commercial tenders from OUP and CUP. For his part, Edwards sought more legal and financial advice and, just two days before the task force's meeting in Capri on 28th August 1999, submitted yet another proposal for independent publication, his third of the year. The essence of this third proposal was that the ESHRE journals would be run by a UK-based company operating under English law but under the eye of a board of directors appointed by the EC. So yet again in Capri, the task force



In August 1999 at the consensus meeting on Capri Edwards's case for the self-publication of the ESHRE journals was heard by a newly formed chairmen's task force chaired by Basil Tarlatzis. Seated clockwise around the table are Lynn Fraser, Tarlatzis, Bruno Van den Eede, Hans Evers, Klaus Diedrich, André Van Steirteghem, Robert Edwards, Pier Giorgio Crosignani and Jean Cohen. The task force made its final decision the following November.

heard the renewed proposals, but yet again there were still many hard questions for the task force to ask, and many answers for Edwards yet to provide, not least on the proposed company's legal and fiscal status and on the issue of electronic publishing, to which ESHRE still felt itself vulnerable.

"What made us feel threatened in this situation," Tarlatzis recalls, "were developments like PubMed Central or other initiatives we heard of to offer all journals on the web, free of charge. We also heard of big libraries in the USA starting to discontinue their individual subscriptions to journals because they would get them through conglomerate sources - libraries therefore would subscribe in groups and share the journal. All these new trends in journal publishing raised a fear of what was to come - maybe less revenue, fewer subscriptions."

Thus, with the task force's questions ringing in his ears, and increasingly frustrated at his lack of progress, Edwards returned from Capri and set about the composition of one more proposal before the task force made its final recommendations in November. The task force's specific questions on legal and fiscal issues were addressed point by point, as were its questions on corporate structure and management, and on finance. But even so, there were still omissions from this fourth proposal - and with these Edwards's editorial colleagues in Cambridge were now palpably uncomfortable, particularly with regard to pensions and salaries, training, IT support, financial control, personnel support and management structure. A few days later these concerns were raised at a staff meeting at the editorial offices and later expressed more formally in a joint letter to Tarlatzis.

Events would subsequently show that this letter would finally be the beginning of the end of Edwards's bid for self-publication and to this most sensitive and difficult of issues for ESHRE.

Edwards met with each of his editorial colleagues individually to try to resolve their personal issues and assuage their doubts. But the fact remained that most of the staff at Moor Barns Farmhouse felt that a move to independence as reflected in Edwards's fourth proposal would compromise work and efficiency and challenge their pension rights and job security. Thus, when the task force met on 6th November at Central Office to make its final decision, Edwards agreed that his plans could not be pursued without the support of his editorial staff, and he therefore called for two votes as a basis for the task force's conclusions: the first on independent publication in principle, and the second on independent publication in reality and thus without the support of his editorial staff.

Three voted in favour of the first motion, and six against; no-one voted in favour of the second motion, although one of the nine abstained.

There was thus no further debate, no more discussion, no more acrimony. The task force would recommend to the EC that ESHRE should pursue a contract with a professional publisher and abandon any notions of self-publication. Without the support of the editorial and administrative staff, any proposal for independence was a non-starter, and this, Tarlatzis recalls, had changed the entire discussion.

Thereafter, the task force took more advice from its consultants and set about the less contentious task of deciding to which of OUP or CUP the ESHRE contract would be awarded. Financially and editorially there were not many differences between the two, but now the taskforce had new questions to ask on pension schemes, reporting structures, job appraisal and career opportunities. Site visits to Oxford and Cambridge took place, where more questions on electronic publishing and subscriptions were raised and answered. The EC would make a final decision at its 68th meeting on 11th December, to which Edwards as editor of the journals was invited. In those discussions Edwards appeared to express no clear preference, acknowledging the pros and cons of both bids. So in the end it was left to a vote and, with the view prevailing that CUP's bid was not sufficiently advantageous to warrant a change, the vote went unanimously in favour of OUP.

ESHRE's new contract with OUP was scheduled to start right away, from January 2000, and not 2001 as the former contract would have allowed. Thus, the new terms would be in place for six and not five years, providing a guaranteed income for ESHRE of 65 per cent of the journals' revenue, or at least £200,000. "The guaranteed minimum income will provide ESHRE and the journals with a safety net at a critical time, when it is unclear just how publishing will evolve or, indeed, whether it will survive at all," Fraser wrote at the time.

However, if Fraser and her colleagues on the EC thought the saga was drawing to an end, there were still more dramas to come. Just weeks into the new contract Edwards was yet again voicing concerns to Tarlatzis and Fraser over organisational arrangements in the editorial office, but behind the details of his complaints there surely lay a far more deeply rooted awareness that he now felt less able to edit the journals as he wished. And even he, with such an apparently endless supply of energy and commitment, had back in November acknowledged to Lynn Fraser and her colleagues that the task of editing three

titles of such wide acclaim and attracting such a huge number of manuscripts was probably now beyond the capabilities of any one individual. He would, therefore, step down as editor of the journals at some point during 2000.

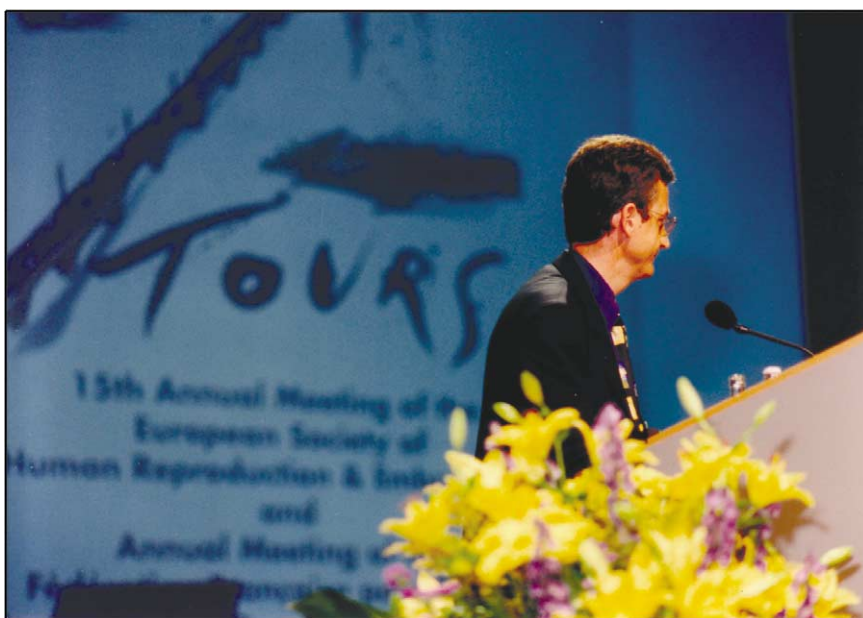
Thus, sooner rather than later, on the morning of 30th January 2000 Basil Tarlatzis as head of the chairmen's task force received the fax he knew would eventually arrive. Edwards gave three months' notice of his resignation as editor of the ESHRE journals. He insisted that his decision was not influenced by the EC's new contract with OUP, nor by the "difficulties" he encountered in the "independence debates". He was, he said, intending "to cut his duties on the journals" anyway, and now apparently was the right time.

Thus, in this brief and deeply felt fax Robert Edwards cut himself adrift from the journals he had created over the past 15 years. Throughout that time, at Bourn Hall and latterly Moor Barns Farmhouse, he had worked tirelessly and selflessly on manuscripts whose publication would depend ultimately on just one criterion, the belief that there was worth in all scientific study and merit in almost all the papers he received. It was his intention back in 1985 that *Human Reproduction* would offer a home to scientific work in Europe, and it was testimony to the realisation of that ambition that, just weeks before he announced his resignation, *Human Reproduction* and *Human Reproduction Update* occupied the first two impact factor positions in the two categories of O&G (ahead of *Fertility and Sterility* and the *American Journal*) and reproductive biology. And within a few months *Molecular Human Reproduction*, as its evaluation criteria fell into place, would achieve the highest rating in reproductive biology, putting the three ESHRE journal into the top three positions in their fields.

Eras come and go with remarkable frequency in medicine. No sooner does a new age dawn than another looms large on the horizon. But for ESHRE the resignation of Edwards from his editorship of the journals truly was the end of an era. Back in 1987, when Jean Cohen had succeeded Edwards as chairman of ESHRE, Cohen had set himself the task of giving ESHRE "the energy to find its own way", to take on a momentum of its own. And it's testimony to that same continuing energy and self-momentum that the resignation of Edwards from the journals caused so little disruption to the society's day-to-day business. And even the transition of each journal from one editor to the next seemed - at least to most - a seamless passage.

Thus, when the dust had settled and the EC could take stock of its other more routine activities the records would show that the 1999 annual meeting in Tours - despite the potential “catastrophe” at the AGM - would prove to be ESHRE’s most successful event ever, and the starting-point of its press initiatives. The meeting was held in conjunction with the Fédération Française pour l’Etude de la Reproduction and the event’s local secretary, Dominique Royere, would report a total attendance of almost 3500. Records were also broken in the number of abstracts submitted and papers presented.

It was also in Tours that ESHRE’s self-contained website (www.eshre.com) was formally launched, with a bank of computers at the first cyber-café whose home pages defaulted unashamedly to ESHRE. The EC tentatively hoped that the website would take over from *Focus on Reproduction* as the society’s main communication channel, and this quickly proved the case, with each of the SIGs appointing their own page editors and all annual meeting procedures - programmes, abstract



ESHRE’s 15th annual meeting in Tours, chaired by Dominique Royère, launched ESHRE’s website and was the first to run a dedicated press centre for journalists. Every attendance and abstract record was broken in Tours. Royère served on the Executive Committee from 1995 to 1999, and was a member of the European IVF Monitoring committee.

submission, registrations - available on-line. ESHRE's first webmaster, Herman Merckx, was a Central Office appointment, but within a year traffic and demand on the website had forced the formation of a website sub-committee chaired by the young Dutch gynaecologist Jan Kremer. By December 2000, when Kremer described the sub-committee's technical challenges to the 72nd EC meeting, the ESHRE site was taking more than 450 hits a day, the most popular pages being "How to become a member" and abstracts from the annual meeting.

The press programme under the direction of Lynn Fraser and PR consultant Margaret Willson had also taken the work of ESHRE - and reproductive medicine - to a wider European audience, especially in the UK. Not only had the press room in Tours provided journalists with the tools of their trade (telephones, desk space, news releases and a non-stop supply of food and drink), but a pilot project of monthly press releases from selected *Human Reproduction* papers had generated wide coverage throughout 2000. Reports from a diverse selection of studies - that men would take a contraceptive pill, that comprehensive chromosomal analysis was now possible using a whole genome amplification technique, or that very low frequency electromagnetic fields impaired mammalian follicle development - were all widely covered in the press. The criteria for selecting papers for press releases, Fraser told the EC, were "novelty and originality" (especially important in the tabloid-minded UK) and scientific interest (usually assessed as an advance in the field).

It was also in Tours in 1999 that the eventful chairmanship of Basil Tarlatzis came to an end. When he became chairman elect four years earlier he had seen the society gaining in self-confidence and in financial security. Then, with the formation of the Publications and Finance sub-committees, and the re-organisation of the SIGs, a phase of restructuring had begun. "My personal goal," says Tarlatzis, "was to make the running of the society and the handling of our success more efficient. That was my main objective, to impose a more formal structure. We did extend our collaborations with other international societies - the mutual exchange of courses with AFS, our ties with Canada, Australia, the Middle East - to make ESHRE into a truly international society. But extroversion was not our only objective; institution was another, and that's why we pursued the sub-committee policy, and put more formal structures in place."

The year 1999 also marked the less momentous end of another era for ESHRE in the discontinuation of Serono's support of the Campus

workshop programme. Since 1989, at the suggestion of Crosignani, Cohen, Edwards and Van Steirteghem, Serono had agreed to fund four Campus workshops a year, a total sum of \$48,000. This posed yet another problem for the EC, especially as, under the common-sense eye of Hans Evers, the whole ESHRE training programme had settled down into a simple system of Campus events (hands-on workshops or teaching courses) or ESHRE-endorsed activities (in which the society had no financial involvement). By now, ESHRE's role in meeting requirements for continuing medical education in reproductive medicine was considerable: in Tours that year more than 450 had registered for the six pre-congress courses offered, and in 2000 nine pre-congress courses were planned for Bologna in addition to three Campus events and a winter course staged by the SIG in reproductive endocrinology. Whatever the funding situation, the EC agreed, the training programme would have to continue, with funding arranged with other outside sponsors or from the society's own reserves. Serono's withdrawal of funding was a headache for the EC, but not one likely to disrupt the programme which Evers had set out for the next year or two.

The EC anyway had more immediate and threatening issues to resolve in finding a successor to Edwards as the editor of the journals - and not just one, because, as Edwards himself had already acknowledged, the job of editing three titles each at the top of its field was a job beyond the capabilities of one individual. Three editors would be needed, and needed quickly before Edwards stepped down at the end of April 2000.

II

THE AGENDA FOR THE FUTURE: 2000-2004

Speed was of the essence, but the task force knew that their choice of editors for the three ESHRE journals should leave no room for error. The transition from Edwards to his three new successors should be at no cost to editorial quality or commercial success. The Publications Committee first asked for nominations from the Executive Committee (EC), journals task force and editorial boards. There were, of course, certain minimum requirements for each of the posts, not least of which were availability and an absence of conflict of interest - with other societies or the pharmaceutical industry. That reduced the pool considerably, but finally short-lists were produced for the EC's 69th meeting on 15th April 2000. That meeting agreed that three names from each short-list would be contacted and asked first if they were interested, and next if they met the basic requirements. Those fitting the bill would be interviewed in May by a committee composed of Fraser (ESHRE chairman), Evers (chairman elect), Tarlatzis (past chairman), Van Steirteghem (executive director) and Mandelbaum and Heineman from the Publications Committee, and a final decision taken shortly after.

The three successful candidates were formally and unanimously approved by the EC at its 70th meeting just prior to the 16th annual meeting in Bologna, and their names publicly announced at the AGM three days later. They were David Barlow as editor-in-chief of *Human*

Reproduction, Bart Fauser as editor-in-chief of *Human Reproduction Update*, and Richard Ivell as editor-in-chief of *Molecular Human Reproduction*.

Barlow, who was Professor of O&G at the University of Oxford as well as Clinical Director of the Assisted Reproduction Unit at the city's John Radcliffe Hospital, had enormous clinical and administrative experience. From 1998 he had been a member of the HFEA, Britain's statutory licensing authority for assisted reproduction, as well as a member of council of the Royal College of Obstetricians and Gynaecologists. Ivell, a zoologist by training, was Director of Reproductive Sciences at the Institute for Hormone and Fertility Research of the University of Hamburg. He too had huge research and publishing experience, and was on the editorial board of many journals, including *Molecular Human Reproduction*. However, of the three Bart Fauser was perhaps best known to ESHRE and its members. He was then Professor of Reproductive Medicine at the Erasmus Medical Center in Rotterdam, had been a regular speaker at recent annual meetings, and for the past several years had also been chairman of ESHRE's Special Interest Group (SIG) in reproductive endocrinology.

In the May 2000 issues of all three journals Edwards explained the circumstances of his resignation, reaffirming his belief "that scientists and clinicians should organise their own publishing affairs". He added: "It is my failure to persuade others of the benefits of this course of action that precipitated my resignation." But he was warm in his thanks to his colleagues and to ESHRE's "Executive Committee at the time" for founding and administering *Human Reproduction*. He acknowledged that the rising number of submitted papers, as well as "new challenges", would certainly demand changes in editorial structure. And with that, this brief record of gratitude to those who had supported him and the journals, he was gone.

Behind him, however, he left a record of unequivocal achievement - both in the founding of the society and in the creation of *Human Reproduction* - which will not be matched again. Those early days, let's not forget, were the days when manuscripts were edited as hard copy and set in type as galley proofs, when letters were written by typewriter (or hurriedly by hand) and sent by post, when slides did not appear at the click of a PowerPoint button. For Edwards - and his founding-father colleague Jean Cohen - ESHRE and its journal were a mission, to bring scientists and clinicians in reproduction together and give a welcome to their work. And those young scientists - like Arne Sunde - who remember Edwards in those

Lynn Fraser

ESHRE's first woman chairman: 1999-2001

Lynn Fraser joined ESHRE's Advisory Committee in 1990 and two years later became co-ordinator for the Special Interest Group in andrology. She joined the Executive Committee the following year and in 1999 became the society's first female chairman, taking charge of the society during the two most difficult years of its history.

Lynn Fraser grew up and was educated in the USA. She took her first degree in zoology at the University of Colorado and her doctorate at Yale, where she was awarded a Ford Foundation postdoctoral fellowship. In 1972 she moved to London to take up a scientific post for the Medical Research Council, where she remained for five years.

In 1977 she became a lecturer at Chelsea College and in 1993, following its merger with King's College, Professor of Reproductive Biology in the division of Anatomy, Cell & Human Biology, School of Biomedical Sciences.

In 1990, after a decade of membership, Lynn Fraser was elected chairman of the Society for Reproduction and Fertility (until 1993), and has also been chairman of the management council of that society's journal, the *Journal of Reproduction and Fertility* (now named *Reproduction*). From 1994 to 2001 she was a member of the editorial board of *Human Reproduction*, and since 1991 has been an inspector for the UK's Human Fertilisation and Embryology Authority.

pioneer ESHRE days remember that mission, the inspiration which would fire others to follow. Like Coleridge's ancient mariner, who "holds him with his glittering eye", Edwards too was compelling, and few could resist his inspiration. But ESHRE finally said no. Inspiration and belief were not enough, the risks to the society too great alongside the certainties which a commercial contract would offer.

