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PETER ROSSDALE AND EQUINE REPRODUCTION: THE STORY OF A MAN WITH VISION, "THE GREAT CATALYST"

PETER ROSSDALE ET LA REPRODUCTION ÉQUINE : HISTOIRE D'UN VISIONNAIRE, "THE GREAT CATALYST"

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ABSTRACT

Dr. Peter Rossdale (1927-2021) practised throughout his career in Newmarket, England. Founder of the most important equine clinic in Europe, he was also one of the major contributors to the modernisation of equine veterinary medicine, particularly in perinatology. His contribution to this discipline results from his clinical research and from multiple scientific collaborations with veterinary and medical colleagues throughout the world. He published widely in peer-reviewed journals, was the author of many textbooks and a founder of the British Equine Veterinary Association. He was the Editor of Equine Veterinary Journal and Equine Veterinary Education for many years. His remarkable career illustrates his vision of combining advanced veterinary medicine, clinical research and dissemination of knowledge to peers, students and professionals in the equine industry.

Keywords: Horse, Perinatalogy, Foal, Mare, Veterinary Medicine

RÉSUMÉ

Le Dr. Peter Rossdale (1927-2021) a exercé toute sa vie à Newmarket, en Angleterre. Fondateur de la plus importante clinique équine d'Europe, il est aussi l'un des grands contributeurs à la modernisation de la médecine vétérinaire équine, en particulier en périnatalogie. Son apport à cette discipline résulte de sa recherche clinique mais aussi de multiples collaborations scientifiques avec le monde vétérinaire et médical dans le monde entier. Auteur de multiples ouvrages destinés à la profession, il est à l'origine de l'association britannique des vétérinaires équins (*British Equine Veterinary Association*). Il a été l'Éditeur de *Equine veterinary Journal* pendant 30 ans et créé *Equine veterinary Education*. Son parcours remarquable illustre sa vision de la profession vétérinaire alliant médecine vétérinaire de pointe, recherche clinique et diffusion des connaissances aux étudiants et aux professionnels de la filière équine.

Mots-clés : cheval, périnatalogie, poulain, jument, médecine vétérinaire

INTRODUCTION

Dr Peter Rossdale (Figure 1) was born on 8th September 1927 and died on 26th November 2021, at the age of 94. During his career he revolutionised veterinary medicine in equine reproduction and perinatology. With a father devoted to medicine and a personal affinity for horses (his first ambition was to become a jockey), Peter chose to become a veterinary surgeon in equine medicine because this combined his childhood interests with an instinctive attraction to biology and research. In 1948 he obtained the equivalent of a BSc in Natural Sciences at Trinity College, Cambridge. His time there set the tone for his future scientific career and the starting point for a close collaboration for over forty years with Marian Silver (Ousey and Fowden, 2012), the future professor of physiology at Cambridge University. Peter went on to study veterinary medicine at the Royal College of Veterinary Surgeons in London (Hunt *et al.* 2021; Marr and Mair, 2022). After completing his studies, Peter joined a veterinary practice in Newmarket, the birthplace of racing and thoroughbred breeding, and then opened his own equine practice in 1959, again in Newmarket, where he remained throughout his career.

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During this period, he developed a particular interest in breeding and foals. With his first partner in 1961, Michael Hunt, he created 'Rossdale and Partners', which became over the years one of the largest European equine clinics in Europe. Stimulated by an insatiable curiosity, Peter wanted to increase the knowledge of the origin of pathologies in order to be able to offer treatments based on scientific data, realising very early on that the lack of knowledge was the main cause of the physical and mental suffering of his equine patients. Being above all a dedicated clinician, his motto was always based on the concept of '**horse welfare**', an innovative concept at the time, which he developed and which is now part of our daily lives. As there was little published in the field of equine reproduction in the 1950s, Peter devoted much of his time to observing, documenting and publishing his clinical cases, specialising in perinatal medicine (Mahaffey and Rossdale, 1957, 1959, 1965) and with a particular interest in comparing pathologies and their treatment with those of human medicine (Mahaffey and Rossdale, 1957, 1959; Rossdale, 1967a). On the basis of his work published in the following years (Rossdale, 1967b, a, 1968a, b; Rossdale and Short, 1967; Rossdale *et al.* 1967), Peter was awarded the FRCVS by thesis, Fellowship of the Royal College of Veterinary Surgeons in 1966. He believed that clinicians like himself were ideally placed to conduct research. He thus paved the way for a new type of clinical research and probably became the first clinician to do what is known, 50 years later, as **Evidence based medicine** (Rossdale 1978, 2000; Rossdale *et al.* 2010). Newmarket and the surrounding area proved an ideal area to meet other medical and veterinary scientists. Peter's enthusiastic nature and innate ability to collaborate on the one hand and delegate on the other, has enabled him, despite the limited time available for research, to increase his publication output exponentially, publishing over 200 scientific papers in peer-reviewed journals (Ousey and Fowden, 2012; Hunt *et al.* 2021; Marr and Mair, 2022) and numerous books dedicated to the profession and translated into several languages (Rossdale and Ricketts, 1974, 1983; Rossdale, 1976; Rossdale and Wreford, 1993). His main collaborators were Drs Leo Mahaffey, Roger Short, Desmond Leadon and Jenny Ousey; and Professors Leo Jeffcott, Twink Allen, Marian Silver, Robert Comline and Ian Silver. In addition, Peter's enthusiasm attracted a multitude of people to assist him in his research work as they were recruited as soon as they expressed an interest in his areas of interest, be they clinicians (veterinarians and medical doctors), researchers, students, various staff and even secretaries, all of whom earned him his reputation as 'Great Facilitator' or 'Great Catalyst'.

