Presentation given at unveiling of Oxford Blue Plaque for Professor John Chassar Moir
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given by Professor David H Barlow

Blue Plaques honouring individuals are for those, from a huge range of activities, who have made important contributions. It is very appropriate that Professor John Chassar Moir is now to be included in that esteemed list. He is much less well known than he should be considering the impact of his contributions which were amongst the most important of the twentieth century to the health and wellbeing of women having babies.

Chassar Moir, as he was known, was one of the giant figures in the medical fields of obstetrics and gynaecology and women's health, a few professional generations before me. To me he was one of the greats from the recent past. His relevance to Oxford is that he was the first Nuffield Professor of Obstetrics and Gynaecology at the University of Oxford and I am asked to speak about him having been, myself, the fourth Nuffield Professor. His Chair was one of five Nuffield Chairs in different medical disciplines established when, William Morris, Lord Nuffield endowed the Oxford Medical School in 1936. He served in that role from 1937 to his retirement in 1967. He later became a close friend to Lord Nuffield.

Before describing his landmark work I must give the wider context.

He was a native of Montrose, born in 1900 and was a 1922 graduate of Edinburgh University Medical School and his landmark work was carried out in the 1930s in University College Hospital in London. His Oxford Nuffield Chair is associated with Oriel College so he was a Fellow then Honorary Fellow of Oriel and he served two terms as Vice-Provost of that College. He also made a significant contribution to the work of the Royal College of Obstetricians and Gynaecologists.

His thirty-year Oxford career was spent at the Nuffield Maternity Home at the Radcliffe Infirmary whereas, by my time, his Department was based at the John Radcliffe Maternity Hospital in Headington. He gave priority to his clinical responsibilities and it is said that he visited the wards every day that he was in Oxford. He made many innovations for the care of the women of Oxford and as a result was a much-loved and respected clinician. As a teacher and researcher he played an important role in promoting the careers of many future clinicians and researchers. Despite his eminent position he was described as a modest man, a trait he shared with his friend, Lord Nuffield.

Chassar Moir's key contributions were in the areas of surgery and the safety of childbirth.

Along with Munro Kerr he became the author of Munro Kerr's *Operative Obstetrics* which remains the leading British textbook of its field, and is now in its twelfth edition under his successors. However, his particular contribution to surgery was his commitment to improving the surgical management of vesico-vaginal fistula: a condition which involves the constant leakage of urine from the bladder or urethra directly into the vagina; which results in social isolation as well as distress and discomfort; and for which the results of surgery were poor. Vesico-vaginal fistula was usually a consequence of obstructed labour since this involves prolonged pressure on the mother's deep pelvic tissues by the head of her baby

which is not finding enough space to pass through for delivery. In obstetrics today this risk should be minimised by the onset of obstructed labour being recognised and the baby delivered by caesarean section. As a result the problem is now rare in the UK. Sadly in some parts of the world where access to good pregnancy care is limited obstructed labour and its consequences remain a real problem. Over many years Chassar developed innovations that improved the results of surgery so that he became an authority on the subject. In 1961 he published the first edition of his textbook *The Vesico-Vaginal Fistula* which became the standard work on the subject. Thus in addition to personally changing the outlook for affected women he raised standards of care internationally.

His landmark work, however, was the isolation of the key component of ergot, ergometrine, which has become a fundamental agent in managing the safety of childbirth. Mothers dying in childbirth is very rare in the 21st century in developed countries and increasingly rare in developing countries but any readers of novels from the nineteenth or early twentieth centuries will be aware that this was not always the case and that widowed fathers and orphaned children were common in plots. The two most important causes of maternal death were infection (puerperal fever) and poor contraction of the uterus after delivery of the baby resulting in bleeding which could be massive (post-partum haemorrhage). Chassar Moir's contribution was to bring about a major reduction in maternal haemorrhage by isolating and validating the action of the agent that would induce controllable uterine contraction after delivery.

Ergot is a fungus that grows especially on rye. It produces a cocktail of chemicals that can cause serious consequences for humans, known as ergotism. Consumption of contaminated rye bread giving ergotism has been recognised since the Middle Ages and was known as St Anthony's Fire because the Brothers of St Anthony were prominent in the primitive care of sufferers. Symptoms, which were diverse and very serious, included spasms, hallucinations, being struck dumb, paralysis and tremors, and blood-vessel spasm causing gangrene of limbs. In the early nineteenth century it was discovered that ergot caused contraction of the uterus and it was postulated that this might help with post-partum haemorrhage so an extract was given as 'labour tea' or crude ergot extract was injected. Looking back at this era, the *BMJ* stated that, "The indiscriminate use of ergot in the second stage of labour has probably done more harm than good, and such abuse has earned it an evil reputation."

At the start of the twentieth century a young physiologist, Henry Dale, working for the Wellcome company, was given the task of trying to make a more satisfactory extract from ergot. Dale was a talented physiologist and was later to become Sir Henry Dale and receive the 1936 Nobel Prize for Physiology and Medicine for his work on acetylcholine as the agent involved in the transmission of nerve impulses. By 1904 Dale and Barger had isolated an alkaloid which they named ergotoxine. Ergotoxine was commercialised for use in post-partum haemorrhage but in those days rigorous clinical trials were not a requirement. In 1907, however, Dale and Barger wrote of their scepticism that ergotoxine was truly the main product of ergot responsible for its uterine action. Just after World War I a Swiss pharmacologist isolated another ergot alkaloid, ergotamine, which turned out to be biologically indistinguishable from Dale's ergotoxine but this was also commercialised. Thereafter there do not appear to have been further efforts to pursue the matter though in

1923 the British Pharmacopoeia reported, “ergotoxine is disappointing, and gynaecologists are now generally agreed that it is not the active constituent they want.”