For Lynn Fraser this protracted and eventually sorry episode had been one which she never foresaw, nor one for which she was ever prepared. "I now know a lot more about publishing than I did in 1998," she ruefully told OUP's editorial director when the new contract had finally been signed. For her it had been a stormy as well as challenging chairmanship, and, as she now says, she "hadn't really bargained for everything which came her way". Looking back, she now cites the conclusion of the new journal contract with OUP - with its revised staff structures as well as a new associate editor scheme for the review of manuscripts - as her major achievement, but it was also under Fraser's chairmanship that ESHRE's public profile was raised, its boundaries opened up, with a well developed website and dedicated press programme.



Lynn Fraser's chairmanship was one of the most stormy of ESHRE's history. When her term ended in Lausanne in 2001, new contracts for the journals had been negotiated, new editorial structures were in place, and ESHRE was taking on broader, more public responsibilities. She had also taken a critical look at the composition of ESHRE's committees and the criteria by which members were selected.

And of course, as ESHRE's first woman chairman she cast a critical look at the composition of ESHRE's committees and the criteria by which members were drafted in. So when the time came for nominations to be heard, she always made sure that female members were properly represented. In fact, when Fraser became chairman elect in Edinburgh in 1997, there were no other female members of the EC. However, in Tours in 1999, when Fraser herself became chairman, Jacqueline Mandelbaum also joined the EC (and would stay in place for two two-year terms) to be followed in 2001 by the Swedish gynaecologist Christina Bergh, the

Eighth Executive Committee 1999-2001

Chairman

Lynn Fraser

Chairman elect

Hans Evers

Past chairman

Basil Tarlatzis

Treasurer

Johan Smitz

Members

Anders Nyboe Andersen

Luca Gianaroli

Maas Jan Heineman

Jacqueline Mandelbaum

Joseph Neulen

Karl Nygren

Antonio Pellicer

Paul Devroey (co-ordinator SIGs)

Ronny Janssens (paramedical)

Belgian clinical embryologist Josiane Van der Elst, and the Spanish embryologist Anna Veiga, and in 2003 by the London geneticist Joyce Harper. All three of the 2001 appointments continued to a second two-year term; thus, during 2003-2005, four of the EC members were female.

It was towards the end of Fraser's chairmanship - at the December 2000 EC meeting where next year's committee changes were discussed - that Fraser and chairman elect Hans Evers proposed a firmer principle for the composition of the EC. Until then, as Evers himself had noted, a place on the EC was earned by selection, not election, but to earn that selection candidates had to have shown their energy and commitment to ESHRE - usually in the training programme, or SIGs or Advisory Committee (AC). "It quickly became quite clear to me," says Fraser, "that whoever we proposed for Executive Committee membership should be somebody with the potential to be a chairman of ESHRE." But even that, she felt, as ESHRE grew and grew, would not be enough to give backbone to the ESHRE of the 21st century in a new and expanding Europe. "We also had to look at the Executive Committee in a much more dispassionate way - and we

Representation in the new Europe

ESHRE's forays into eastern Europe gathered pace after the unification of Germany in 1991, with several training courses organised in Moscow (1991), Budapest (1996), Kharkov (1997), Kiev (1999) and Prague (1999 and 2002).

Moreover, by the end of 2003 (from a total membership of 4547) ESHRE had 61 members from the Czech Republic, 49 from Hungary, 50 from Poland, 33 from Romania, 86 from Russia, 15 from Slovakia, 16 from Slovenia, and 14 from Ukraine. By then it had also been agreed that the 23rd annual meeting in 2006 would be held in Prague.

In a bid to engage further the representational input of the Advisory Committee - which yet again had increased in size as a result of border changes and in compliance with article 15 of the by-laws - membership was extended to four years and the committee's advisory and policy-making duties more clearly defined. In 2003 the Executive Committee agreed that the Advisory Committee should meet at least once a year on its own and also with the EC at the annual meeting.

In 2002 the Advisory Committee comprised:

Thomas Abyholm (Norway)	Frank-Michael Kohn (Germany)
Margarita Anshina (Russia)	Leonid Kuzmichev (Russia)
Antal Borsos (Hungary)	Dimitris Loutradis (Greece)
Angelina Correia Tavares (Portugal)	Nicholas Macklon (Netherlands)
Fedir Dakhno (Ukraine)	Tonko Mardesic (Czech Republic)
Erik Ernst (Denmark)	François Olivennes (France)
Anna Pia Ferraretti (Italy)	Marian Senczuk (Poland)
Robert Fischer (Germany)	Alex Simon (Israel)
Richard Fleming (UK)	Anne-Maria Suikkari (Finland)
Juan Garcia-Velasco (Spain)	Marian Szamatowicz (Poland)
Joep Geraedts (Netherlands)	Filippo Ubaldi (Italy)
Stephan Gordts (Belgium)	Bulent Urman (Turkey)
Claes Gottlieb (Sweden)	Greta Verheyen (Belgium)
Mark Grossman (Spain)	Stéphane Viville (France)
Mark Hamilton (UK)	Veljko Vlajsavljevic (Slovenia)
Hikmet Hassa (Turkey)	Valeris Zukin (Ukraine)
Karl Illmensee (Austria)	

achieved that by automatic representation of certain countries. In addition, we tried to ensure that each member of the Executive Committee should have one or more identifiable roles. It now means that everyone has a job, and everyone is actively involved."

The scheme which Fraser and Evers proposed effectively ensured that those countries with more than 250 members - such as the UK, Belgium, Germany, The Netherlands and Italy - should always be represented on the EC, and others, with smaller memberships, would be represented as

before on the AC. It would also mean that the number of EC members would probably rise, to a maximum of 11 or 12.

It was also at this time that ESHRE forged closer links with the European Board and College of Obstetrics and Gynecology (EBCOG) for the development of more formalised sub-specialist training in reproductive medicine. EBCOG was a group commissioned by the European Union of Medical Specialists, which was affiliated to the EU to harmonise and improve the quality of medical specialist practice within Europe. Education was deemed the key to such harmonisation and the EUMS was pursuing a common policy in medical training. EBCOG had in turn approached Tarlatzis as ESHRE chairman in 1999 to develop guidelines for training in reproductive medicine. Both Tarlatzis and Paul Devroey pursued this collaboration with EBCOG such that in November 2000 a draft contract with ESHRE was proposed and accepted by the EC in December 2000. The contract meant that ESHRE would always participate in EBCOG council meetings, and that ESHRE would run postgraduate training courses in reproductive medicine at EBCOG conventions.

ESHRE, as reflected in the andrology SIG's efforts to establish commonly agreed parameters in semen analysis, was keen to augment its role in the medico-political environment of Europe. Indeed, one reason for Tarlatzis's support of the EBCOG initiative was that it might bring ESHRE closer to the EU. However, ESHRE's links with the EU had not been as great as Edwards and the pioneers might have hoped for more than a decade ago. Back in 1987 Edwards had secured formal consultative status for ESHRE with the Council of Europe by which the rapporteurs of the various advisory committees of the Council would consult ESHRE for advice along with other scientific societies. However, over the ensuing years that advisory function had been rarely exercised, and ESHRE, while committed to guidelines and harmonisation through the SIGs, had not played such a role at the political level.

However, in the mid-1990s the andrology SIG had taken part in an EU initiative to develop guidelines on the medical and ethical aspects of gamete donation in Europe, then deemed necessary not just because of inconsistent medical standards but especially because of the free movement of Europeans within the EU. Members of the andrology SIG had retreated with other nominees to the ancient priory of Corsendonk in Belgium and there, under the direction of Chris Barratt, Yvon Englert, Claes Gottlieb and Pierre Jouannet, had produced the Corsendonk consensus for the EU (which was discussed at an andrology SIG

workshop in Maastricht in 1996 and published in *Human Reproduction* in 1998 (13; 500-501) and as a supplement to volume 13 that same year). The Corsendonk agreement was not the usual exercise in Euro-unity, but more a consensus on minimum standards which in some respects would be “mandatory” (in the recruitment and screening of donors, some technical procedures and evaluation), and in others “strong recommendations”. The thorny issue of donor payment was not ignored, and took the line that payment may well compromise the informed consent of the donor. “Medical care should be independent of money,” Englert said at the time, and based on need, not profit.

Although with less formalised authority, and more at the initiative of the SIGs, other sets of guidelines were now taking shape with such frequency that Fraser and other members of the Publications Committee felt that a more systematic means of publication in *Human Reproduction* was necessary. Luca Gianaroli and his colleagues in the embryology SIG had published their guidelines for good practice in IVF laboratories in October 2000, the PGD Consortium had published three data collection reports by May 2001, and the EIM committee was by now committed to the publication of continuing data returns.

But by far the greatest output in terms of guidelines was set to emerge from the SIG in ethics and law recently revived by Françoise Shenfield. Already, by the start of 2000, Shenfield’s group had three drafts of guidelines in circulation, the first on the moral status of the embryo, the second on gamete and embryo donation, and the third on cryopreservation. Approval of the drafts was not a simple procedure, and the EC felt obliged to recognise in the production of all ESHRE guidelines that some, like those of the ethics SIG, would simply reflect the position of ESHRE, while others, such as those on semen analysis or good laboratory practice, would set out a benchmark on minimum standards.

For Paul Devroey, who by now had been co-ordinator of the SIGs for four years, this was the direction he had always wished the SIGs to take. Guidelines, he says, “are the final goal of the SIGs”, and in their development he saw a coming together of expertise, discussion and consensus. “But it was not always like this,” he recalls. “Many in ESHRE thought that the principal task of the SIGs was purely educational - to devise Campus workshops and pre-congress courses. I disagreed with that. I thought it should be both. And now I think that ESHRE’s progress will be found in those meetings of people with the same interests, who come together to discuss their projects, or organise some educational

activity - to instruct others in the state of the art, and instruct themselves in mutual discussion.”

The activities of the ethics and law SIG (known now as a “task force”) embodied all that Devroey wanted to see. It was active, it brought experts together, it organised training, it developed guidelines, and its recommendations were based on clinical and scientific evidence, not on local legal policy. By the time the ethics task force had published its first statement in 2001 - on the moral status of the pre-implantation embryo (Hum Reprod 2001; 16: 1046-1048) - its members comprised Shenfield, Guido Pennings, Claude Sureau, Jean Cohen (who had headed the first ethics committee shortly after ESHRE’s foundation), Devroey and Tarlatzis, and its aim was clearly set out: “to establish a code of ethical practice . . . rather than to take part in a theoretical philosophical debate.” These were hard, not soft, endpoints. The statement first defined the “embryo” according to the biological sequence of its development, noting particularly that the “pre-implantation embryo is human and deserves our respect as a symbol of future human life”. The statement next summarised the “lack of consensus” in Europe over the legal status of the embryo, and went on to review and advise on those areas of practical concern - PGD, embryo freezing, embryo donation and research, which included gene therapy, cloning and embryonic stem cells. All these issues would in time be addressed more specifically by the task force. In the meantime, however, the statement reiterated ESHRE’s public positions - such as the five-year moratorium on reproductive cloning declared in February 1997 or acceptance of the principle of somatic cell gene therapy.

The task force’s second statement - on the cryopreservation of embryos - appeared the following year (Hum Reprod 2001; 16: 1049-1050) and sought to address two questions: who decides what should happen to human embryos which are supernumerary to a fresh IVF cycle, and what should be done with them. The task force presented a seven-point answer which was effectively based on the informed agreement of both parties involved and in the full knowledge of the options available to them. The delicate issue of deciding an embryo’s fate after the death of one of the partners was also addressed, and outlined the possible options when the female partner survived - as had occurred in Britain in the well publicised case of Diana Blood: that the surviving partner decides, or she decides only with prior written consent of the deceased, or no transfer is possible. The task force was “reserved” in its opinion, but did note that prior written consent

by the deceased should be available in order to meet the basic principle that parenthood should not be imposed on someone against his or her will.

The third statement of the task force was published in 2002 (Hum Reprod 2002; 17: 1407-1408) and reviewed the ethical issues of gamete and embryo donation. As a basic principle the statement agreed that it was indeed ethical for families to be created through the donation of gametes and embryos, but recognised, as a matter of public interest, society's right to regulate by law. The question of anonymity raised three basic rights - the parents' right to anonymity, the donor's right to privacy, and the child's rights to know his or her origins. There was no simple answer, but the task force proposed a "double track" whereby both donors and recipients would choose identity or anonymity before entering the donation programme. As in the Corsendonk agreement, the task force described payment for gametes as unethical, but did not exclude the reimbursement of expenses. "Excessive payment", as was now evident in all egg donation programmes in the USA (where sums up to \$5000 were advertised for oocytes), was deemed "to challenge the very notion of informed consent by the donor".

The ethics and law task force was just one of six SIGs to organise pre-congress courses at ESHRE's 16th annual meeting in Bologna in 2000, which yet again broke all attendance records (with almost 3700 participants). Not all those courses, however, were well attended, and it gave the EC some room to tighten up the pre-congress programme at future meetings, with perhaps fewer courses (there were nine in Bologna) and subjects covered less frequently.

However, among the active SIGs in Bologna was that in endometriosis, which had been formed in 1999 and was now running its first training event. Both the SIG and the pre-congress course - run as a mini-symposium to review new developments and treatments in endometriosis - had been steered by the Swedish gynaecologist Agneta Bergqvist and the Belgian gynaecologist Thomas D'Hooghe. The conclusions of the course, which were published in *Human Reproduction Update* (2002; 8: 79-83), were that both intrafollicular and intraperitoneal inflammation at the time of menstruation are each important processes in the biology of endometriosis and may therefore affect oocyte quality, and thereby fertility. Surgical treatment preceded by hormone therapy appeared the best means for treating the infertility, the symposium concluded.

It was also in Bologna that ESHRE's EIM committee presented its first report on IVF and ICSI - data returns from 500 clinics in 1997 with pregnancy follow-up through 1998. Nyboe Andersen and Nygren

presented data from more than 200,000 treatment cycles performed in 18 countries, a half of them in France, Germany and UK, with the other 15 countries making up the rest. However, they noted that the availability of IVF treatment was highest in the Scandinavian countries and The Netherlands - with 1500 treatments per million population in Finland, compared with just 580 in the UK and 330 in Portugal. In countries with such high availability, IVF would now account for around 2 per cent of all children born. However, live birth rates were found fairly consistent among different countries, at around 22 per cent per cycle. This first EIM report, with more than 200,000 cycles monitored, put into perspective the huge scale of ART in Europe when seen alongside similar exercises in the USA (SART's 1999 report for 1996 with 65,000 cycles), Latin America (5332 cycles) or Australia/New Zealand (24,124 cycles).

The local secretary of ESHRE's millennium meeting in Bologna was Luca Gianaroli, who had been elected to the EC in 1999 after successfully steering the SIG in embryology. Three years earlier Gianaroli, from his own SISMER clinic in Bologna, had begun a collaboration in preimplantation genetic screening with the Spanish biologist Santiago Munné, then working with the group of Jacques Cohen at Saint Barnabas hospital in New Jersey.

Subsequent results from the collaboration, presented at ESHRE's annual meeting in Tours and derived from 982 consecutive ART cycles performed between September 1996 and October 1998 in patients aged between 29 and 43, showed that the highest implantation rate was in those patients aged 38 to 43 years who had had embryo screening - a rate of 26.6 per cent. Embryos from this group were screened by FISH for aberrations of chromosomes X, Y, 13, 14, 15, 16, 18, 21 and 22. By contrast, those in the same age group who did not have PGD screening achieved an implantation rate of just 15.6 per cent. The 38-43 years PGD group also achieved a remarkable cumulative pregnancy rate of 90 per cent after three cycles of treatment. The investigators thus proposed that the use of PGD screening for aneuploidy would give older women the same probability of pregnancy as younger women.

With such results and such local interest, it was inevitable that pre-implantation genetics would be high on the agenda for ESHRE's millennium meeting in Bologna. The international scientific committee had scheduled invited lectures on nuclear transfer (from Ian Wilmut of the Roslin Institute, the "father" of Dolly), autosomal genes in infertility and a report from ESHRE's own PGD Consortium. Munné himself spoke and confirmed that the risk of aneuploidy rises up to 70-fold as women get



The 16th annual meeting in Bologna, with Luca Gianaroli (left) as congress secretary and Pier Giorgio Crosignani as congress chairman, once again broke all records. Gianaroli himself had joined the Executive Committee in 1999, had revived the Special Interest Group in embryology in 1996 and had been a member of several ESHRE committees, notably the European IVF Monitoring committee and the PGD Consortium.

older. Many embryos don't implant, he said, and of those that do the result can be an early miscarriage or handicap.

What was notable about the Bologna programme - as Gianaroli himself observed and was evident in the PGD and high-tech embryology sessions - was the re-emergence of basic science as a major influence in assisted reproduction. Gianaroli saw it as a trend coming full circle, in which the initial place of science - characterised in the work of Edwards or Testart in the 1970s - was once more taking on a leading directional role. "In the beginning," Gianaroli explained, recalling the early difficulties of clinicians like Jean Cohen in Paris, "the major part of IVF was done in

Preimplantation genetic screening

Although there were by now many single (or even multiple) gene defects amenable to diagnosis by PCR (a technique by which a single copy of DNA could be amplified millions of times), Gianaroli and Munné were concentrating on numerically abnormal chromosomes in the embryos of couples at risk of IVF failure (and not on individual couples at risk of transmitting inherited disease). They were not using PCR, but fluorescent in situ hybridisation (FISH), a technique allowing the simultaneous analysis of multiple chromosomes in a single cell by fluorescently labelled probes.