Figure 1 : *Peter Rossdale, Ocala, Florida, 1992 (photo P. Chavatte)*

Further, Newmarket's proximity to the academic world at the University of Cambridge enabled Peter to develop another of his passions: the combination of several complementary activities. He pursued his vision of a veterinarian that embraces three activities at once: practising veterinary medicine, conducting clinical research and ensuring the dissemination of knowledge gained (Rossdale, 1985).

ROSSDALE & PARTNERS

When Michael Hunt joined Peter Rossdale in 1961, the clientele continued to grow. Peter realised early on the importance of having those with specialist interests in his clinic and developed the concept of '**specialism**' which he would recommend to the veterinary world throughout his career (Rossdale, 1999). In 1965 Colin Peace joined the clinic to develop surgery, Raymond Hope in 1968 specialised in medicine and the management of racehorses in training. In 1973 they were joined by Sydney Ricketts, a reproductive specialist who developed the laboratory into a reference service centre (Rossdale, 1999). Nick Wingfield-Digby then introduced cytological tests as an aid to diagnosis and set up the first diagnostic laboratory with Jo Mahaffey and Ian Silver (for blood gas analysis). More than 60 years later, Rossdale and Partners became Rossdale Veterinary Surgeons (https://www.rossdales.com), officially opened by Her Majesty the Queen in 1998 (Rossdale, 1999). It is among the largest private equine clinics in Europe, a world-renowned centre, housing over 50 veterinarians, a diagnostic centre, laboratory, pathology centre and a large outpatient practice in Newmarket with two additional regional branches. Peter retired in 2002 while allowing his name to be used for life (Hunt *et al.* 2021). The opening of the new £1.9 million modernised laboratory took place the day before his death.

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CLINICAL RESEARCH: FOETAL MATURATION AND FOAL HEALTH

Peter's greatest legacy is undoubtedly the breadth of published scientific knowledge that resulted from his work in equine perinatology (Ousey and Fowden, 2012) and for which - among other things - he was awarded a Doctor of Philosophy (PhD) degree by Cambridge University in 1985. The knowledge accumulated by Peter and his numerous collaborators, including Dr Anne Koterba, Dr Tim Cudd, Dr Phil Kosch, Dr Frank Pipers and Dr Willa Drummond at the University of Gainesville in Florida, led to the establishment of intensive care units for new-born foals (Figure 2) in the 1980s in both Europe and the USA. In this chapter, we will present only part of his work in relation to foetal maturation and the role of foetal progestagens.

Figure 2 : *Pascale Chavatte-Palmer in the first intensive care facility at Rossdale & Partners.)*

