RBMO

OBITUARY

Obituary: Ivo Brosens (1931–2022)

It was with great sadness that we recently learned of the loss of a major figure in our field. On Wednesday 23 November 2022, age 91, Ivo Brosens, Professor Emeritus of Gynaecology and Obstetrics at the Catholic University of Leuven and a giant in the field, passed away peacefully after a long life professionally dedicated to the study of reproductive biology and its clinical applications. His influence was as broad as it was deep.

Professor Brosens was born in Flanders near Antwerp, the fourth child of a large family, and studied philosophy and philology before enrolling in the medical school of the Catholic University (KU) in Leuven.

His initial field of research was feto-maternal medicine, specifically the physiopathology of the placental bed. After the discovery by *Browne and Veall (1953)* that preeclampsia was characterized by a decreased maternal blood flow to the placenta, at the suggestion of Marcel Renaer, at the time Chairman of the Department of Gynaecology and Obstetrics at KU Leuven, Ivo became interested in the study of placental specimens. He then moved to London to prepare his PhD thesis on the placental bed, using the methodology proposed by *Dixon and Robertson (1958)*. With his colleagues in Leuven, he collected uteri with the placenta *in situ* from Caesarean hysterectomies carried out in women with and without hypertensive disease. This research, published as Ivo's Thesis (*Brosens, 1965*) revealed for the first time the vascular pathology associated with the 'great obstetrical syndromes' (GOS).

Upon return to the Leuven University Hospital in 1966, Ivo was appointed Associate Professor and then Full Professor in 1975. There, he created a research unit that quickly became a focal point for placental bed research, hosting in 1974 the first international symposium on this promising field of research.

After establishing himself as a pioneer in the study of placenta, Ivo moved on to other fields of reproductive medicine, establishing in Leuven a pioneering Centre for Reconstructive Reproductive Microsurgery (*Gordts et al, 1984*). He gave an international hands-on microsurgery course for gynaecologists there for 10 consecutive years. After the success of the first pregnancy following IVF and embryo transfer in Cambridge, Ivo realized that this technique would replace surgery for tubal occlusion and started an IVF programme at KU. Because the Catholic Church had rejected the technique on ethical grounds, the Dean of the Medical School decided that the news of the birth of the first IVF baby in Leuven should not be divulged and eventually IVF was discontinued at KU Leuven and the team was dismantled. This forced Ivo and his co-workers to create, not without controversy, a private Centre in Leuven, still active today (The Life Expert Centre).

Over the years, Ivo Brosens became involved in a number of areas of reproductive medicine and, typical of his character, he quickly became an internationally recognised leader in each of them. An important new area of his interest was endoscopy to explore the pelvis and its content in infertile patients. A first achievement was the adaptation of salpingoscopy, originally performed during laparotomy, to endoscopy (Gordts et al, 2007). His group then set-up the technique known as transvaginal hydrolaparoscopy as an outpatient procedure for the investigation of infertility, using culdocentesis to access the pouch of Douglas, followed by hydroflotation. This led, in 1992, to the creation of the Centre for Surgical Technologies, one of the oldest and most prominent research and training centres for endoscopic surgery and microsurgery in Europe.

Using the laparoscope, Ivo described a somewhat mysterious phenomenon coined LUF for 'luteinized, unruptured follicle' in women with endometriosis (*Brosens and Koninckx, 1980*).

At this stage, he became more and more involved in work on the clinical and pathophysiologic aspects of endometriosis and adenomyosis with a focus on the endometrioma. Here it is important to recall that in the endless debate on endometriosis, he took a firm stand: 'Endometriosis is a disease because it bleeds' (*Brosens, 1997*).

As a teacher, Ivo supervised a number of talented PhD students from several European countries and his work was internationally acknowledged, allowing him to teach and establish collaborations around the world. He acted as Visiting Professor at the University of Bristol, UK; at Columbia University, New York, USA; at the University of New Mexico, Albuquerque, USA, at the King Edward Memorial Hospital for Women, Perth, Australia; at the University of Hong Kong; and at the University of the Free State, Bloemfontein, South-Africa.

He received numerous awards and honorary memberships from national societies including the Royal Society of Medicine in the UK (Section Obstetrics and Gynaecology); the Royal College of Obstetrics and Gynaecology (fellow *ad eundem*); the American Society of Reproductive Medicine. He was among the founding members of the World Endometriosis Society.