The first paper of Gianaroli and Munné, published in *Fertility and Sterility* in December 1997 (68; 1128-31), confirmed that there was a high proportion of chromosomally abnormal embryos (55 per cent) in poor prognosis IVF patients - such as those of an older maternal age or with a history of failed IVF. Identification and deselection of the aneuploid embryos would allow the transfer of only those embryos which appeared chromosomally normal. In the 1997 *Fertil Steril* study embryo transfer with at least one normal embryo was performed in ten cycles, while in the non-analysed control group 41 embryos were transferred in 17 cycles. Results revealed an implantation rate of 28 per cent in the study group (40 per cent pregnancy rate), but a 12 per cent implantation rate in the control group. "It was quite clear," said Gianaroli at the time, "that the ability to select and transfer embryos with normal FISH results has an immediate impact on implantation."

In 2000, at ESHRE's annual meeting in Bologna, Munné described 65 translocation diagnoses made in New Jersey, whose spontaneous abortion rate was only 15 per cent after transfer - compared with 95 per cent of non-screened pregnancies. Further data from Gianaroli's group showed that 30 per cent of screened embryos successfully implanted after transfer - even in women over 38. Indeed, said Gianaroli, pregnancy rates in the PGD cycles were around three times higher than in comparable non-PGD cycles.

the laboratory. However, once the technique was established, clinicians took it over. Today, we want to treat more patients, different patients, we want to treat them better. But to do this we need basic research, so again we are going back to the laboratory." According to Gianaroli, it was the beginning of a trend which would take reproductive medicine - for the first time - beyond the "mere" treatment of infertility, and towards the creation of opportunities which were partly driven by the human genome project and which lay largely beyond the confines of reproduction.

A further hot topic for discussion in Bologna - and one which had some overlap with embryo screening - was the potential of blastocyst transfer to improve implantation rates and thereby reduce the high rate of multiple pregnancies. Data pouring out of the USA - particularly from the Colorado group of Schoolcraft and Gardner - had shown high implantation and pregnancy rates in strictly selected patients following the transfer of embryos at day 5 rather than day 2 or 3. Day 5 transfers in Colorado had been made possible by the development of a new two-stage culture medium which reflected the embryo's changing nutritional requirements

as it moves from the eight-cell to the blastocyst stage. The two-stage culture system was therefore modelled on the concentrations of ions and nutrients to which embryos are naturally exposed in the reproductive tract.

The success rates achieved in Colorado were viewed with caution by many in Europe, and even the Stanford, USA, embryologist Barry Behr, speaking in Bologna, described blastocyst transfer as “a tool in IVF”, and not the panacea for an improvement in pregnancy rates. The endpoint of the blastocyst learning-curve, he said, was the opportunity to transfer fewer embryos - and thereby reduce the incidence of multiple pregnancies. Certainly, in *Human Reproduction* and *Fertility and Sterility* the blastocyst results looked impressive, but in Europe there were concerns, not least the question of whether the development of a blastocyst is nothing more than the mark of a viable oocyte which anyway would have fertilised and implanted. While visionaries like Alan Trounson saw a combination of new sequential culture systems and PGD as a way to the holy grail of single viable blastocyst transfer (*Hum Reprod* 1998; 13: 169-77), within a few years most European ART programmes seemed reassured that embryo viability can be adequately assessed at day 3.

Because the 2000 annual meeting broke all attendance records (an increase of almost 6 per cent on Tours in 1999), plans for 2001's gathering in Lausanne were worrisome to the EC, even in Bologna. Hotels in and around Lausanne - which were even then block-booked - could provide no more than 3000 rooms, while as many as 4000 registrants might now be expected. Thus, local organising committee chairman Marc Germond told the EC that hotel bookings would have to be made along the lake in Geneva, thus imposing once again a daily commute to the congress centre for some delegates. As the EC had concluded following huge expansion in Maastricht (attendance 31 per cent up on the previous year), Edinburgh (25 per cent up), Tours and Bologna, small-city academic environments were no longer appropriate for the annual meeting; thus, the EC now agreed to Vienna in 2002, Madrid in 2003, and Berlin in 2004. Such planning seemed logical, but it did pose a problem of principle for the EC: should ESHRE simply let its annual meeting grow and grow and accommodate all comers in large-city venues; or, as chairman elect Hans Evers tentatively suggested, should ESHRE now call a halt and take steps to reduce numbers? Not surprisingly, there was little enthusiasm in the EC for the latter option, and ESHRE thus committed its annual meeting to the grand event of big convention cities.



The Beaulieu Centre in Lausanne would prove the last of ESHRE's low-cost congress venues for the annual meeting. Thereafter, ESHRE committed its annual meeting to the grand event of big convention cities.

By now, Evers as chairman elect was also chairman of the Publications Committee and had therefore stepped down as co-ordinator of ESHRE's training activities. He would now be replaced - after some friendly persuasion - by Arne Sunde, who as an unknown and fledgling embryologist had taken up that same position at ESHRE's first AGM in Bonn. He had subsequently remained in post until 1994, when, somewhat disappointed that training was not given more resources - financial and human - he had resigned. But now, following the involvement of the SIGs in training plans and a rationalisation of the programme by Evers, Sunde returned to an EC whose commitment to training was clearly stronger. Indeed, at the 69th EC meeting in April 2000 - at which Sunde was confirmed as co-ordinator of training - the EC agreed to allocate €10 from each membership fee to educational purposes.

Among the forthcoming Campus workshops outlined by Sunde at that meeting was one in Antwerp the following month - for which the EC had allocated \$12,000 - aimed at the prevention of twin

pregnancies. The workshop was organised by Jan Gerris of the Middelheim Hospital in Antwerp, where a programme of elective single embryo transfer was already in place. Multiple pregnancy was already a hot topic, and one which had prompted statements from ESHRE itself, the ASRM, IFFS and other voluntary and regulatory bodies. Gerris had called twin pregnancies in IVF and ICSI “an epidemic”, and the key to their prevention, he proposed, was in recognising those embryos with high implantation potential. Workshop contributions from Finland, Sweden, Ghent and Antwerp itself would recount experiences so far. Just after the workshop Gerris had joined a *Human Reproduction* Debate (2000; 15: 1884-1888) in which, based on data from his own and the Scandinavian groups, he proposed that an ongoing pregnancy rate of 35 per cent or more was possible with single embryo transfers. The target population, he said, were those IVF or ICSI patients under the age of 34, who collectively were accountable for more than 80 per cent of all ART twins. It was Gerris’s case that in such patients a progressive programme of elective single embryo transfer would yield pregnancy rates no different from the natural outcomes of normally fertile people.

Despite the plethora of pleas for fewer multiple pregnancies, there was a worldwide reluctance to bite the bullet of single embryo transfer. The USA’s SART registry report of 1999 still showed an average of four embryos transferred per cycle, and a multiple pregnancy rate of 40 per cent. And even in Europe - as ESHRE’s EIM reports showed - Mediterranean countries still felt more confident with higher order transfers. Thus, the clinical example was left mainly to Scandinavian, Dutch and Belgian groups, to demonstrate that in younger patients with at least two good quality embryos pregnancy rates need not be reduced by single embryo transfer. A randomised trial in Finland, for example, found a pregnancy rate per transfer of 32.4 per cent in a single embryo transfer group and 47.1 per cent in a two embryo group, a non-significant difference. However, there were 11 twin deliveries in the two embryo group, and just one pair of monozygotic twins in the one embryo group (Martikainen H, Tiitinen A, Tomas C, et al. *Hum Reprod* 2001; 16: 1900-1903).

The ESHRE Campus course organised by Gerris in 2000 had concluded that a twin pregnancy rate of 25 per cent or more is unacceptable; the aim should be around 10 per cent, with an ongoing “acceptable” pregnancy rate of around 30 per cent. With such intensity of discussion (and a *Human*

Identifying the single embryo likely to implant

A randomised trial published by the group of Jan Gerris the year before the 2000 Campus workshop (Hum Reprod 1999; 14: 2581-2587) had defined high quality embryos as those characterised by four or five blastomeres at day 2 and at least seven blastomeres on day 3 after insemination, the absence of multinucleated blastomeres and less than 20 per cent anucleate fragments on days 2 and 3 after fertilisation. Using such criteria, a prospective study in women under 34 showed that 26 single embryo transfers resulted in an implantation rate of 42.3 per cent and an ongoing pregnancy rate of 38.5 per cent. A subsequent report from the group (Hum Reprod 2002; 10: 2626-2631) confirmed that elective single day 3 embryo transfer had halved the twinning rate in Antwerp without any decrease in the ongoing pregnancy rate.

By 2004 one Finnish centre (Oulu) would report that "single embryo transfer is routinely carried out among women under the age of 36 in the first or second treatment cycle when a top-quality embryo is available" (Hum Reprod 2004; 19: 1364-1366), while in Gerris's own group in Antwerp 39 per cent of all transfers in 2002 were with single embryos; the ongoing pregnancy rate remained stable at 30.6 per cent and the twin (multiple) pregnancy rate declined to 11.7 per cent (Reprod Biomed Online 2003; 7: 615-622). Similarly, the proportion of elective single embryo transfers increased from 11 to 56 per cent at the University Hospital in Helsinki between 1997 and 2001, with multiple pregnancies falling from 25 to 7.5 per cent (Hum Reprod 2003; 18: 1449-1453).

Reproduction debate) this was clearly an issue which the EC took seriously, and in December 2000, following representations from Gerris and his proposal for a further meeting in Lausanne, the EC agreed to form a task force on the risks and complications of ART, with multiple pregnancy as its number one target.

It was a reflection of such concerns that in 2003 Sweden updated legislation to restrict all transfers to one embryo except in women over 39 or with a history of two failed cycles. Similar restrictions - to a maximum of two - were agreed in Belgium and the UK as part of proposals to extend the state reimbursement of ART treatment cycles. But ESHRE, as the ethics and law task force had already made clear, chose not to get involved in the legal discussions of individual countries - at least, not until 2002, when legislative proposals in Italy would finally draw formal comment and lobbying pressure from the society.

In the meantime, however, the EC had other operational procedures to address, particularly changes to the EC's composition which would become effective in Lausanne. Five stalwarts of the EC, Pellicer, Nygren, Nyboe Andersen, Heineman and Smitz (after two two-year terms) would each be standing down, while Basil Tarlatzis as past chairman would also be leaving the EC after eight years' executive service and chairmanship of

some of the most difficult committees. Evers, of course, would become chairman, while EC members Mandelbaum, Gianaroli and Joseph Neulen would continue for a second two-year term until 2003. But the first question for the EC, at its 72nd meeting in Brussels, was the successor to Evers as chairman elect. The principle of a scientist following a clinician was now chiselled in stone, and the EC's natural inclination was towards Arne Sunde, a veteran of the pioneer days but now back in the EC as co-ordinator of training. Moreover, Sunde represented the Nordic countries and had strong links with fast-moving developments in embryology.

"So I gave it some thought," says Sunde, "and said yes. It was the kind of offer I couldn't refuse - even though I knew how demanding it would be. It takes six years of your life, dictates what you're going to do for six years. You can't just leave, you have to be available for ESHRE." Sunde's name, therefore, would go before the AGM in Lausanne for approval as chairman elect, alongside the EC nominees (meeting the new national representative criteria of Fraser and Evers) of Christina Bergh, the Hungarian

Hans Evers

ESHRE's ninth chairman 2001-2003

By the time Hans Evers became chairman elect of ESHRE in 1999, his experience in the society's activities was already vast. He had been a member of the editorial board of *Human Reproduction* since 1995, had been chairman of ESHRE's 12th annual meeting in Maastricht, had sat on the international scientific committees for every annual meeting from 1992 to 2001, and had been the co-ordinator of ESHRE's training activities from 1992 to 2000.

Hans Evers qualified in medicine in 1976 at the University of Nijmegen, where he began work in obstetrics. In 1982 he was invited to establish an infertility unit at a new university hospital in Maastricht, where he has remained to the present day. Evers became Director of the Division of Reproductive Endocrinology and Fertility at the Academisch Ziekenhuis in Maastricht in 1982, and Professor of Obstetrics and Gynaecology at the University of Maastricht in 1990.

He was Vice President of the World Endometriosis Society from 2002, a member of the International Affairs Committee of the ASRM from 1998 to 2003, and a board member of the Dutch/Flemish Fertility Society from 1995 to 2000 and of numerous other learned societies and expert groups. He is currently the chairman of the Dutch National Committee on Biomedical Research. Evers has been an associate editor of *Human Reproduction* since 2000 and was a member of the editorial board of *Fertility and Sterility* from 1992 to 1997. With interests in evidence-based medicine, he became a member of the Cochrane Review Group for Subfertility and Menstrual Disorders in 1996.

Ninth Executive Committee 2001-2003

Chairman

Hans Evers

Chairman elect

Arne Sunde

Past chairman

Lynn Fraser

Members

Christina Bergh

Luca Gianaroli

Jacqueline Mandelbaum

Ioannis Messinis

Joseph Neulen

Juha Tapanainen

Janos Urbancsek

Josiane Van der Elst

Anna Veiga

Paul Devroey (co-ordinator SIGs)

Mark Van den Bergh (paramedical)

gynaecologist Janos Urbancsek, Ioannis Messinis, Josiane Van der Elst, Anna Veiga, and Juha Tapanainen, whose work in Oulu, Finland, was already steering the issue of single embryo transfer.

When the EC met in June 2001, just days before the opening of the 17th annual meeting in Lausanne, it was clear that the attendance forecasts made in Bologna would easily be reached. More than 3000 had registered before the opening, and even the eight pre-congress courses - whose organisation had now almost exclusively devolved to the SIGs - were well booked: 105 registered for the joint ESHRE/ASRM course on the "mid reproductive years" and 170 for the embryology course.

It was also at this meeting that the EC confirmed that Robert Edwards would deliver an honorary keynote lecture at next year's annual meeting in Vienna on "the ancient and modern world of IVF". Edwards's departure from the journals had been peremptory, and in a subsequent letter to Lynn Fraser he had asked for his name as founding editor to be removed from the mastheads of all three titles. The EC had reluctantly acceded, but were gratified that in his agreement to deliver this first honorary lecture

Edwards was not disposed to sever all his links with ESHRE. Indeed, at the AGM 12 months earlier in Bologna, Jean Cohen had proposed a motion from the floor to formally acknowledge Edwards's achievements for ESHRE - the honorary R G Edwards keynote lecture which began in Vienna in 2002 was a reflection of that acknowledgment.

Lausanne would also mark the end of the first year for the three journals' new editors. All three reported to the EC in Lausanne and all three were upbeat. While readers might not have noticed much difference, *Human Reproduction* had in fact been tightened up under David Barlow and his (now) managing editor Helen Beard, particularly with respect to manuscript review. Barlow's appointment had been announced in the August 2000 issue of *Human Reproduction* and, by the first issue of 2001, the editorial board had been replaced by a roster of associate editors chosen for their specialist and sub-specialist knowledge. In fact, many of the names were the same, but the 50+ new editors, wrote Barlow in a rare editorial that January, "will have a role in the co-ordination of the refereeing process within distinct areas of specialism". Barlow's own role, therefore, would be to oversee that process and to make final editorial decisions. Barlow also trimmed down the range of material applicable to the journal, noting that only those subjects recognisably within the field of reproduction would be deemed appropriate. The effect of a tighter review process was already evident in Lausanne, where Barlow told the Publications Committee that *Human Reproduction's* rejection rate was now 60 per cent and its place maintained at the top of the impact factors for O&G (with *Update* just behind in second).

Human Reproduction and *Update* continued to thrive, while Richard Ivell, the new editor of *Molecular Human Reproduction*, was also looking to tighten the editorial scope of his journal and introduce reviews. The three titles now accounted for 12 per cent of ESHRE's revenue under the terms of the new OUP contract and, as the EC had recognised, had become an important and guaranteed source of income. However, it was the grand event of the annual meeting which now made the biggest contribution to ESHRE's reserves, with congress revenues accounting for 75 per cent of all ESHRE's income. Although membership had reached 4243 by July 2001, fees accounted for just 8 per cent of total revenue.

So, as the new millennium unfolded, ESHRE yet again found itself on the up and up: the annual meeting breaking all records, membership still growing, and the journals safely nested at the top of their tree. But, as the EC found following ESHRE's last leap forward in the mid-1990s, with

growth comes pain, and growing pains were now high on the agenda of Hans Evers. To be fair, what Evers saw as wanting within the institutions of ESHRE was not simply of ESHRE's own making, for the world outside had also changed. ESHRE's higher public profile in the late 90s was not just that the society wanted its voice to be heard, but that this was how it was, everywhere. Information ran round the world in seconds; the world *was* involved and wanted to know. Scrutiny, transparency and public accountability were the politics of the new global age, and to Evers it seemed almost out of step with the times that ESHRE could float along, from one EC meeting to the next, riding on the crest of a wave of success which may or may not capsize and leave the society sunk. What Evers wanted was a long-term objective, a goal which would take ESHRE from here to there according to a carefully plotted route. What he wanted was a strategic plan.



Hans Evers' first priority when he became chairman of ESHRE in 2001 was the composition and adoption of a long-term strategic plan. The management overhaul of ESHRE which this entailed was the first since 1990 and has set the standards by which ESHRE is run today.

Immediately after he and Sunde were confirmed in their new roles in Lausanne, Evers set about his strategic overhaul of ESHRE. The discussion paper which followed was indeed a radical review, but no more radical than that of the business consultant William Metcalf in 1989 which Crosignani had commissioned to underpin ESHRE's finances. Evers prepared the paper jointly with Arne Sunde and invited contributions from Devroey (for the SIGs), Gianaroli (for annual meetings and sponsorship) and Nygren (for registries and guidelines) - and they lost no time in putting the paper together. The 76th meeting of the EC in December 2001 was the first full meeting which Evers chaired, and the 12-page strategy report was the first item on the agenda.