Neonatal Maladjustment Syndrome

Early in his career, Peter met Professor Leo Mahaffey, an Australian pathologist at the Animal Health Trust's Equine Research Station in Newmarket. From this meeting, Peter learnt a lesson for life - and taught it: the importance of clinicians attending the autopsy of their patients! Leo Mahaffey guided Peter in his early research and several publications resulted from their collaboration (Rossdale *et al.* 1967; Mahaffey and Rossdale, 1957; Mahaffey and Rossdale 1958; Rossdale and Mahaffey, 1958; Mahaffey and Rossdale 1959; Mahaffey and Rossdale, 1965). One of their earliest publications appeared in the Lancet (Mahaffey and Rossdale, 1959) and described the symptoms observed in Thoroughbred foals occurring most often during the first 6 hours after an easy and rapid birth. Symptoms begin suddenly with the onset of abrupt, uncoordinated movements of the neck and head, followed by periods of convulsion often accompanied by guttural or whistling sounds made by the foal which are sometimes reminiscent of a dog's bark. Parallels are drawn with a human neonatal syndrome described as 'barker syndrome'. Necropsy of these foals reveals pulmonary and central nervous system abnormalities (Palmer and Rossdale, 1976), suggesting post-natal maladaptation of the nervous and/or cardiopulmonary systems, although a definitive causal link cannot be made. The concept of Neonatal Maladjustment Syndrome (NMS) was proposed, with Peter Rossdale pioneering its clinical description, early aetiological investigations and management of foals suffering from this syndrome (Toribio, 2019), which are also known as barkers, wanderers, dummies and/or convulsives. The NMS syndrome belongs to group II of the four groups of neonatal diseases that Peter described in 1972 (Rossdale, 1972) based on the symptoms observed in foals. He suggested that the causes of this syndrome are related to hypoxia and/or circulatory problems before, during or after birth, also recognising that various pathophysiologies can lead to the same syndrome. He later proposed the classification of this syndrome into two categories based on length of gestation, course of parturition and time of onset of clinical symptoms. Category 1 had a good prognosis, including normal length of gestation, unproblematic parturition and normal new-born behaviour at birth, with the onset of neurological symptoms occurring only within 6-24 hours after birth. Category 2 foals had a much poorer prognosis (less than 50% survival rate) often having experienced an abnormal delivery and/or abnormal placenta and/or showing abnormal behaviour immediately after birth suggesting that these foals were delivered while already suffering pre-natal 'insults' as a consequence of placental deprivation and hypoxic or acidaemic episodes *in utero*. Peter was thus one of the first to link certain pathologies to problems occurring during foetal development (Clement, 1987; Hess-Dudan and Rossdale, 1996). In 2019, Toribio (2019) proposed that the terms NMS, dummy foal and/or equine neonatal encephalopathy should be used to describe this syndrome as they are based on clinical signs and not on pathophysiological processes that are still poorly defined. Peter Rossdale's observations remain relevant in the light of current knowledge based on anamnesis, clinical signs, autopsy findings and the recent association of this syndrome with neuroactive steroids, strongly suggesting that different syndromes share the same clinical symptoms. The aetiopathology of these syndromes remains unclear although periods of ischaemia and/or hypoxia and endocrine and metabolic dysfunction remain suspected (Madigan *et al.* 2012; Dembek *et al.* 2017; Aleman *et al.* 2019; Toribio, 2019). While progestagens that are elevated at birth disappear very quickly from the circulation in

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normal foals, they remain elevated in diseased foals, particularly in foals with NMS (Holtan *et al.* 1991; Houghton *et al.* 1991; Rossdale *et al.* 1991). It should be noted that Peter was the first to link the severity of his patients' condition to elevated circulating progestagens, including neuroactive steroids (Rossdale *et al.* 1995). The characterisation of these progestagens already demonstrates the presence of 3 b-hydroxy-5 a-pregnan-20-one or 3b5P, to which the name allopregnanolone was later given and which was recognised as a powerful neurosteroid, modulator of the $GABA_A$ receptor, crossing the blood-brain barrier. Madigan, building on Peter's work, suspected that the neurosteroid allopregnanolone was responsible for both the physiological sleepiness of the foetus *in utero* and the pathological sleepiness of foals suffering from NMS. Indeed, injection of allopregnanolone into healthy foals in the perinatal period induces symptoms similar to those observed in NMS (Madigan *et al.* 2012). Madigan *et al.* proposed that an abnormality in foetal maturation, particularly in the hypothalamus-pituitary-adrenal axis, is responsible for the persistence - or reappearance - of neurosteroids in foal's plasma. Thus, the reduction of allopregnanolone concentrations in the plasma would allow the resolution of the pathology. Other work hypothesises that the thoracic pressure exerted by the passage through the cervix during normal parturition activates a transition from a state of relative sleepiness to a state of full consciousness (Diesch and Mellor, 2013), which may be related to the suppression of these neurosteroids. Madigan *et al.* (2012), then speculated that the typically rapid birth of NMS foals does not allow for complete suppression of allopregnanolone precursor and other neurosteroid production by the adrenal gland and/or by other tissues. A new treatment consisting of applying high pressure with a rope wrapped around the foal's thorax (squeezing), for approximately 20 minutes, mimicking the foetal expulsion phase of parturition has been shown to be effective as an adjunct therapy for the treatment of foals with NMS and/or somnolence (Aleman *et al.* 2019). It is proposed that this squeezing procedure induces adrenal maturation although the mechanisms involved remain to be explored.