Because of his long life, Ivo Brosens spent 25 years in retirement, but – as he repeatedly stated – 'would continue to work for as long as my physical conditions

will allow'. In fact, thanks to the internet, he not only continued his collaboration with scientists across the world, but developed novel concepts and opened new research avenues. In the end he was able to produce and publish until the final year before his death.

During these long, yet productive years, he not only retraced his early work summarising and updating his findings (e.g., *Brosens et al, 2019*), but dedicated his time to uncovering old, forgotten scientific literature. Specifically, neonatal uterine bleeding (NUB), also named 'neonatal menstruation' had been frequently reported as interesting case reports in the old literature and even in religious books (see the *Mishneh Torah*, the code of Jewish religious law authored by Rabbi Moshe ben Maimon, towards the end of the 12th century) (*Benagiano et al., 2021*). In recent times, NUB has been considered a physiologic event due to progesterone withdrawal at birth and therefore of no clinical relevance. This position, however, ignored the fact that progesterone withdrawal occurs in all neonates, whereas NUB manifests itself in only 3–5% of them. Brosens not only re-discovered the fundamental results of a remarkable autopsy study by the Harvard pathologists *Ober and Bernstein (1955)*, but produced a theory linking NUB to the rare occurrence of very early endometriosis (*Brosens and Benagiano, 2013*). Subsequently, with his collaborators he published a series of articles on the subject, not only explaining the mechanism of NUB, but also reporting evidence that it occurs significantly more frequently in neonates born following pre-eclampsia and fetal growth restriction. This suggests that in these fetuses decidualisation followed by menstrual shedding is caused by chronic fetal distress.

His latest work provided additional evidence that the GOS may have their roots in early neonatal life, stimulating research in this area.

As we celebrate his life and work, we believe that Professor Brosens' legacy in obstetrics, gynaecology and reproductive medicine will continue to positively influence research, clinical practice and the care we provide to our patients for many years to come.

REFERENCES

Benagiano, G., Habiba, M., Lippi, D., Brosens, I.A., 2021. A History of Neonatal Uterine Bleeding and its Significance. Reprod. Med. 2, 171–184. https://doi.org/10.3390/reprodmed2040018.

Brosens, I., 1965. The placental bed. Thesis Faculty of Medicine, University of London, London.

Brosens, I.A., Koninckx, P.R., 1980. Luteinized unruptured follicle (LUF) syndrome and endometriosis. Fertil. Steril. 34, 179–181. https://doi.org/10.1016/S0015-0282(16) 44906-x.

Brosens, I.A., 1997. Endometriosis – a disease because it is characterized by bleeding. Am. J. Obstet. Gynecol. 176, 263–267. https://doi.org/10.1016/s0002-9378(97)70482-4.

Brosens, I., Benagiano, G., 2013. Is neonatal uterine bleeding involved in the pathogenesis of endometriosis as a source of stem cells? Fertil. Steril. 100, 622–623. https://doi.org/10.1016/j.fertnstert.2013.04.046.

Brosens, I., Benagiano, M., Puttemans, P., D'Elios, M.M., Benagiano, G., 2019. The placental bed vascular pathology revisited: A risk indicator for cardiovascular disease. J. Matern., Fetal., Neonatal Med. 32, 1556–1564. https://doi.org/10.1080/14767058.2017.1409718.

Browne, J.C., Veall, N., 1953. The maternal placental blood flow in normotensive and hypertensive women. J. Obstet. Gynaecol. Br. Emp. 60, 141–147. https://doi.org/10.1111/j.1471-0528.1953.tb07668.x.

Dixon, H.G., Robertson, W.B., 1958. A study of the vessels of the placental bed in normotensive and hypertensive women. J. Obstet. Gynaecol. Br. Emp. 65, 803–809. https://doi.org/10.1111/j.1471-0528.1958.tb08876.x.

Gordts, S., Boeckx, W., Brosens, I., 1984. Microsurgery of endometriosis in infertile patients. Fertil. Steril. 42, 520–525. https://doi.org/10.1016/s0015-0282(16)48132-x.

Ober, W.B., Bernstein, J., 1955. Observations on the endometrium and ovary in the newborn. Pediatrics 16 (4), 445–460 Oct.

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