Where the report of Metcalf in 1989 had taken as its starting-point ESHRE's strengths - to repackage them as added value to the membership - Evers and Sunde began with ESHRE's weaknesses and the feeling of "a perceived distance between the membership and their Society". This, they explained, arose from a lack of transparency in ESHRE's political structure, inadequate long-term financial planning, and obscure definition of roles within ESHRE's institutions (including the EC). Their strategy, therefore, to provide an agenda for ESHRE from 2001 to 2004, was to address these issues, to "streamline the activities of the Society and its governing bodies and to create more transparency of the Society's structure and functioning". The catalyst for the report, they added, were the difficulties which always follow rapid growth.

It was a wide-ranging paper, covering every aspect of ESHRE's daily life from Edwards's original mission statement of the 1985 by-laws to the practical problems of running a meeting for 4000+ participants. "Our main concern," says Evers, "and I think we succeeded here, was to involve the Executive Committee on a more permanent basis in the running of the society. Until then, it seemed like a bunch of guys meeting three times a year and looking from one meeting to the next. Our strategy was to plan ahead, to set out what we were trying to achieve with one committee and the next. So we were looking four years ahead, with refreshed ideas every two years, but what we always had in mind was the future of ESHRE."

Not least among the future views was the possibility that the annual meeting - by now responsible for around three-quarters of ESHRE's total revenue - could be struck by disaster. The Madrid railway bombings in June 2003, and not March 2004? "So our main strategy was to secure the financial basis of the society," says Evers. In 2004, with a revised

programme of investment in place, that security had been achieved and the finances were such - despite a falling stock market - that ESHRE could indeed survive the complete failure of one annual meeting.

But the strategy report offered more for discussion than financial planning. The EC picked through every item raised and the first agreement, in a bid to rationalise and open up executive activity, was that the five core areas of EC responsibility should be allocated to designated members. Thus, Evers and Sunde would be responsible for internal and external affairs, Bergh and Mandelbaum for publications, Veiga and Urbancsek for annual meetings, Gianaroli and Tapanainen for finances and sponsoring, and Van der Elst, Neulen and Messinis for education, SIGs and services. The Finance and Publications sub-committees would, of course, continue. It was, as Fraser had explained, that everyone now had a job.

The ongoing issue of election to the EC, AC and SIG co-ordinators was deferred; however, the EC did recognise that the role of AC members remained poorly defined and that their involvement should be stepped up. In April 2002 it was agreed to increase the term of office for AC members to four years, and, for those countries eligible for two representatives, voting nominations should be for a scientist and a clinician. The AC, said Evers, would become the "elected Parliament" of ESHRE and should feel free to make proposals and comment to the EC. Also identified for added support was the ESHRE website, which in 2001 had taken around 1 million hits. Every aspect of ESHRE's activities - but especially the annual meeting and the SIGs - should be fully described on the site, which would eventually become ESHRE's "home", its premises in cyberspace somewhat grander than the offices in Grimbergen. Indeed, by April 2002 around half the registrations for June's annual meeting in Vienna had been received on-line, and 90 per cent of the abstracts.

But most importantly the strategy report recommended a grand plan for training and for the SIGs in which each SIG would take a long-term view in the planning of "basic", CME and high science courses. Such courses should be properly funded (despite Serono's withdrawal from the Campus funding, the EC had still allocated €10 per member to training) and logically planned. Similarly, each of the SIGs would have annual budgets and a clear view of its responsibilities, with requirements each year to hold business meetings and organise courses. In streamlining the scope of ESHRE, Evers proposed to disband the ever-struggling SIG in contraception and menopause and to create new SIGs for stem cells,

evidence-based medicine in infertility, and risks and complications in ART (out of the task force on multiple pregnancy devised by Gerris). Once again, Paul Devroey was delegated to oversee the SIGs' operational and financial planning.

It's fair to say that not everyone in ESHRE's hierarchy fully subscribed to the strategic plan. Sunde concedes that, even today, much of ESHRE's disposition is not far removed from "that modest academic society, cautious in its thinking" of the 1980s. "If there is a clash of cultures within the society," Sunde adds, "it's between those who want ESHRE to be bigger with its focus on finance and long-term growth, and those who still see ESHRE in the mould of the 1985 society. There has to be a balance between these two views, but I lean more towards those who say, well, ESHRE *is* important, we need to be more organised, to structure our activities according to a plan. We need our mission for the future and to know where we're heading. We need to do what a business would do, without becoming a business."

In line with the new continuity policy of smoothing one EC meeting into the next, there were many action steps to be picked up by the EC when it next met in Vienna in June 2002. Among them was the composition of the SIG in stem cells, which Luca Gianaroli had agreed to convene at the annual meeting. But before that meeting opened he had more immediate concerns to bring before the EC. There, at the 78th meeting, Gianaroli described proposals made by the Lower House of the Italian parliament to ban embryo freezing in Italy and to restrict the number of oocytes fertilised in any one ART cycle to three. Because cryopreservation would now be banned, all fertilised oocytes from that cycle - thus, a maximum of three - would have to be transferred. Gianaroli and his colleagues in Italy were angered and upset by what they saw as a pro-life political proposal which ultimately would encourage multiple pregnancies and increase risks to mother and baby. Paradoxically, the freezing of oocytes and sperm was ignored. If subsequently approved by the Italian Senate, the proposal would become law in Italy - and embryo freezing, as in Germany, would be outlawed. Gianaroli asked the EC to publicly oppose the proposal.

The EC agreed, basing its immediate statement on "strict scientific arguments" and not on politics. ESHRE described the proposal as "unethical", and a measure likely to increase multiple pregnancies. Oocyte freezing, its public statement added, "is of low efficacy" and its safety "still a concern". However, ESHRE's support for its Italian

colleagues didn't end there. A year later, as the legislation came before the Senate for a final verdict, Gianaroli assembled yet more ESHRE delegates (Sunde, Nygren, Shenfield) for a press conference in Bologna in which the restrictive nature of the law and its implications were once more explained . . . multiple pregnancies, poor quality embryos, reduced success rates, reproductive tourism to other countries. A spreadsheet of ART legislation showed how Italy would become the most restrictive country in Europe, allowing only limited IVF and ICSI but banning embryo freezing, heterogenic egg and sperm donation, PGD (which Gianaroli had helped pioneer in Bologna), and embryo research. Feelings ran high, and ESHRE's commitment never flinched, but in the end it counted for nothing. On 11th December 2003 the Italian Senate approved legislation 1514 by which cryopreservation in Italy was forbidden, access to ART restricted to documented cases of infertility (ie, no PGD for medical reasons), and "embryo production" limited to the number required for transfer, "which should be no more than three". The legislation became active in March 2004, subject to new guidelines and under a wave of protest from Italy's ART establishment. There was even talk that clinics would close and re-open beyond Italy's borders.

Meanwhile, in Vienna the 18th annual meeting progressed as planned, with both the abstract scoring and award systems tightened up. There were still seven awards open to participants - for an established clinician or scientist, for the exchange lectures, for the paramedics, for the poster, and for the most promising young scientist and clinician. The last award, incidentally, was renamed in memory of Michael Hull, the Bristol professor of reproductive medicine and surgery whose death at the age of 60 occurred in November 1999. Mike Hull's widow presented the award in Vienna.

The ever changing face of reproductive medicine - as forecast by Gianaroli in Bologna - was much in evidence in Vienna. Here, sessions were allocated to embryonic stem cells (with Trounson invited to speak), adult stem cells, and the genetics of ovarian dysfunction, while pre-congress courses included single cell genetic diagnoses and, from the andrology SIG, the use of functional genomics in male fertility.

The meeting also reaffirmed ESHRE's continuing good - if selective - relations with other societies. Reciprocal exchange awards continued with the Fertility Society of Australia, the Canadian Fertility and Andrology Society, and even the Pacific Coast Fertility Society (though the exchange lectureship would be brought to an end in 2003). ESHRE's association with

MEFS, the Middle East Fertility Society, formed in Thessaloniki in 1993, had flourished such that in Beirut in November 2000 Lynn Fraser on behalf of ESHRE had signed a “protocol of collaboration” with MEFS whereby both societies would develop joint training and lecture activities, exchange free announcements in publications, and share relevant data information. In March 1998 a celebration of the first 20 years of IVF, devised by Edwards and Mohammed Aboulghar, had been jointly organised by MEFS and ESHRE in Marakech, Morocco, and by now MEFS would regularly stage its own board and clinical meetings to coincide with ESHRE’s annual event.

However, it was with the ASRM that relations proved most cordial and most abundant. By the end of the 1990s ASRM exchange lectures occupied two sessions of the scientific programme of ESHRE’s annual meeting, and the reciprocal pre-congress training courses had become a well attended institution. Basil Tarlatzis remained ESHRE’s main liaison with the ASRM, and it was at the latter’s annual convention in Orlando in 2000 that suggestions were first made about some form of collaborative consensus on the definitions and treatment protocols for polycystic ovary disease. Tarlatzis brought the idea back to the EC, and was encouraged to press ahead.

It was, in fact, clear on both sides of the Atlantic that there were discrepancies and anomalies in the diagnostic criteria then applied to polycystic ovary syndrome. Most clinicians, especially in the USA, based their diagnosis on NIH guidelines drawn up in 1990 on the basis of majority opinion, not evidence-based trials. If the patient had clinical or biochemical evidence of hyperandrogenism and chronic anovulation, with evidence of any other disorder excluded, the diagnosis was PCOS. “The NIH criteria did not include the appearance or the presence of polycystic ovaries,” explains Tarlatzis. “And that was heavily debated by us in Europe, especially in the UK. How can you call it PCO if the ovary doesn’t need to be polycystic?”

The debate and the possibility of consensus were first put in the hands of the SIG in reproductive endocrinology headed by Bart Fauser. “There was such a gap between the US researchers and others,” says Fauser. “How could we ever agree on anything when we seemed to be talking about different patients. Those in the UK were strongly in favour of ultrasound for diagnosis, whereas our US colleagues relied almost completely on endocrine and metabolic markers.”



Members of the ESHRE/ASRM consensus workshop on polycystic ovary syndrome, which met in Rotterdam in May 2003. Seated on the decking are Bart Fauser (left), chairman of ESHRE's Special Interest Group in reproductive endocrinology until 2000, and Basil Tarlatzis (centre), who took over the chairmanship from Fauser.

The consensus statement was published jointly in *Human Reproduction and Fertility and Sterility*.

Both Fauser and Tarlatzis knew the US establishment first-hand and sounded out their US colleagues on the possibility of a new consensus based on evidence, not opinion. There was some enthusiasm, and first a joint US and ESHRE workshop in Thessaloniki was proposed under the umbrella of the reproductive endocrinology SIG. While Thessaloniki was thought too remote for the Americans, a subsequent plan for a joint meeting in Rotterdam did receive ESHRE and ASRM approval (as well as some funding) and - to Fauser's surprise - everyone involved in the discussions agreed to attend. "Our plan for the meeting was an original one," says Fauser. "One public day with lectures and 1.5 days of closed workshops on allocated themes with invited speakers and discussants. The consensus paper would be written by the organisers and be based on the contributions of the speakers. Once written, the paper would be sent to all participants and after amendments approved by all participants.

And that's exactly how it went. The paper was eventually published simultaneously in both *Fertility and Sterility* and *Human Reproduction*, and this was never done before."

In the event the 2003 consensus on the diagnostic criteria related to PCOS (Hum Reprod 2004; 19: 41-47/Fertil Steril 2004; 81: 19-25) concluded that PCOS is a syndrome of ovarian dysfunction but that no single feature (such as hyperandrogenism) is sufficient for a clinical diagnosis. Its "cardinal features" were defined as hyperandrogenism and polycystic ovary morphology (as determined by ultrasound) and its clinical manifestations defined to include "menstrual irregularities, signs of androgen excess, and obesity". The bottom line of the consensus was that PCOS "encompasses a broader spectrum of signs and symptoms . . . than those defined by the original diagnostic criteria".

Another SIG making progress since its formation in Vienna in 2002 was that in stem cells, now chaired by Luca Gianaroli. ESHRE had entered the stem cell debate that same year when *Human Reproduction* (2002; 17: 1409-1410) had published the fourth statement from the ethics and law task force considering issues related to the research and use of such cells, particularly those derived from human embryos. As in its previous statements, the task force reviewed the scientific background and then raised the ethical issues. The most contentious, of course - as had already been debated within forums as grand as the UN and European Parliament - was the use of stem cells derived from embryos created (by nuclear transfer) solely for such purposes. Thus, in the task force's view the real ethical issue on therapeutic stem cells was dependent on the more fundamental issue of cloning for therapeutic or reproductive purposes - and on that matter ESHRE had already delivered its unequivocal verdict in November 1997: a yes to therapeutic cloning and a five-year moratorium on reproductive cloning. The latter would be renewed during ESHRE's 20th annual meeting in Berlin.

ESHRE's position on embryonic stem cells, therefore, was predictable, as the task force's 2002 statement made clear: "We do not object to embryo research on supernumerary embryos, nor do we find any major ethical differences with embryos created for research within the constraints expressed in a previous Task Force publication (on the moral status of the pre-implantation embryo): 'The creation and the possibility of research on pre-implantation embryos specifically created for the purpose is appropriate only if the information cannot be obtained by research on supernumerary zygotes.' "

However, as the furore after the birth of Dolly forewarned, the cloning debate was not now going to go away, whatever ESHRE had to say. Theirs was just one small voice in what was becoming a major international discussion - which was not helped by occasional headline-grabbing claims that a cloned baby was being planned (Antinori in Italy in August 2001) or even on its way (Panos Zavos in January 2004).

The European Parliament had been basically sympathetic to embryo research and in 2001 had allocated more than €2 billion over four years to health-related genetic research. However, with a serious slice of this funding destined for embryo research, there was much consternation among conservative members, who had introduced numerous amendments to the bill. But in December that year the European Parliament threw out the amended report and thereby rejected - for the time being at least - any ban on public funding of human embryo research.

However, at its April 2003 meeting ESHRE's Executive Committee heard that deliberations under another EU heading - a directive on the safety of gamete and tissue storage and donation - could again jeopardise embryo research in Europe. Following debate in March that year amendments to the drafted bill would, if accepted by the Council of Ministers, effectively close down any avenues of support for research designed to create human embryos solely for the supply of stem cells. The EC thus agreed to an urgent programme of lobbying before the EU's Council of Ministers next met in June: both Evers and Devroey met with their national health ministers, while Evers on behalf of the EC wrote to the chairman of the European Commission.

And in Madrid that June, as ESHRE's 19th annual meeting got under way, the society's incoming chairman Arne Sunde told a press conference that a ban on embryonic stem cell research would not only impede progress in infertility research but also damage the prospect of treatments for diseases such as Parkinson's and Alzheimer's. "It's not an either/or situation," Sunde told the press. "Most scientists working with stem cells, whether embryonic or adult, agree that in order to find clinically viable treatments research must continue on both types."

The June meeting of Europe's Council of Ministers turned down the amendments, and devolved the matter of stem cell research to the local legislation of member states. But in November that year, following a second reading, the European Parliament did back the public funding of research on stem cells derived from human embryos - and thereby appeared to back therapeutic cloning. The vote, according to the official

communiqué from the Parliament, was “highly charged and emotional”, and reaffirmed that the research could only take place in countries which made it legal, such as the UK, Belgium and Sweden. Europe’s first application to create embryos by nuclear transfer as a source of stem cells - from the group of Alison Murdoch in Newcastle, UK - was approved by the British regulators in August 2004.

Therapeutic cloning had also come before the United Nations in 2003, when Costa Rica (backed by the USA) called for a vote on the subject in the General Assembly. But an outright ban was averted in December following a compromise deal which effectively postponed debate on any cloning treaty until October 2004. While there was no doubt of the universal repugnance for reproductive cloning, a ban on all cloning, which would seem to have the support of the USA, the Vatican and some Catholic countries, would have caused a deep rift at the UN, particularly with those European nations now committed to the pursuit of new medical treatments through stem cell research. (The UN continued to reject any total ban on “cloning”, while the State of California in 2004 allocated \$10 billion over ten years to stem cell research, its first public funding in the USA.)

It was indeed a political time in reproductive medicine, and one which forced on ESHRE a greater awareness of its public role. In Vienna at its 82nd meeting the EC agreed “as a general rule” not to invite politicians to speak at any future opening ceremony on the basis that ESHRE should not offer them a stage on which to speak “unopposed”. The following November, at its 84th meeting, the EC recognised the importance of up-to-date guidelines and position papers, as ready-to-use solutions to clinical issues raised by politicians or the press. Such a public role for ESHRE had been outlined in the strategy report of Evers and Sunde, and now in Brussels Sunde as chairman set the initiative in motion. Designer babies? ESHRE had no position - but would in future.

In fact, by that same 2002 EC meeting in Brussels, almost three years after it was first presented as a draft, the strategy report was beginning to take shape as a hard programme of action. The society’s future, said Sunde, would become “more complicated and more in-depth knowledge would be needed to make the right decisions”. Thus, in addition to the administrative “portfolios” carried by each member of the EC, the day-to-day running of the society would now be put in the hands of a “chairmen’s group” (composed of the past, present and future chairmen) working alongside Central Office. Individual EC members’

responsibilities, as defined by their portfolios, would lie in four key sub-committees - for training, annual meetings, finance, and publications.

It was not surprising that training should be accorded such importance, for both Sunde and Evers had in the past co-ordinated ESHRE's training programme - when they had each recognised under-funding and a lack of long-term planning. Now, under a new administrative structure, was the chance to rationalise training once and for all. As the strategy report had recommended, training would now be organised at three levels - basic, postgraduate as part of CME, and specialist. The training sub-committee, which would include the SIGs committee, would now organise all training activities, including the pre-congress events, but do so within the framework of the society's grand plan for training. Courses "under the auspices of ESHRE" would be no longer allowed, although the committee would still be able to "endorse" training activities.

