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Preface “50 Years of Gonadotropin Therapy”

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FÜR KLINIK & PRAXIS

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Freuen Sie sich auf spannende Vorträge und den lebendigen Austausch mit Kolleg:innen und Expert:innen aus Klinik und Praxis. Freitagabend laden wir Sie herzlich zu einem entspannten Empfang ein – eine perfekte Gelegenheit, Kontakte zu knüpfen und den Tag genussvoll ausklingen zu lassen.

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Preface “50 Years of Gonadotropin Therapy”

The purification of gonadotropins from the urine of menopausal women was certainly a key step towards differentiated methods of controlled ovarian stimulation and hyperstimulation. As we have come to know hyperstimulation as a core component of IVF or ICSI treatment, we tend to forget what was the original goal of gonadotropin therapy, i.e. treating infertile patients with central, hypogonadotrophic amenorrhea.

At the time, it was a sensation to find that these chronically anovulatory women all of a sudden developed intense ovarian activity and in most cases also had ovulations after being injected with gonadotropins, although the ovulations were often multiple ones. As a consequence, the delight over the resulting pregnancies was tainted by the problem of frequent higher-grade multiple pregnancies. The lessons have been learned and the risk of multiple pregnancies have been reduced over time.

Another 15 years went by from the first steps of ovarian stimulation treatment to the birth of Louise Brown. The first German “IVF baby” was born 30 years ago, and the method spread rapidly.

Only 10 years later, the German IVF register (DIR) was established – by the way on the initiative of the doctors themselves and long before any plans for legal or professional rules were made. The DIR has now grown into a substantial and internationally much-respected statistical database: The annals of 1996–2010 record data from 1.006.266 treatment cycles leading to 156.809 live births, more than 22.000 of which are based on the transfer of cryopreserved oocytes.

IVF treatment was mainly aimed at women with tubal problems. Leaving aside the “option” of sperm donation, severe male subfertility continued to be a problem. The introduction of intracytoplasmic sperm injection (ICSI) was another revolutionary step: It even helped men with azoospermia to have a child of their own after extracting sperm from their testicles (TESE).

With the advent of ICSI if not before, it became clear that IVF labs and biologists were taking center stage. So the post-ICSI era is marked by the attempt to customise the different techniques to suit the individual situation of the couple, but also to find objective, highly prognostic biomarkers for the development and implantation potential of an oocyte or embryo.

This search is not just about prognostic parameters, but also techniques: One example is intracytoplasmic morphologically selected spermatozoa injection (IMSI), where it is hoped that the targeted selection of sperms based on morphological criteria will lead to higher pregnancy and birth rates.

Although this method is still under highly controversial discussion, it illustrates the constant quest for better treatment results. Further examples are studies into gene expression (e.g. in cumulus cells, in the endometrium) and metabolic changes in the culture medium (metabolomics) or the application of cytokines or growth factors systemically or in the culture medium (G[M]-CSF). At this point, we should also mention time-lapse imaging (TLI), i. e. the continuous documentation of embryonic development, helping to identify the characteristic morphokinetic parameters potentially determining a successful implantation.

Even though these methods have not yet become routine and some of the concepts still have to be further developed, they already indicate future trends influencing lab work in the future.

Human genetics is another recent addition to the field of reproductive medicine based on the possibility to diagnose monogenic diseases in oocytes (using polar body



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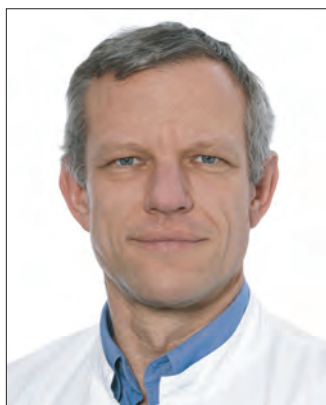
Thomas Rabe



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Jens Hirchenhain

biopsy) or embryos (using preimplantation genetic diagnosis [PGD] by blastomer biopsy or trophoctoderm biopsy [TEB]). On the other hand, it is increasingly recognised that many human preimplantation embryos show aneuploidy, frequently of the mosaic type.

The obvious question as to whether the diagnosis of aneuploidies or mosaicisms influences the implantation rate has been the object of many studies. It is too early for a conclusive answer to this question, but there is no doubt (any more) that human genetics have become a part of reproductive medicine.

The increasing scope for the customised treatment of couples is complemented by improvements in cryopreservation such as vitrification. This procedure as well as the improved conventional techniques have opened up new therapeutic options such as “freeze all but one”. Since it has emerged that the natural cycle offers better conditions for implantation than the stimulated cycle, cryopreservation will become even more important.

This is also true for fertility protection in the context of curative malignoma therapy. Both the cryopreservation of ovarian tissue and of oocytes (increasingly unfertilised ones, e.g. if there is no steady relationship) have just about become routine now. “Social freezing” is also on the rise, i.e. a woman’s oocytes are frozen at a young age in order to fertilise them at a later stage when she wants to have children but has a reduced fecundity due to higher age.

All these procedures and methods are of course closely related to hormonal stimulation treatment. With the introduction of gonadotropins, the range of pharmacological options has widened enormously: Genetically produced, i.e. recombinant gonadotropins and long-acting “designer molecules” such as corticofollitropin, GnRH agonists and antagonists have made the stimulated cycles more plannable and reliable, and antiestrogens or SERMs (selective estrogen receptor modulators) such as aromatase inhibitors have also been developed. Recently, the first selective progesterone receptor modulators have become available, so the range of options is continuing to grow.

In a space of decades, therefore, a completely new medical field has emerged which is very exciting, innovative and fast-moving.

Without the pioneering work of Professor Bruno Lunenfeld the development of the first urinary human menopausal gonadotropins would not have been possible. He gave the impetus for the development of further preparations and supported the switch from urinary to recombinant gonadotropins in the 1980s and 1990s.

Introducing urinary human gonadotropins opened the way to finish the use of human pituitary gonadotropins (HPG) and pregnant mare serum gonadotropins (PMSG) in the treatment of subfertile patients. This was an enormous health benefit for the patients and finally only possible because of Prof. Lunenfelds scientific and clinical studies in this field.

Most of the procedures and methods in reproductive medicine are closely related to hormonal stimulation treatment. Beside urinary gonadotropins nowadays recombinant gonadotropins and long-acting “designer molecules” such as corticofollitropin are available.



Bruno Lunenfeld



Bruno Lunenfeld



Bruno Lunenfeld with HRH King and Queen of Malaysia, 2001



Bruno Lunenfeld and his wife with Wolfgang Wagner in Bayreuth, 2002



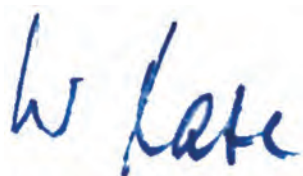
Bruno Lunenfeld with Robert Greenblatt (left) and VB Mahesh (right), 1962



Bruno Lunenfeld and his wife with Thomas Strowitzki (left) and Thomas Rabe (right) in Heidelberg, 1995

Dear Bruno,

you have made a major contribution to the development of modern reproductive medicine and we are extremely grateful to you. We hope you will stay as creative and innovative, but most importantly, as healthy as ever!



Prof. Dr. med. Thomas Rabe

Präsident der Deutschen Gesellschaft
für Gynäkologische Endokrinologie und
Fortpflanzungsmedizin e.V.



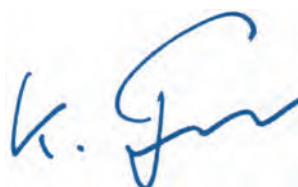
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