The subject was opened again in the early 1930s when Chassar Moir, a registrar researcher at University College Hospital (UCH), London, was asked to try to improve the methods for assessing the contraction of the uterus with a view to further exploring the effects of ergot and its products. He was a talented innovator and developed an apparatus that he modestly described as involving a piece of bent wire, a pivot, and a tin lid. He was apparently proud that this cost only one shilling. An important innovation was to carry out the assessments of uterine activity at around seven days after delivery. This delay was safer for the mother since by this stage the placement of a balloon in the uterine cavity was more acceptable. The balloon was connected to the measurement apparatus by means of a long rubber tube with mercury in the balloon and tube as the pressure-transmitting liquid. I understand that this fragile equipment was located in the room adjacent to that of the mother being studied. Initially the rubber tube passed from the mother to the equipment via two adjacent windows until it was discovered that local pigeons were attracted by the reddish colour of the rubber and their interference caused the mercury to leak, thus invalidating the results. A further innovation was to pass the tube through a hole in the wall, and therefore safe from pigeon assault. Chassar now had the most sensitive and reproducible system yet developed for the testing of the uterine response to drugs given to the mother. He could distinguish between ergotoxine or ergotamine inducing uterine contraction in 20 minutes and ergot inducing contraction in 5 minutes. This was a landmark observation and in his paper in the *BMJ* in 1932 he published that the characteristic and traditional effect of ergot was caused, not by any so far identified components of ergot, but by an unknown substance. Moir told Dale about these results and he later recollected that Dale had been delighted and said again and again, ‘I told them so’.

Chassar collaborated with Dr Harold Dudley, a respected UCH biochemist, and with the sensitivity of the equipment and Dudley’s expertise they were able to isolate the active constituent. They published their classic paper in the *BMJ* in March 1935 entitled “The substance responsible for the traditional clinical effect of ergot”. In this paper they state, “in spite of some criticisms and scepticism our clinical and chemical observations kept us convinced of the truth of our conclusions, and we are now able to prove their correctness by reporting the isolation of the substance to which ergot rightly owes its long-established reputation…. We propose to name it Ergometrine.” Sadly and unexpectedly by October of the same year the journal *Nature* had published the obituary of Dr Harold Ward Dudley OBE FRS. He had been 48 years old. “Nearly three weeks after a serious operation he died in a London Nursing Home.”

Dudley’s 1935 *BMJ* obituary stated “Until 1932 the nature of the active principles of ergot was regarded as a closed chapter, but the clinical observations of Dr J Chassar Moir proved the existence of a principle which acted promptly on uterine muscle when taken orally. The collaboration of Dudley and Moir led to the isolation and characterisation of a new simple water-soluble alkaloid, ergometrine, from ergot. This discovery of ergometrine, made only a few months before Dudley’s fatal illness, solves a long-standing problem of the pharmacology of ergot and its use in therapeutics.”

The immediate clinical use of ergometrine, acknowledged by some to have brought about a 'renaissance in obstetrics', was a major factor in reducing obstetric mortality. By the late 1940s maternal deaths from post-partum haemorrhage (PPH) had declined to less than one third their 1931 levels. The reduction in deaths from massive PPH was a consequence of a major reduction in all PPH events; PPH usually being defined as a blood loss in excess of half a litre of blood following delivery. In the early 1950s reports on the effect of giving ergometrine to the mother at the delivery of the baby were very positive; with a paper from Edinburgh reporting a reduction in PPH from 16% to 0.4% of deliveries and a UCH paper reporting a fall from 13.1% to 1.2%.

Chassar Moir's lasting legacy is that since that time giving ergometrine to the mother as the baby delivers has become the standard practice and for the past few decades the ergometrine has been supplemented with oxytocin in the preparation Syntometrine. This remains a standard of care today and is recommended by the World Health Organization (WHO).

Through the nineteenth century and to around 1940 in the UK the risk of a woman dying as a result of pregnancy or delivery was approximately 1 in 200. By the mid-1950s, in the wake of the introduction of antibiotics, blood transfusion and ergometrine the rate had fallen to 1 in 2,000. With ongoing improvements in care, the rate today is so low (1 in 11,000 in the UK by 2015) that healthy women do not usually consider that they are risking their survival to have babies. This safety remains dependent on the platform of care that includes Chassar Moir's ergometrine.

Those standards of care are, sadly, not available to all pregnant women around the world since access to care varies hugely. WHO reported that in 2015 in developing countries globally around 1 in 400 pregnant women die compared with 1 in 8,000 in developed countries globally. In some Sub-Saharan African countries the rate is near to 1 in 100. Death resulting from post-partum haemorrhage is a major contributor to the worldwide WHO statistic that approximately 830 women die every day from preventable causes related to pregnancy and childbirth.

Chassar Moir's legacy is the countless women over the decades whose lives and wellbeing were secured by his contribution. His achievements justify the recognition of an Oxfordshire Blue Plaque.