The main task of the annual meetings sub-committee, which would be chaired by the current chairman of the international scientific committee, was the selection of future venues. The annual congress was by now the

Tenth Executive Committee 2003-2005

Chairman

Arne Sunde

Chairman elect

Paul Devroey

Past chairman

Hans Evers

Members

Christina Bergh

Joyce Harper

Ioannis Messinis

François Olivennes

Juha Tapanainen

Janos Urbancsek

Josiane Van der Elst

Anna Veiga

Luca Gianaroli (co-ordinator SIGs)

Jan Kremer (website)

Liz Corrigan (paramedical)

biggest in the world in reproductive medicine. Despite ESHRE's "self-organisation" policy, some tasks, such as accommodation, had necessarily been put out to specialist agencies. For the new committee there was still a huge check-list of requirements for eligibility for the annual meeting, and a line of would-be hosts with applications. The annual meetings sub-committee would also oversee the scientific committee and have final responsibility for the content of the meeting, including the pre-congress courses.

It was unlikely that the Publications sub-committee would face the kind of problems met by Lynn Fraser and her colleagues in 1999 and 2000, but there was still plenty lying ahead. One of the committee's designated tasks was a strategy for future developments and there were no clear signs of how medical journals might move ahead in the near future. Open-access electronic publishing - raised by the committee as a contentious issue in its discussions with Robert Edwards - would inevitably shape developments, but to what extent was not clear. In 2002 the three ESHRE titles had generated a €500,000+ gross surplus, but the possibility of free-access web-based publishing was real, and such high levels of profit could not be guaranteed. Already, access to abstracts of *Human Reproduction* papers via sites like PubMed Central was free, and the EC recognised the possibility that within a few years only those journals with high impact factors would survive, financed, maybe, not by readers but by authors willing to pay for the refereeing and publishing process.

The imponderables of the future would also determine the responsibilities of the Finance Committee, chaired as before by ESHRE's chairman. The worldwide stock market slump from 2000 onwards had hit ESHRE no differently from other organisations, and in 2002 the Finance Committee had asked its accountants, Deloitte and Touche, to review the society's investment policy. Both medium and long-term investments were performing poorly and in April 2003, following proposals from two investment banks, the EC agreed to move ESHRE's reserves to a more varied investment programme. Arne Sunde, the chairman of the Finance Committee at the time, also agreed that Bruno Van den Eede should investigate the possibility of ESHRE buying and not renting its office space; property, after all, was seeing a much better return on investment than the stock market, and staff at Central Office, which now numbered four but was due for at least one addition, was bursting at its seams in Grimbergen. Van den Eede duly found new offices nearby which were available for purchase; contracts

Arne Sunde

ESHRE's tenth chairman 2003-2005

Arne Sunde's own history with ESHRE is as old as the society itself. He joined the temporary committee in Helsinki in 1984 and became a member of the first Executive Committee the following year, becoming special advisor on workshops in 1988 until 1994. He was a member of the editorial board of *Human Reproduction* from 1986 to 1992 and head of the newly formed training committee from 2000 to 2003. Sunde became chairman of ESHRE in 2003.

Arne Sunde trained as a scientist in Norway, and in 1980 took his PhD in biophysics on the hormonal activation of androgens. From 1980 to 1988 he worked as a research associate at the Institute for Cancer Research in Trondheim, and later at the national laboratory for molecular biology. In 1984 he moved to the University Hospital of Trondheim as laboratory director of the newly formed IVF unit, and in 1994 became Professor of Cell Biology at the University of Trondheim.

Sunde has been a member of numerous Norwegian boards in the fields of biotechnology, fertility and ethics, and a prolific investigator, lecturer and author. In 1985 his centre in Trondheim won the Schering prize for its work in gynaecology in Norway, which included the country's first IVF babies.

were finally signed and sealed in December 2003. Meerstraat 60 in Grimbergen would thus become ESHRE's new registered address, and a new addition to its investment portfolio.

Another long-term strategic view taken by the Finance Committee concerned the contribution to revenue of registrations from the annual meeting. In Madrid almost 60 per cent of the 5000+ participants were group registered by the pharmaceutical industry. ESHRE's working relations with its sponsoring companies had remained cordial, especially after they had been given independent responsibility for the scientific content of their sponsored symposia. Both Organon and Serono had remained long-standing supporters and would inevitably look on the "big event" status of the annual meeting as an important platform for their activities. Yet however the companies viewed the event, it was increasingly clear to them - as it was to ESHRE - that any unlimited support for doctors to attend congresses could not continue in the same ways as before. In both Europe and the USA regulatory authorities would surely impose restrictions on such drug company spending, as was already the case in countries like Italy, where a whole rigmarole of administrative requirements was necessary before any doctor could be sponsored to a medical congress. Such support, claimed the authorities, could potentially create a conflict of interest in the mind of the doctor if a sponsor's generosity was more than reasonable. Thus, if the revenue from company

registrations was likely to decline, where, asked the Finance Committee, would alternative sources lie? There was no simple answer, but, as 2003 came to an end, it was clear that the options lay more in ESHRE's own activities than in the hands of outside contributors, whether journal advertisers and subscribers, or drug industry sponsors. With CME accreditation available for most ESHRE training courses, would an ESHRE accreditation system also be applicable to laboratories and clinics? With ESHRE membership fees simplified to full, paramedic and student status, would it be possible to double membership from 4500 to, say, 10,000? Would a more structured training programme with more investment attract more participants and generate more income?

As 2003 came to an end these were the issues facing the EC as it took stock of the 21st century and looked ahead into the future. It was, as Sunde had said, ESHRE now acting more and more like a business, without actually being a business. Of course, there were no immediate concerns for ESHRE - far from it. Both annual meetings of 2003 and 2004 had been enormously successful, with pre-congress courses and content fulfilling the very latest scientific agendas, attendance approaching 6000, membership of the society at 4500, the journals as strong as ever, and ESHRE's own activities - in particular training, the SIGs and data collection - operating on realistic budgets with properly planned expectations.

Both Karl Nygren for the EIM committee and Joyce Harper for the PGD Consortium had put proposals to the EC in 2003 to expand their data collection activities. The EIM group's fourth report was imminent in *Human Reproduction* but Nygren was now keen to scale up the exercise to establish a reference database and build into ESHRE a more permanent structure for ART surveillance in Europe. The EC's view was that ESHRE was indeed the only body - in Europe for sure - with the ability, responsibility and resources to take on such a project. Similarly, Joyce Harper looked to enhance the PGD Consortium's data collection operation, which by 2003 was assembled by means of electronic processing. Reception and checking of data on referrals, cycles, pregnancies and outcomes had by now become a time-consuming task, but still the only initiative of its kind. It was important work, the EC agreed, and still the world's only data collection programme in PGD.

For the incoming chairman Paul Devroey the future of ESHRE, for all its strategic planning, would lie as ever with its members' interests in science and clinical medicine. To this extent he sees the role of the SIGs, properly defined in the strategy report of Evers and Sunde, as now embodying

Paul Devroey

ESHRE's eleventh chairman 2005-2007

Although Paul Devroey will be ESHRE's tenth chairman, he, like his predecessor Arne Sunde, has a history with ESHRE which stretches back to the society's foundation. He represented Belgium on the first and second Advisory Committees (from 1986 to 1990) and, with André Van Steirteghem, organised ESHRE's second annual meeting in Brussels in 1986 (having served on the organising committee for the first meeting in Bonn in 1985). Devroey joined the Executive Committee in 1993, and was treasurer from 1993 to 1995, when he became co-ordinator of the Special Interest Groups (until 2003).

Paul Devroey qualified in medicine in 1971 at the Dutch-speaking Catholic University of Louvain. In 1989 he was awarded his PhD (on oocyte donation) at the Dutch-speaking Free University of Brussels (VUB). Two years later he pioneered the technique of intracytoplasmic sperm injection at the VUB with Van Steirteghem.

Paul Devroey has extensive clinical and research experience in infertility, and is currently Professor of Reproductive Medicine and Clinical Director of the Centre for Reproductive Medicine at the VUB. He is a member of the Belgian National Committee for Bioethics, a past president of the Belgian Society of Reproductive Medicine, a member of the editorial board of *Fertility and Sterility*, and an associate editor of *Human Reproduction Update*.

ESHRE's future. "The SIGs will bring young people and new scientists together to meet," says Devroey. "ESHRE itself can no longer be a meeting place – there are nearly 5000 members, 6000 at the annual meeting, how can you meet? We have to meet in small groups, defined by common interests - strong groups with strong leaders and good subjects behind them."

Yet for all its focus on the SIGs, the basic common denominator of Devroey's view of the future of ESHRE is not far removed from that of Edwards and Cohen as they talked over dinner in Paris in March 1984 - a society for European scientists and clinicians to come together and share their work with each other, in meetings, in a journal or in presentations and discussion at a scientific congress. This is what they wanted, and what ESHRE has surely delivered - and what Devroey still wants for the society's future. Yet out of all ESHRE's achievements it's no surprise or coincidence to find that all the past chairmen, and all those whose own histories have touched ESHRE's, unfailingly identify the foundation and growth of *Human Reproduction* as the greatest jewel in ESHRE's crown. "ESHRE created the best journal in infertility," says Pier Giorgio Crosignani, "and the credit for that lies with Bob Edwards."

If the essentials of ESHRE today - the journal, the mission - are not much different from the vision of Edwards and Cohen more than 20 years



Arne Sunde, left, became ESHRE's tenth chairman in 2003, 19 years after he first joined the temporary committee in Helsinki; Paul Devroey, centre, confirmed as chairman elect in 2003, joined the Executive Committee in 1993, and was treasurer from 1993 to 1995, when he became co-ordinator of the Special Interest Groups (until 2003); Bart Fauser, right, after heading the Special Interest Group in reproductive endocrinology, became editor of *Human Reproduction Update* in 2000.

ago, the new visionaries of the society - Evers, Sunde, Devroey - also recognise the more formalised structures of ESHRE and the new public role which the society will necessarily take on in the years to come, and these two developments, more than anything else, define its difference from those early days of the 1980s. "Now," says Evers, "we are invited to take part in - indeed, seek involvement in - a number of European activities, like the stem cell debate, or the political changes in Italy. This is relatively new to the society. So we've had to develop ways of being involved. That's the kind of thing expected of an organisation like ESHRE. So we need to have authority. We need to be officially recognised by the press, by the politicians as a group of authority."

Such a broadened view is also evident in revisions to the by-laws, which grew out of Evers and Sunde's strategy report, their first major overhaul since adoption in 1985. And the mission today, finally approved under Article 3 at the AGM in Berlin in 2004, is more pragmatic, more specific, more accountable than the visionary mission of the by-laws 20 years ago:

The main aim of ESHRE, a non-profit organization, is to promote interest in, and understanding of, reproductive biology and medicine. It does this through facilitating research and subsequent dissemination of research



All ten of ESHRE's past and present chairmen met in Capri in August 2004. From left to right Pier Giorgio Crosignani, Basil Tarlatzis, José Egozcue, Lynn Fraser, Klaus Diedrich, Jean Cohen, Robert Edwards, André Van Steirteghem, (seated) Arne Sunde and Hans Evers.

findings in human reproduction and embryology to the general public, scientists, clinicians and patient associations; it also works to inform politicians and policy makers throughout Europe. On a more applied level, it aims to promote improvements in clinical practice through organizing teaching, training and continuing medical education activities, developing and maintaining data registries and implementing methods to improve safety and quality assurance in clinical and laboratory procedures.

No-one, neither the founding fathers nor the new executives, believe that ESHRE's future will run and run in blissful security. The society's first 21 years were enormously progressive, though largely trouble-free, and punctuated only by contractual dramas with publishers. André Van Steirteghem described his chairmanship from 1991 to 1993 as "uneventful"; other chairmen, like Cohen or Crosignani, had challenges to meet in laying a basis for ESHRE's financial security, while Tarlatzis or Evers looked to the incorporation of administrative structures within the society

Absent friends...

It would be remarkable if in ESHRE's 21-year history there were no setbacks to report, but the deaths of three men who figured substantially in ESHRE's history were felt deeply by the society, especially as they all died well before their careers and contributions were complete.

Professor Gerard Zeilmaker (1936-2002) was one of the true pioneers of IVF. It was from his clinic at the Erasmus University of Rotterdam that the Netherlands' first IVF baby was born (in October 1982), as well as Europe's first live births (in May 1983) from frozen-thawed embryos. Zeilmaker, a biologist by training and always a careful innovator in the science and clinical applications of reproductive medicine, recognised the ambitions of Edwards and Cohen and in 1985 was elected to the first Advisory Committee as a representative of The Netherlands. He joined the Executive Committee in 1987, and was treasurer from 1989 to 1991. He was also chosen by Edwards as one of five initial associate editors of *Human Reproduction*, and served on the first Safety and Standards Committee (whose first report was published in 1990).

Professor Mike Hull (1939-1999) had been a supporter of ESHRE from the pioneer days in Bonn and was elected to the second Advisory Committee in 1988 as a UK representative. Hull moved to the department of O&G in Bristol in 1976 and 13 years later was appointed Professor of Reproductive Medicine and Surgery. Following his death in 1999 he left behind in Bristol - and in Britain - a legacy of outstanding work and research which still remains much quoted today.

Herman Merckx (1962-2002) joined Bruno Van den Eede in ESHRE's Central Office in 1994. It was a year which proved an important turning-point in the society's history, when the annual meeting became fully organised in-house and many new developments lay ahead. Herman's first responsibility was in the management of membership and registration of participants for the upcoming annual meeting in Hamburg (1995). He soon started work on databases for processing membership and registrations. His interest in computer systems proved invaluable in converting the old databases into an integrated system linking membership and registration records with the society's financial administration. A few years later it was Herman who played a key role in the development of ESHRE's website and he who laid down the foundations of the ESHRE website today. By the time of his sudden and unexpected death on 23rd December 2002, he had as ESHRE's webmaster developed a dynamic website offering on-line facilities for registration and abstract submission.

to prepare it for the future. However, as the changes to the by-laws suggest, ESHRE's growth in the past 20 years has been in a steady broadening of outlook, in a wider range of activities to embrace the society's more public responsibilities.

So what ESHRE's 21-year history has really achieved throughout this time of growth is that self-momentum which Cohen spoke of at the end of his chairmanship in 1987, that self-perpetuating drive which gives an organisation a life of its own over and above the sum of its individual members. And that surely remains evident today as ESHRE begins the next two decades of its history. ESHRE, as Arne Sunde told the AGM in Berlin, is today a "dynamic" society. Thus, as stand crews dismantled the

exhibition booths from ESHRE's 20th annual meeting, the second announcement had appeared for the next gathering in Copenhagen, the scientific committee had concluded its planning, and arrangements were already unfolding for Prague in 2006 (ESHRE's first congress in the "new" Europe), and Lyon in 2007. Five stand-alone training courses had been prepared for 2004, including a symposium on data monitoring in Thessaloniki in September, the ethics and law task force was about to present its eighth statement (on ART in HIV-positive patients) for publication, the Rotterdam PCO consensus had been published simultaneously in *Human Reproduction* and *Fertility and Sterility*, and a re-allocation of funds to Central Office in support of SIG and training initiatives as well as data collection would ensure that membership activity would continue where it was felt necessary and useful.

As for the pioneers who had gathered in Hall B at the Finlandia Hall in 1984, they could surely never have foreseen how far their ambitions would take them, how fully their faintest hopes would be realised. History would show that in the years which followed these same pioneers, men like Van Steirteghem or Edwards himself, would indisputably shape the future of reproductive medicine in Europe. ESHRE gave a single voice to the work they were doing, and brought it before their peers and the outside world. And in the provision of a society to scientists and clinicians alike they shared their achievements with all around them, according to the basic principles of investigation, reporting and discussion. ESHRE made all that possible, but, with so much in reproductive technology likely to unfold in the coming years - ethical, clinical and scientific - the story has surely only just begun.

APPENDIX A

Articles of Incorporation

The creation of constitutional by-laws (alongside the agreement of a name and election of an Executive Committee) was one of three formal responsibilities for the temporary committee. Before they left Helsinki in 1984, Edwards told each of the national representatives to forward to him details of other societies' constitutions "to serve as a model for our Society". He meanwhile would produce a draft for discussion at the second meeting in London in September.

By the time of the first AGM in Bonn in 1985 the draft text had been subject to some discussion, principally on the composition of the Advisory Committee. The agreed text, formally adopted in Bonn, is set out below, and has been largely left intact by the Executive Committee and AGM until Berlin in 2004, when changes to Article 3 revised the society's mission and activities in line with its more pragmatic, educational and advisory roles.

NAME, REGISTERED OFFICE, PURPOSES

Article 1

A scientific society will be constituted, named "The European Society of Human Reproduction and Embryology", called hereafter "The Society". This Society is regulated by the Belgian Law of October 25, 1919, modified by the law of December 6, 1954.

Article 2

The Society has its registered address at “Centrum voor Internationale Verenigingen, Washingtonstraat 40, 1040 Brussels, Belgium”. The registered office can be transferred by simple decision of the Executive Committee, published in the annexes of the “Moniteur Belge-Belgisch Staatsblad” (The Bulletin).

Article 3

The Society is a non-profit association. The purpose of the Society will be to facilitate the study and the analysis of all aspects of human reproduction and embryology. It will co-operate with other scientific and medical societies, universities and any organisation with related interests.

MEMBERSHIP

Article 4

The Society consists of a General Assembly, an Executive Committee and an Advisory Committee. Members can be full members, student members and honorary members. Each category of members has the same rights and obligations.

Article 5

Full members and student members will be elected by a majority of the votes cast at the General Assembly if recommended by two members of the Society.

Eligible candidates for student membership are those carrying out postgraduate research for a medical or scientific degree.

Honorary members will be recommended by the Executive Committee and be approved by the Advisory Committee and the General Assembly. Members can resign from the Society by registered cover to the Chairman. A membership is terminated by failing to pay membership fee for two consecutive years. A member may be expelled from the Society at the recommendation of the Executive Committee and after ratification of the General Assembly.

All members without exception have the right of information concerning the scientific activities of the Society.

Article 6

Full members and student members pay annual fees. The amount of those annual fees is proposed by the Executive Committee and ratified by the General Assembly.

GENERAL ASSEMBLY

Article 7

The General Assembly has all rights permitting the realization of the purposes of the Society. The General Assembly is composed of scientists, medical doctors or any other person who has contributed to the aims of the Society and has been elected to membership as a full member, a student member or an honorary member.

Article 8

The General Meeting will be held once a year under the authority of the Chairman. The Chairman elect will preside in the absence of the Chairman. Otherwise an officer of the Society will act in this capacity. All members have one vote each. Each member present at the General Assembly can cast the mandate vote of one absent member provided he has previously received the signed consent of the absent member. The Chairman will have the deciding vote. Any motion can be raised at the General Assembly if at least 10 Members submit a signed resolution 45 days before the date of the General Assembly. The Agenda for the General Assembly and any submitted resolution must be sent to all members 30 Days before the date of the Annual Assembly.

An extraordinary meeting of the General Assembly can be called following a resolution submitted to the Chairman and signed by at least 50 members of the Society, to be held within 90 days following the receipt of the signed resolution

The Chairman and the Executive Committee must convoke any extraordinary General Assembly.

Article 9

All recommendations and decisions taken by the Executive Committee must be confirmed by a majority vote of members at the General Assembly or referred back to the Executive Committee. All decisions affecting motions raised at the General Assembly will be taken by a majority vote. These rules apply to all motions except resolutions to amend the present articles of incorporation or to dissolve the Society. The minutes of the General Assembly will be communicated to all members. The quorum for the General Assembly will be 10% of the membership or 50 members present or mandated.

AMENDMENTS TO THE ARTICLES OF INCORPORATION AND LIQUIDATION OF THE SOCIETY

Resolutions to amend the articles of incorporation or to dissolve the Society may only be passed by the Executive Committee or by members of the Society. The Executive Committee must communicate the date of the General Assembly, which will decide on the above-mentioned resolution, at least 3 months before. No resolution will be passed if there is not a two-thirds majority of members. If this quorum is not attained another General Assembly shall be called on the same conditions as described above, at which valid resolutions may then be taken with respect to the foregoing by a two-thirds majority of the members present.

The amendments to the articles of incorporation will take effect only after approval by royal decree and after fulfillment of the conditions concerning publication, claimed by Art. 3 of the Law of October 25, 1919. In the event of dissolution of the Society, the liquidation shall take place under such provisions as the General Assembly shall determine.

ADMINISTRATION OF THE SOCIETY

Article 11

The Administration of the Society is assured by an Executive Committee of at least 7 members and elected by the General Assembly. One member of the Executive Committee must have the Belgian nationality. The names

of the Chairman, the Chairman elect, the Secretary, the Treasurer and the other members of the Executive Committee of the Society will be proposed by the Executive Committee and ratified by the General Assembly. At the end of his mandate the Chairman will be succeeded by the Chairman elect. The members of the Executive Committee are appointed and may be dismissed by the General Assembly.

Article 12

On its responsibility the Executive Committee can assign special and well defined duties to one or more persons. The Chairman will preside at the meetings of the Executive Committee. The Chairman elect will preside in his absence, otherwise an officer will act in this capacity.

Article 13

The Chairman, Chairman elect, Treasurer and other members of the Executive Committee will be appointed for two years. Notwithstanding this article the first Secretary will be appointed for three years. A mandate of a member of the Executive Committee may be renewed only once. The Chairman elect will accept his office from the Chairman at the General Assembly after the minutes of the previous General Assembly have been called.

Upon retirement, the Chairman will be an ex officio member of the Executive Committee for the next two years without the power of voting on this Committee. A member can form part of the Executive Committee for a maximum of two consecutive terms of office. A member of the Executive Committee, except the Chairman, may be re-elected to the same or to another office or to the next Chairmanship. The power to bring, defend or carry on actions on behalf of the Society is vested in the Executive Committee and the Chairman (or another member of the Executive Committee nominated by the Chairman) shall be the individual authorised by these articles to represent the Society and to execute any necessary documents.

The Society is validated by the Executive Committee.

Article 14

The Executive Committee will meet bi-annually if possible. A majority vote will be decisive on any motion; the Chairman having the deciding vote. Twenty members can raise any motion for submission to the Executive

Committee, provided the signature of each member is obtained three months in advance. The Executive Committee is qualified for all acts of disposition, management, and conservation concerning movable and immovable property.

Article 15

The Advisory Committee will be elected by the General Assembly and its members shall reflect the geographical basis of the countries of Europe. As many scientists as clinicians will preferably be represented and elected by members of each representative country. Its composition will be defined by a byelaw, to be accepted by the General Assembly.

The Chairman of the Executive Committee will preside at the meetings of the Advisory Committee.

The Chairman elect will preside in his absence, otherwise an officer will act in this capacity.

BUDGET AND BALANCE

Article 16

The financial year will correspond to the calendar year. The Executive Committee must submit to the General Assembly the balance of the past year as well as the budget for the following year.

For any contribution to the Society the Executive Committee will define how this right to the assets, if the contribution may be considered as a right to the assets, will cease to exist in consequence of death or dismissal or retirement.

GENERAL DISPOSITIONS

Article 17

Any matter not mentioned in the present articles of incorporation such as the publications of these articles of incorporation in the "Moniteur Belge - Belgisch Staatsblad" (The Bulletin), will be done according to legal prescriptions.

SPECIAL STIPULATION

Article 18

The Society will guarantee the publication of an official journal. In order to realize this goal, an editor in chief, editors and an editorial board, will be appointed under the proposals of the Executive Committee, which proposal shall be ratified by the General Assembly.

The General Assembly will define how the editor in chief, editors and the editorial board can be dismissed.

APPENDIX B

Honorary members

It was at the fourth meeting of the temporary committee in Paris in December 1984 that Robert Edwards proposed that each year two distinguished figures in reproductive science and medicine might be honoured as Honorary Members of ESHRE. The first two nominations were Dr Raoul Palmer, the French gynaecologist who had been the inspiration in laparoscopic surgery for Kurt Semm, and Professor Friedrich Seidel, a zoologist from the University of Marburg, Germany, whose pioneer work in developmental biology had achieved live births from isolated rabbit blastomeres. The idea was that each should be presented with their honorary membership at the first annual meeting in Bonn (though in the event neither could be present).

Subsequently, two honorary members were proposed each year, and their memberships formally awarded at the following annual meeting. It became a convention that they were “retired” from their formal posts and that at least one of the two recipients was from the host country of the annual meeting. At the AGM in Barcelona in 1988 it was agreed that all nominations for honorary membership - a scientist and a clinician - should be approved by vote at the previous year’s AGM.

The second recipients in 1986 at the annual meeting in Brussels were Patrick Steptoe and the Belgian molecular biochemist Jean Brachet, whose work with RNA explained the chromosomal control of cell differentiation. Over the next 20 years ESHRE continued the annual tradition, and in 1993 in Thessaloniki honoured Edwards himself with the award. Jean Cohen

was made an honorary member in 1999 in Tours, Anne McLaren in 1997 in Edinburgh, and José Egozcue in 2003 in Madrid.

1985 Bonn

Raoul Palmer
Friedrich Siedll

1986 Brussels

Patrick Steptoe
Jean Brachet

1987 Cambridge

Pietro Donini
Tadeusz Mann

1988 Barcelona

Charles E Ford
Jose Botella Llusia

1989 Malmo

Carl Gemzell
Hannah Peters

1990 Milan

CR Austin
Marco Fraccarro

1991 Paris

Charles Thibault
Egon Diczfalusy

1992 The Hague

Walter Hohlweg
Hans Rumke

1993 Thessaloniki

Robert Edwards
Alexandre Psychoyos

1994 Brussels

Jacques Mulnard
Georges David

1995 Hamburg

Gerhard Bettendorf
Bruno Lunenfeld

1996 Maastricht

Jan Kremer
Roger Short

1997 Edinburgh

Anne McLaren
Etienne Beaulieu

1998 Gothenburg

Howard and Geoganna Jones
Lennart Nilsson

1999 Tours

Jean Cohen
Ryuzo Yanagimachi

2000 Bologna

Luciano Martini
Carl Wood

2001 Lausanne

Albert Jacquard
Colin Matthews

2002 Vienna

David Baird
John Collins

2003 Madrid

José Egozcue
Alex Tsafiriri

2004 Berlin

Mohammed Aboulghar
Dieter Krebs

APPENDIX C

A short history of ESHRE

1984


- * First assembly of temporary committee (May) during III World Congress of IVF and Embryo Transfer, Helsinki.
- * Second meeting of temporary committee (September) at the Westmoreland Hotel, London.
- * At its third meeting (Monte Carlo, September), the temporary committee “decided that the Society should be formed”; minutes of the previous meeting are titled “ESHRE”, the first time the name is used.
- * Draft by-laws outline ESHRE’s aims to “facilitate the study and the analysis of all aspects of human reproduction and embryology”.

1985

- * Proposals take shape for ESHRE’s journal, to be published by IRL Press.

SECOND ANNOUNCEMENT

**THE FIRST MEETING
OF THE EUROPEAN SOCIETY
OF HUMAN REPRODUCTION
AND EMBRYOLOGY**



THE "REDOUTE" - BAD GODESBERG

**BONN, GERMANY
June 23–26, 1985**

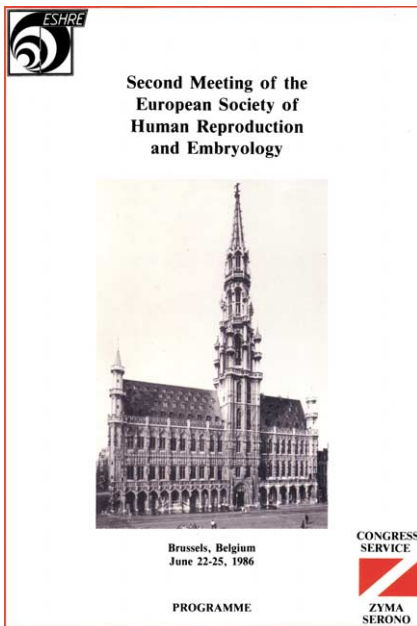
- * 1st Annual Meeting at the Stadthalle, Bad Godesberg, Bonn, 23rd-26th June
 - 650 attended
 - Klaus Diedrich local chairman
 - First executive committee confirmed as:
 - Robert Edwards (chairman)
 - Jean Cohen (chairman elect)
 - Klaus Diedrich (secretary)
 - André Van Steirteghem (treasurer)

- Pier Giorgio Crosignani
- José Egozcue
- Arne Sunde

- * An ethics committee is formed under the chairmanship of Jean Cohen.
- * Arne Sunde is given responsibility for training.

1986

- * First issue of *Human Reproduction* published in January, with Robert Edwards as editor; eight issues a year are initially planned.



- * 2nd Annual Meeting at the Hospital of the Dutch-speaking Free University of Brussels (VUB), 22nd-25th June

- 800 attended
- André Van Steirteghem chairman, Paul Devroey secretary
- First pre-congress workshop (on reproductive endocrinology)

- * ESHRE organises ethics workshop at SAC meeting in Bordeaux.

- * ESHRE's first three training courses are held - Zeilmaker and Alberda in Rotterdam on the practical aspects of IVF; Brambati in Milan on prenatal diagnosis; and Van Steirteghem at the VUB on reproductive endocrinology.

- * ESHRE's first consensus workshop, organised by Crosignani on Capri, features treatment with GnRH analogues.

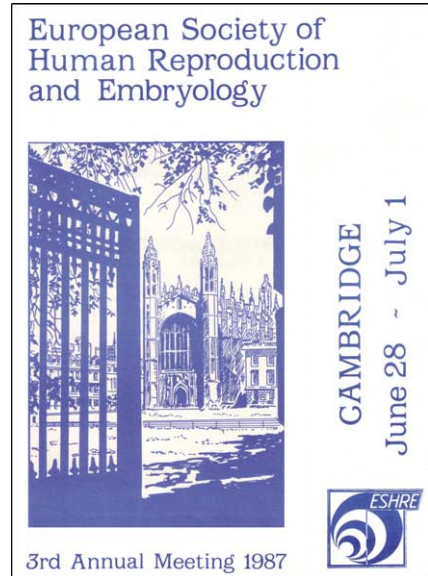
1987

* ESHRE given formal “consultative status” with Council of Europe.

* Berndt Kjessler takes over chairmanship of ethics committee.

* 3rd Annual Meeting at The Guildhall,
Cambridge, 28th June-1st July

- 850 attended
- Patrick Steptoe chairman of local organising committee
- Paramedical Group formed, with Hilde Olbrechts as chairman
- Second executive committee confirmed as:
 - Jean Cohen (chairman)
 - Pier Giorgio Crosignani (chairman elect)
 - Robert Edwards (past chairman)
 - Klaus Diedrich (secretary)
 - André Van Steirteghem (treasurer)
 - José Egozcue
 - Lars Hamberger
 - Anne McLaren
 - Gerard Zeilmaker
 - Berndt Kjessler (chairman ethics committee)
 - Arne Sunde (special advisor workshops)



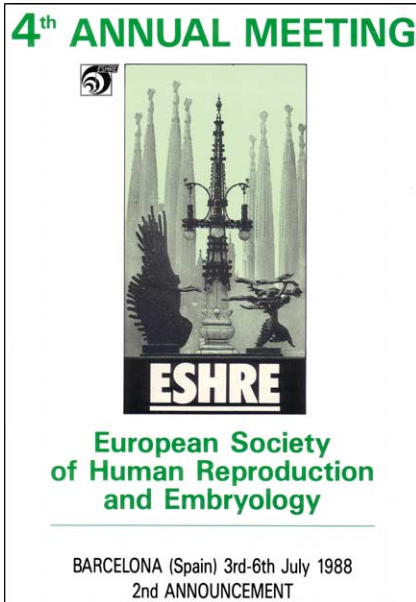
* ESHRE and ESCO joint congress in Budapest, with Rezso Gimes as local chairman and Robert Edwards as chairman of the European Scientific Committee (September); an ESHRE-ESCO congress committee is formed to organise the next joint meeting in 1990.

* Bruno Van den Eede joins ESHRE as part-time administrative assistant; Central Office accommodation is found at the VUB.

* Subscriptions to *Human Reproduction* total 500 (September).

1988

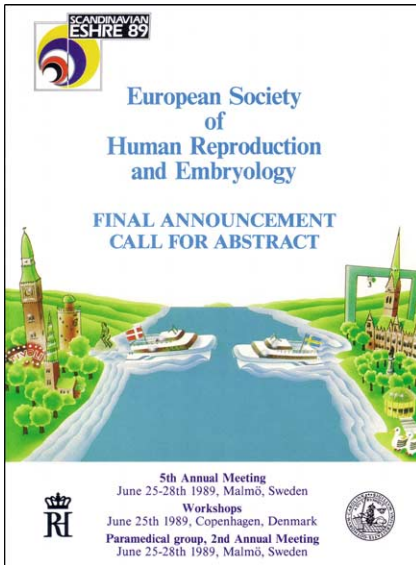
- * Membership reaches 1000.
- * Oxford University Press takes over publication of *Human Reproduction*.
- * ESHRE begins its first multicentre trial - on the treatment of unexplained infertility.



- * 4th Annual Meeting at The Princesa Sofia Hotel, Barcelona, 3rd-6th July
 - 800 attended
 - Juan Antonio Vanrell local chairman
 - Pedro Barri and José Egozcue co-chairmen of scientific committee
 - Parmamedical Group organises its first annual meeting (as a pre-congress event)

1989

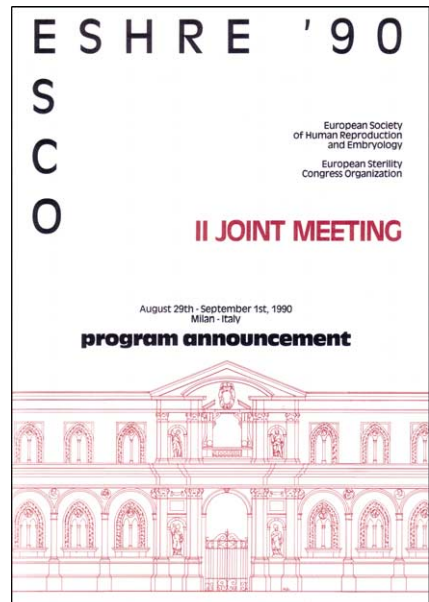
- * 5th Annual Meeting at The Malmo Theater, Malmo, 25th-28th June
 - 700 attended
 - Nils-Otto Sjoberg congress president
 - The idea of "Campus" workshops is announced - originally based on basic training courses run in Brussels and Bonn
 - Third executive committee confirmed as:
 - Pier Giorgio Crosignani (chairman)
 - André Van Steirteghem (chairman elect)
 - Jean Cohen (past chairman)
 - Klaus Diedrich (secretary)
 - Gerard Zeilmaker (treasurer)
 - Pedro Barri
 - Henning Beier



- Lars Hamberger
 - Steve Franks
 - Anne McLaren
 - Michelle Plachot
 - Berndt Kjessler (chairman ethics committee)
 - Arne Sunde (special advisor training)
 - Hilde Olbrechts (paramedical)
- * Safety and Standards Committee formed under chairmanship of Klaus Diedrich, following contamination of culture medium in The Netherlands.
- * Ethics Committee begins its task of developing guidelines for application of ART and PGD.

1990

- * *Human Reproduction* records its first profitable year.
- * First report from Safety and Standards Committee published; advises that the number of embryos transferred in an IVF cycle “should be limited to three”.
- * 6th Annual Meeting, organised jointly with ESCO, at The Università Statale, Milan, 29th August-1st September
 - 916 attended
 - Pier Giorgio Crosignani chairman of local organising committee
 - Congress was organised by “joint organising committee” of ESHRE and ESCO
 - ESHRE ends its active association with ESCO
- * A business consultant is hired to look at ESHRE’s financial structures; on his recommendation a management committee



and sub-committees for other areas of ESHRE's activities (including the Special Interest Groups) are formed.

* The first Campus workshops begin.

1991

* Ethics Committee publishes first draft of "Guidelines regarding medical practice related to assisted procreation and prenatal diagnosis".



* ESHRE's first multicentre clinical trial published.

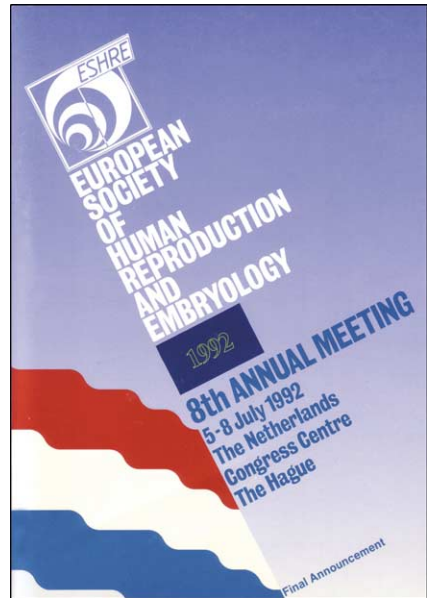
* 7th Annual Meeting, organised jointly with 7th World Congress on IVF and Assisted Reproduction, Palais des Congrès, Paris, 28th-30th June

- 1141 attended
- Jean Cohen and Michelle Plachot represent ESHRE on organising executive committee
- At a session on ethics, Cohen defends IVF against charges of WHO's Marsden Wagner
- Fourth executive committee confirmed as:
 - André Van Steirteghem (chairman)
 - Klaus Diedrich (chairman elect)
 - Pier Giorgio Crosignani (past chairman)

- Michelle Plachot (secretary)
- Basil Tarlatzis (treasurer)
- Pedro Barri
- Henning Beier
- Steve Franks
- Berndt Kjessler
- Carlo La Vecchia
- Arne Sunde (special advisor training)
- Hilde Olbrechts (paramedical)

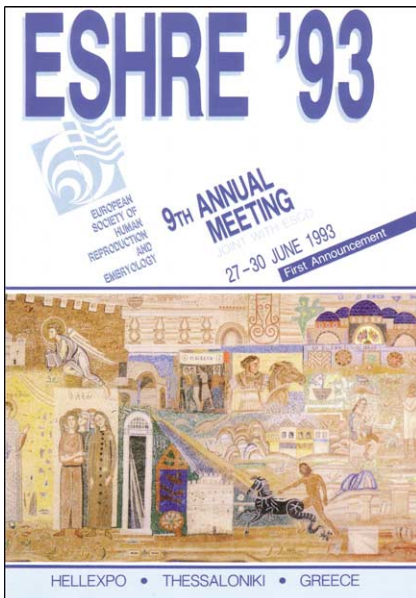
1992

- * 8th Annual Meeting at The Netherlands Congress Centre, The Hague, 5th-8th July
 - 942 attended
 - Frans Helmerhorst president
 - Gerard Zeilmaker chairman of local scientific committee
 - First meeting to assess abstracts by “blind” scoring
 - First Advisory Committee to be elected by full membership ballott



1993

- * First Campus workshop on ICSI (in Brussels).
- * *Human Reproduction* steps up to 12 issues per year; subscriptions reach almost 2000.



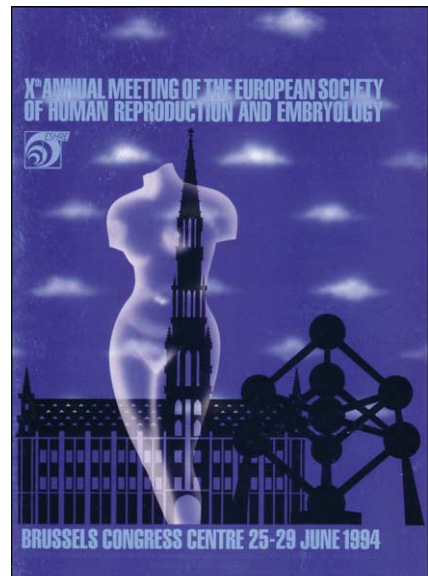
- * 9th Annual Meeting at The Helexpo International Congress Center, Thessaloniki, 27th-30th June
 - 1550 attended
 - Basil Tarlatziss congress president
 - First meeting to be organised independently
 - First programme to be determined by international scientific committee (chaired by Pier Giorgio Crosignani)
 - First exchange session with AFS; reciprocated later in year in Montreal at AFS congress
 - Van Steirteghem’s landmark presentation on ICSI
 - Safety session refutes claims of increased risk of ovarian cancer from ovarian stimulation

- Fifth executive committee confirmed as:
 - Klaus Diedrich (chairman)
 - José Egozcue (chairman elect)
 - André Van Steirteghem (past chairman)
 - Basil Tarlatzis (treasurer)
 - Paul Devroey
 - Hans Evers
 - Lynn Fraser
 - Matts Wikland
 - Carlo La Vecchia
 - Jean-René Zorn
 - Arne Sunde (special advisor training)
 - Frederike Wegener (paramedical)

*ESHRE membership reaches 2000.

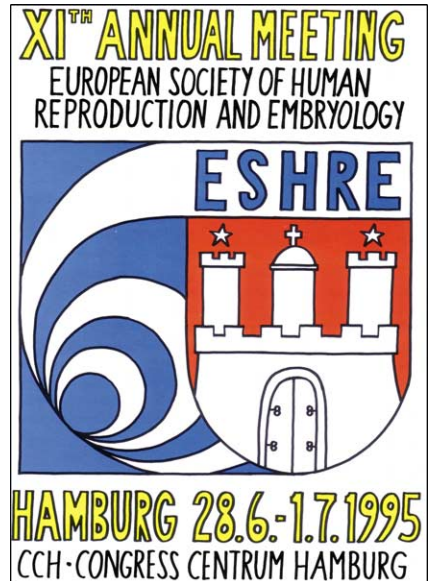
1994

- * ICSI task force formed.
- * New SIG established in reproductive genetics.
- * First course in semen assessment organised jointly by andrology SIG and British Andrology Society.
- * ESHRE's second multicentre clinical trial (in male infertility) published.
- * Hans Evers takes over as co-ordinator of SIGs (from Pedro Barri) and training (from Arne Sunde).
- * 10th Annual Meeting at the Brussels Congress Center, Brussels, 25th-29th June
 - 1702 attended
 - Pier Giorgio Crosignani chairman of international scientific committee
 - Introduction of "weighted" abstract scoring
 - First joint course with AFS



1995

- * Ethics Committee's updated (second) guidelines published.
- * Second guidelines on good laboratory practice published.
- * ESHRE signs new contract with Oxford University Press for publication of *Human Reproduction*.
- * Annual sales of *Human Reproduction* reach 2500.
- * First Campus workshop on reproductive genetics held in Maastricht (November).
- * Brussels workshop in collaboration with NIH on outcome of ART (December); first report from ESHRE's ICSI task force.
- * 11th Annual Meeting at the CCH-Congress Centrum, Hamburg, 28th June-1st July
 - 1484 attended
 - First congress to advertise programme on the Internet
 - First presentation from patient representative
 - Andrology SIG moves towards common standards of semen assessment in Europe
 - Sixth executive committee confirmed as:
 - José Egozcue (chairman)
 - Basil Tarlatzis (chairman elect)
 - Klaus Diedrich (past chairman)
 - Paul Devroey (treasurer)
 - Hans Evers
 - Lynn Fraser
 - Eberhard Nieschlag
 - Dominique Royère
 - Matts Wikland
 - Paulo Vercellini
 - Frederike Wegener (paramedical)
- * André Van Steirteghem appointed as Executive Director of ESHRE.
- * Exchange lectureships agreed with the Fertility Society of Australia and the Canadian Fertility and Andrology Society.

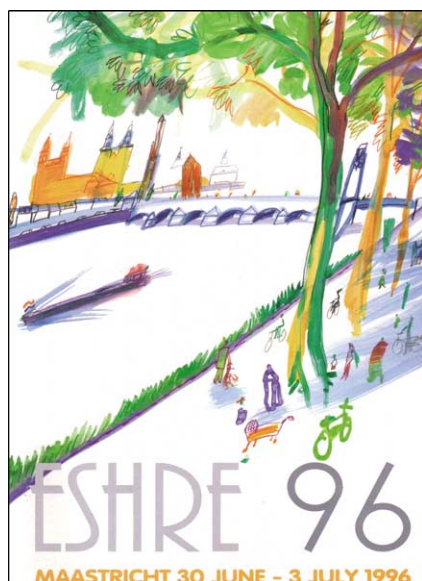


1996

* Central Office moves from the VUB to dedicated premises in Grimbergen outside Brussels.

* Editorial staff of *Human Reproduction* moves from Bourn Hall to Moor Barns Farmhouse outside Cambridge.

* *Human Reproduction Update* and *Molecular Human Reproduction* launched.



* 12th Annual Meeting at the Maastricht Exhibition and Congress Centre, Maastricht, 30th June-3rd July

– 2178 attended

– Hans Evers congress chairman

– André Van Steirteghem chairman of international scientific committee

– Ronny Janssens replaces Wegener as chairman of the Paramedical group

– Clinical tutorials introduced

– SIG in early pregnancy formed

– SIG in embryology revived under Luca Gianaroli

* ESHRE's first website goes live; on-line registration and abstract submission for Edinburgh 1997 is now possible.

* Formation of Publications Committee (to be chaired by chairman elect) and Finance Committee (to be chaired by ESHRE's chairman).

* Two new committees are given responsibility for training (chaired by Hans Evers) and SIG activities (chaired by Paul Devroey)

* Reproductive surgery SIG publishes guidelines for training, accreditation and monitoring in gynaecological endoscopy

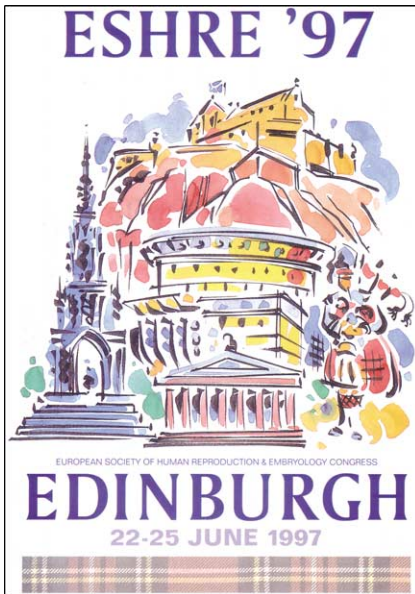
1997

* Membership reaches 3000.

* 13th Annual Meeting at the Edinburgh International Conference Centre, Edinburgh, 22nd-25th June

– 2413 attended

– David Baird congress chairman, Stewart Irvine congress secretary



- Klaus Diedrich chairman of international scientific committee
- Content of satellite symposia determined by scientific committee, not sponsors
- PGD Consortium joins SIG in reproductive genetics
- Seventh executive committee confirmed as:
 - Basil Tarlatzis (chairman)
 - Lynn Fraser (chairman elect)
 - José Egozcue (past chairman)
 - Johan Smitz (treasurer)
 - Anders Nyboe Andersen
 - Maas Jan Heineman
 - Eberhard Nieschlag
 - Karl Nygren

- Antonio Pellicer
- Dominique Royere
- Paulo Vercellini
- Hans Evers (co-ordinator training)
- Paul Devroey (co-ordinator SIGs)
- Ronny Janssens (paramedical)

* ESHRE agrees to a five-year moratorium on reproductive cloning.

1998

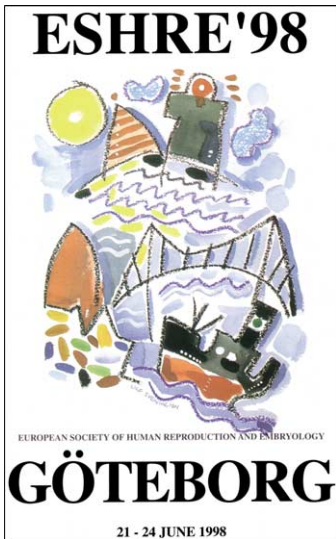
* Celebration of the first 20 years of IVF jointly organised by Middle East Fertility Society and ESHRE in Marakech, Morocco.

* SIG in ethics and law formed under chairmanship of Françoise Shenfield.

* Second and third reports from ICSI task force published.

* Web publication of papers introduced by *Human Reproduction*.

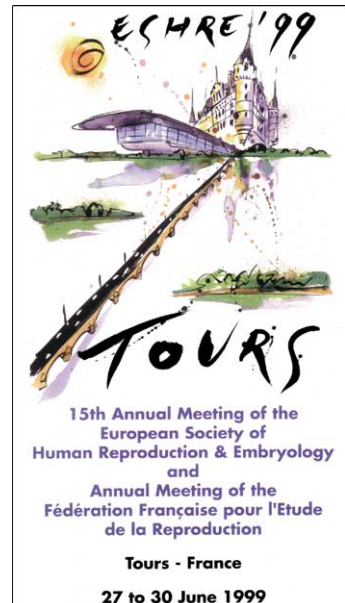
* *Human Reproduction* and *Human Reproduction Update* reach numbers 1 and 2 in impact factor index for O&G.



- * 14th Annual Meeting at the Swedish Exhibition and Congress Centre, Gothenburg, 21st-24th June
 - 2550 attended
 - Lars Hamberger congress chairman, Matts Wikland congress secretary
 - Klaus Diedrich chairman of international scientific committee

1999

- * First report from SIG in reproductive genetics
- * The Executive Committee rejects Edwards's bid for self-publication of the journals and opts to renew its contract with Oxford University Press.
- * 15th Annual Meeting at the Vinci International Conference Centre, Tours, 27th-30th June
 - 2742 attended
 - Jacques Lansac congress chairman, Dominique Royere congress secretary
 - José Egozcue chairman of international scientific committee
 - Press office and communications programme introduced
 - ESHRE's own dedicated website launched
 - European IVF monitoring (EIM) committee formed following proposals from Karl Nygren and Anders Nyboe Andersen

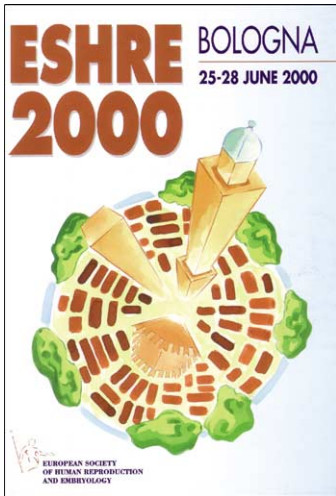


- Eighth executive committee confirmed as:
 - Lynn Fraser (chairman)
 - Hans Evers (chairman elect)
 - Basil Tarlatzis (past chairman)
 - Johan Smitz (treasurer)
 - Anders Nyboe Andersen
 - Luca Gianaroli
 - Maas Jan Heineman
 - Jacqueline Mandelbaum
 - Joseph Neulen
 - Karl Nygren
 - Antonio Pellicer
 - Paul Devroey (co-ordinator SIGs)
 - Ronny Janssens (paramedical)

*Formation of SIG in endometriosis

2000

- * Robert Edwards resigns as editor of ESHRE's three journals.
- * David Barlow appointed as editor of *Human Reproduction*, Richard Ivell as editor of *Molecular Human Reproduction*, and Bart Fauser as editor of *Human Reproduction Update*.
- * Associate editors replace editorial board of *Human Reproduction*.
- * Second report from PGD Consortium.
- * ESHRE is contracted to the European Board and College of Obstetrics and Gynaecologists (EBCOG) for the development of sub-specialist training in reproductive medicine
- * EIM committee publishes first report (on IVF in 1997).
- * Third ESHRE guidelines on good laboratory practice published from SIG in embryology.
- * 16th Annual Meeting at the Palazzo della Cultura e dei Congressi, Bologna, 25th-28th June
 - 3342 attended
 - Pier Giorgio Crosignani congress chairman, Luca Gianaroli congress secretary
 - José Egozcue chairman of international scientific committee



- Mark Van den Bergh succeeds Ronny Janssens as chairman of Paramedical Group
- EIM committee presents first report
- * Arne Sunde replaces Hans Evers as co-ordinator of training.
- * First Campus workshop, organised in Antwerp by Jan Gerris, on the prevention of multiple pregnancies; a task force in risks and complications in IVF is subsequently formed.
- * ESHRE forms "protocol of collaboration" with Middle East Fertility Society.

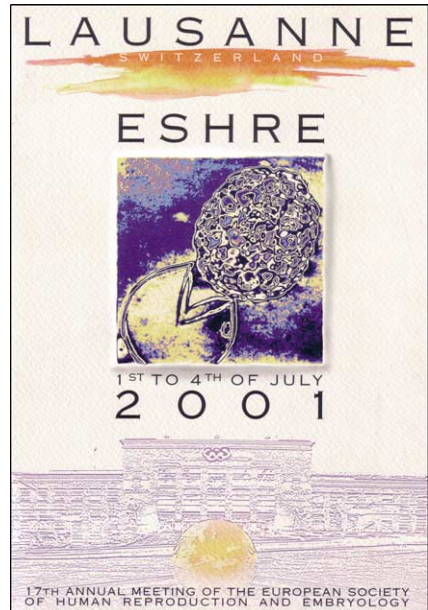
2001

* Ethics and law task force publishes first statement (on the moral status of the pre-implantation embryo); seven more will follow over the next three years.

* Second report from IVF monitoring programme (EIM).

* 17th Annual Meeting at the Palais de Beaulieu Conference Centre, Lausanne, 1st-4th July

- 3466 attended
- Marc Germond congress chairman, Alfred Senn congress secretary
- Basil Tarlatzis chairman of international scientific committee
- Ninth executive committee confirmed as:
 - Hans Evers (chairman)
 - Arne Sunde (chairman elect)
 - Lynn Fraser (past chairman)
 - Christina Bergh
 - Luca Gianaroli
 - Jacqueline Mandelbaum
 - Ioannis Messinis
 - Joseph Neulen



- Juha Tapanainen
- Janos Urbancsek
- Josiane Van der Elst
- Anna Veiga
- Paul Devroey (co-ordinator SIGs)
- Mark Van den Bergh (paramedical)

* Evers and Sunde present their strategy report for next four years; a grand plan for training is devised.

* ESHRE membership reaches 4243 in July.

2002

* Third report from EIM committee.

* Third report from PGD Consortium.

* Ethics and law task force publishes statement on stem cells.

* 18th Annual Meeting at the Austria Centre, Vienna, 30th June-3rd July

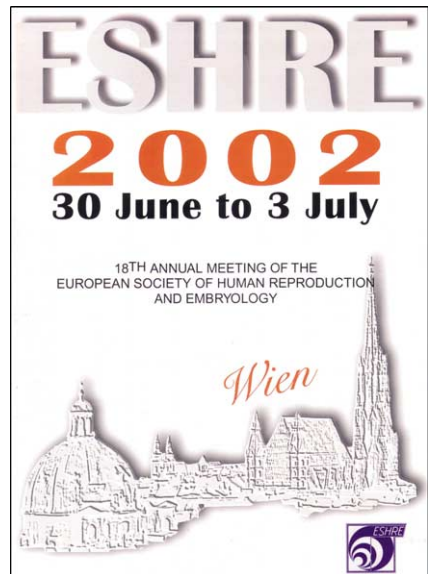
- 3808 attended
- F Fischl congress chairman
- Basil Tarlatzis chairman of international scientific committee
- Robert Edwards delivers first RG Edwards keynote lecture
- Alan Trounson speaks on embryonic stem cells
- SIGs formed in stem cells, evidence-based medicine, and risks and complications (from Gerris's multiple pregnancy task force).

* Portfolio responsibilities allocated to members of EC for training, annual meetings, finance, and publications.

* Term of office of AC membership extended to four years.

* ESHRE publicly condemns proposals in Italy to restrict the scope of ART.

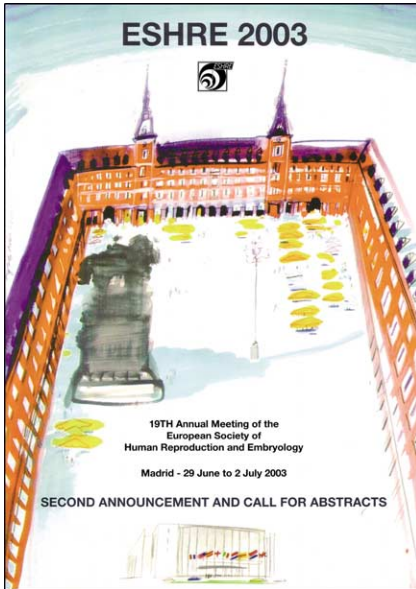
* Politicians no longer invited to speak at opening ceremonies.



2003

* The day-to-day running of the society put in the hands of a “chairmen’s group” (composed of the past, present and future chairmen) working alongside Central Office.

* Joint ESHRE/ASRM consensus on polycystic ovary syndrome held in Rotterdam.



* 19th Annual Meeting at the Palacio Municipal de Congressos de Madrid, 29th June-2nd July

- 4547 attended
- Antonio Pellicer congress chairman, Juan Garcia-Velasco and Carlos Simon congress secretaries
- Lynn Fraser chairman of international scientific committee
- Tenth executive committee confirmed as:
 - Arne Sunde (chairman)
 - Paul Devroey (chairman elect)
 - Hans Evers (past chairman)
 - Christina Bergh
 - Joyce Harper
 - Ioannis Messinis
 - François Olivennes
 - Juha Tapanainen
 - Janos Urbancsek
 - Josiane Van der Elst
 - Anna Veiga
 - Luca Gianaroli (co-ordinator SIGs)
 - Jan Kremer (website)
 - Liz Corrigan (paramedical)

2004

- * Fourth report from EIM committee.
- * ESHRE renews moratorium on reproductive cloning.
- * Reproductive endocrinology SIG publishes Rotterdam ESHRE/ASRM consensus on polycystic ovary syndrome.
- * 20th Annual Meeting at the ICC, Berlin, 27th-30th June
 - 5309 attended
 - Heribert Kantenich congress chairman
 - Lynn Fraser chairman of international scientific committee
 - Belgian group of Donnez announces first ongoing pregnancy from frozen-thawed ovarian tissue



APPENDIX D

ESHRE publications

Clinical trials

1. Crosignani PG, Walters DE, Soliani A. The ESHRE multicentre trial on the treatment of unexplained fertility: a preliminary report. *Hum Reprod* 1991; 6: 953-958.
2. Crosignani PG, Walters DE. Clinical pregnancy and male subfertility; the ESHRE multicentre trial on the treatment of male subfertility. *Hum Reprod* 1994; 9: 1112-1118.

Safety and standards/good practice

1. Safety and Standards Committee. Focus on Reproduction 1990; 1: 10-38.
2. Van den Eede B. Investigation and treatment of infertile couples: ESHRE guidelines for good clinical and laboratory practice. *Hum Reprod* 1995; 10: 1246-1271.
3. Gianaroli L, Plachot M, van Kooij R, Al-Hasani S, Dawson K, DeVos A, Magli MC, Mandelbaum J, Selva J, van Inzen W and Committee of the Special Interest Group on Embryology. ESHRE guidelines for good practice in IVF laboratories. *Hum Reprod* 2000; 15: 2241-2246.

ICSI task force

1. The ESHRE Task Force in Intracytoplasmic Sperm Injection. Assisted reproduction by intracytoplasmic sperm injection. Focus on Reproduction 1995; 3: 9-12.
2. Tarlatzis BC. Report on the activities of the ESHRE Task Force on Intracytoplasmic Sperm Injection. Hum Reprod 1996; 11 (Suppl 4): 160-186.
3. ESHRE Task Force on Intracytoplasmic Sperm Injection. Assisted reproduction by intracytoplasmic sperm injection: a survey on the clinical experience in 1994 and the children born after ICSI, carried out until 31 December 1993. Hum Reprod 1998; 13: 1737-1746.
4. Tarlatzis BC, Bili H. Survey on intracytoplasmic sperm injection: report from the ESHRE ICSI Task Force. Hum Reprod 1998; 13 (Suppl 1): 165-177.

IVF monitoring

1. The European IVF Monitoring Programme (EIM) for the European Society of Human Reproduction and Embryology (ESHRE). Assisted Reproductive Technology in Europe, 1997. Results generated from European registers by ESHRE. Hum Reprod 2001; 16: 384-391.
2. Nygren KG, Andersen AN; European IVF Monitoring Programme (EIM) for the European Society of Human Reproduction and Embryology (ESHRE). Assisted Reproductive Technology in Europe, 1998. Results generated from European registers by ESHRE. Hum Reprod 2001; 16: 2459-2471.
3. Nygren KG, Andersen AN. The European IVF Monitoring Programme (EIM) for the European Society of Human Reproduction and Embryology (ESHRE). Assisted Reproductive Technology in Europe, 1999. Results generated from European registers by ESHRE. Hum Reprod 2002; 17: 3260-3274.
4. Nyboe Andersen A, Gianaroli L, Nygren KG: The European IVF Monitoring Programme (EIM) for the European Society of Human Reproduction and Embryology (ESHRE). Assisted Reproductive Technology in Europe, 2000. Results generated from European registers by ESHRE. Hum Reprod 2004; 19: 490-503.

Ethics and law

1. ESHRE Task Force on Ethics and Law. I. The moral status of the pre-implantation embryo. *Hum Reprod* 2001; 16: 1046-1048.
2. ESHRE Task Force on Ethics and Law. II. The cryopreservation of human embryos. *Hum Reprod* 2001; 16: 1059-1060.
3. ESHRE Task Force on Ethics and Law. III. Gamete and embryo donation. *Hum Reprod* 2002; 17: 1407-1408.
4. ESHRE Task Force on Ethics and Law. IV. Stem cells. *Hum Reprod* 2002; 17: 1409-1410.
5. Shenfield F, Pennings G, Devroey P, Sureau C, Tarlatzis B, Cohen J; ESHRE Ethics Task Force. V. Preimplantation genetic diagnosis. *Hum Reprod* 2003; 18: 649-651.
6. ESHRE Task Force on Ethics and Law. VI. Ethical issues related to multiple pregnancies in medically assisted procreation. *Hum Reprod* 2003; 18: 1976-1979.
7. ESHRE Task Force on Ethics and Law. VII. Ethical considerations for the cryopreservation of gametes and reproductive tissues for self use. *Hum Reprod* 2004; 19: 460-462.
8. ESHRE Task Force on Ethics and Law. VIII. Ethics of medically assisted fertility treatment for HIV positive men and women. *Hum Reprod* 2004; 19: 2454-2456.

Reproductive endocrinology

The Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Hum Reprod* 2004; 19: 41-47.

Preimplantation genetics

1. Geraedts J, Handyside A, Harper J, Liebaers I, Sermon K, Staessen C, Thornhill A, Vanderfaillie A, Viville S. ESHRE Preimplantation Genetic Diagnosis (PGD) Consortium: preliminary assessment of data from January 1997 to September 1998. ESHRE PGD Consortium Steering Committee. *Hum Reprod* 1999; 14: 1667.
2. Geraedts J, Handyside A, Harper J, Liebaers I, Sermon K, Staessen C, Thornhill A, Viville S, Wilton L; European Society of Human

Reproduction and Embryology Preimplantation Genetic Diagnosis Consortium Steering Committee. ESHRE Preimplantation Genetic Diagnosis Consortium: data collection II. *Hum Reprod* 2000; 15: 2673-2683.

3. ESHRE PGD Consortium Steering Committee. ESHRE Preimplantation Genetic Diagnosis Consortium: data collection III. *Hum Reprod* 2002; 17: 233-246.

4. Sermon K, Moutou C, Harper J, Geraedts J, Scriven P, Wilton L, Magli M-C, Michiels A, Viville S, De Die C. ESHRE PGD Consortium data collection IV: May-December 2001. *Hum Reprod* 2005; 20: 19-34.

5. Thornhill AR, De Die-Smulders CE, Geraedts JP, Harper JC, Harton GL, Lavery SA, Moutou C, Robinson MD, Schmutzler AG, Scriven PN, Sermon KD, Wilton L. ESHRE PGD Consortium best practice guidelines for clinical preimplantation genetic diagnosis (PGD) and preimplantation genetic screening (PGS). *Hum Reprod* 2005; 20: 35-48.

Andrology

1. ESHRE Andrology Special Interest Group. Consensus Workshop on advanced diagnostic andrology techniques. *Hum Reprod* 1996; 11: 1463-1479.

2. ESHRE Andrology Special Interest Group. Guidelines on the application of CASA technology in the analysis of spermatozoa. *Hum Reprod* 1998; 13: 142-145.

3. Barratt C, Englert Y, Gottlieb C, Jouannet P. Gamete donation guidelines. The Corsendonk consensus document for the European Union. *Hum Reprod* 1998; 13: 500-501.

4. Bjorndahl L, Barratt CL, Fraser LR, Kvist U, Mortimer D. ESHRE basic semen analysis courses 1995-1999: immediate beneficial effects of standardized training. *Hum Reprod* 2002; 17: 1299-1305.

5. Kvist U, Bjorndahl L. (Eds.) Basic semen analysis. ESHRE Monographs: Oxford University Press, 2002.

Endometriosis

Bergqvist A, D'Hooghe T. Mini symposium on pathogenesis of endometriosis and treatment of endometriosis-associated subfertility. Introduction: the endometriosis enigma. *Hum Reprod Update* 2002; 8: 79-83.

Risks and complications in ART/multiple pregnancy

1. European Society of Human Reproduction and Embryology. Prevention of twin pregnancies after IVF/ICSI by single embryo transfer. ESHRE Campus Course Report. Hum Reprod 2001; 16: 790-800.
2. Land JA, Evers JL. Risks and complications in assisted reproductive techniques: Report of an ESHRE consensus meeting. Hum Reprod 2003; 18: 455-457.

Psychology and counselling

1. Boivin J, Appleton TC, Baetens P, et al; European Society of Human Reproduction and Embryology. Guidelines for counselling in infertility: outline version. Hum Reprod 2001; 16: 1301-1304.
2. Boivin J, Kertenich H. (Eds.) Guidelines for counselling in infertility. ESHRE Monographs: Oxford University Press, 2002.

Reproductive surgery

Chapron C, Devroey P, Duboisson JB, Pouly JL, Vercellini P. ESHRE guidelines for training, accreditation and monitoring in gynaecological endoscopy. Committee of Special Interest Group on Reproductive Surgery. Hum Reprod 1997; 12: 867-868.

Capri workshops

1. Crosignani PG, Edwards RG. Current treatments with LHRH and its analogues. Hum Reprod 1987; 2: 95-97.
2. Crosignani PG, Rubin B. Risks and benefits of steroid replacement therapy. Hum Reprod 1988; 3: 924-926.
3. Crosignani PG, Rubin B. Strategies for the treatment of hirsutism. Hum Reprod 1989; 4: 651-652
4. Crosignani PG, Rubin B. Dysfunctional uterine bleeding. Hum Reprod 1990; 5: 637-638.
5. Crosignani PG, Rubin B. Recurrent spontaneous abortion. Hum Reprod 1991; 6: 609-610.
6. Crosignani PG, Diczfalusy E, Newton J, Rubin B. Sexually transmitted diseases. Hum Reprod 1992; 7: 1330-1334.

7. Crosignani PG, Collins J, Cooke ID, Diczfalusy E, Rubin B. Unexplained infertility. *Hum Reprod* 1993; 8: 977-980.
8. The ESHRE Capri Workshop Group. Male sterility and sub-fertility: guidelines for management. *Hum Reprod* 1994; 9: 1260-1264.
9. The ESHRE Capri Workshop Group. Anovulatory infertility. *Hum Reprod* 1995; 10: 1549-1553.
10. The ESHRE Capri Workshop Group. Guidelines to the prevalence, diagnosis, treatment and management of infertility, 1996. *Hum Reprod* 1996; 11: 1775-1807.
11. The ESHRE Capri Workshop Group. Female infertility: treatment options for complicated cases. *Hum Reprod* 1997; 12: 1191-1196.
12. Crosignani PG, Rubin B. Cardiovascular effects of combined oral contraceptives and hormone replacement therapy. *Eur Menopause J* 1997; 4: 60-67.
13. The ESHRE Capri Workshop Group. Male infertility update. *Hum Reprod* 1998; 13: 2025-2032.
14. The ESHRE Capri Workshop Group. Hormones and cardiovascular disease: Oral contraceptives and hormonal replacement therapy: differential effects on coronary heart disease, deep vein thrombosis and stroke. *Hum Reprod* 1998; 13: 2325-2333.
15. Crosignani PG, La Vecchia C. Concordant and discordant effects on cardiovascular risks exerted by oestrogen and progestogen in women using oral contraception and hormone replacement therapy. *Hum Reprod Update* 1999; 5: 681-687.
16. The ESHRE Capri Workshop Group. Screening before and during the use of oral contraceptives and hormone replacement therapy. *Hum Reprod* 2000; 15: 485-492.
17. The ESHRE Capri Workshop Group. Optimal use of infertility diagnostic tests and treatments. *Hum Reprod* 2000; 15: 723-732.
18. The ESHRE Capri Workshop Group. Multiple gestation pregnancy. *Hum Reprod* 2000; 15: 1856-1864.
19. The ESHRE Capri Workshop Group. Continuation rates for oral contraceptives and hormone replacement therapy. *Hum Reprod* 2000; 15: 1865-1871.
20. The ESHRE Capri Workshop Group. Ovarian and endometrial function during hormonal contraception. *Hum Reprod* 2001; 16: 1527-1535.
21. The ESHRE Capri Workshop Group. Social determinants of human reproduction. *Hum Reprod* 2001; 16: 1518-1526.

22. The ESHRE Capri Workshop Group. Hormonal contraception: what is new? *Hum Reprod* 2002; 8: 359-371.
23. The ESHRE Capri Workshop Group. Physiopathological determinants of human infertility. *Hum Reprod* 2002; 8: 435-447.
24. The ESHRE Capri Workshop Group. Hormonal contraception without estrogens. *Hum Reprod* 2003; 9: 373-386.
25. The ESHRE Capri Workshop Group. Mono-ovulatory cycles: a key goal in profertility programmes. *Hum Reprod* 2003; 9: 263-274.
26. ESHRE Capri Workshop Group. Hormones and breast cancer. *Hum. Reprod Update* 2004; 10: 281-293.
27. ESHRE Capri Workshop Group. Diagnosis and management of the infertile couple: missing information. *Hum Reprod Update* 2004; 10: 295-307.