Foeto-placental biosynthesis of progestagens

Peter's group II classification of foal diseases also includes prematurity, which remains an important clinical problem, particularly in Thoroughbreds (Rossdale, 1972). The observation of a highly variable gestation period in mares and the need to monitor the animals at night to witness foaling (Rossdale and Short, 1967) led to his work to predict the timing of foaling and to understand the mechanisms (Figure 3). Initially, the observation of a relationship between calcium, sodium and potassium concentrations in mammary secretions and imminent foaling led to the proposal of this assay in practice to reduce the time spent monitoring mares. Although other methods have now been developed to predict or detect foaling, this remains the cheapest and most widely used method in equine reproduction (Diel de Amorim *et al.* 2019). In the pregnant mare, in the absence of plasma progesterone from about 120 days of gestation (Holtan *et al.* 1975, 1991), progesterone metabolites or progestagens are present. Their plasma concentrations in the maternal circulation increase very considerably two to three weeks before parturition, whether physiological or premature (Rossdale *et al.* 1991). The study of foeto-placental biosynthesis of these progestagens helps to explain the absence of plasma progesterone (Schutzer and Holtan, 1995, 1996; Chavatte *et al.* 1997) and suggests that the ante-natal increase in progestagens was related to foetal maturation. Furthermore, as progestagens are able to inhibit their own biosynthesis at high concentrations (Chavatte *et al.* 1995), this late increase would also reduce 5-a dihydroprogesterone (5 a - DHP) concentrations, as the progestagen binds preferentially to the progesterone receptor (Chavatte-Palmer *et al.* 2000) and may cause myometrial quiescence (Fowden *et al.* 2002), which has recently been confirmed (Scholtz *et al.* 2014; Conley 2016; Conley and Ball 2019).

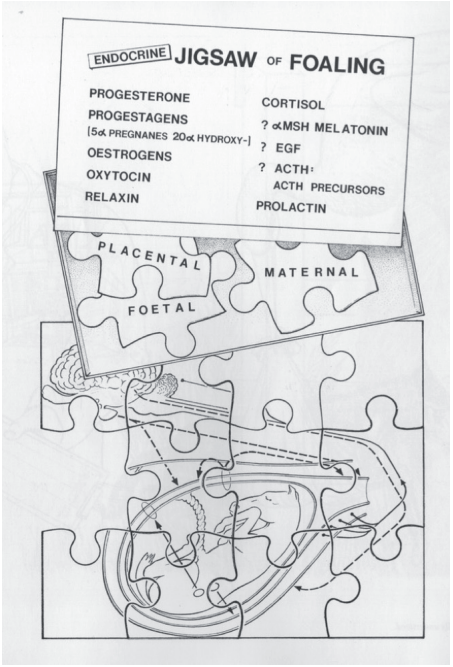

Figure 3 : *Illustration of the complexity of the hormonal mechanisms of foaling created for Peter Rossdale's scientific purposes by John Fuller (Fuller, 1990)*

Foetal maturation

In order to complement his clinical research activities, Peter Rossdale obtained financial support from the Wellcome Trust who supported at the Animal Health Trust Equine Research Station in Newmarket a herd of 10-20 ponies from 1978-1983 and a PhD student for three years (D.P. Leadon). This herd was subsequently maintained by other funding bodies such as the Horserace Betting Levy Board which contributed to research expenses and funded a Masters student (J.C. Ousey). Several collaborative projects were set up with other medical institutes and university departments interested in comparative medicine

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and supported financially from various sources. Thus, during the first 6 years after the establishment of the experimental herd, an important amount of data, still the basis for many studies in foals, was obtained. In particular:
- Prematurely induced foals can be classified according to their post-natal behaviour and their ability to survive.
- blood gas and acid-base status is significantly altered in premature foals (Rose *et al.* 1982).
- Blood count/formula parameters related to the haematopoietic lineage (red cells, haematocrit and haemoglobin) and erythrocyte volume at birth allow estimation of foetal maturity at birth (Jeffcott *et al.* 1982) and the white lineage (total cell count and Neutrophil: Lymphocyte ratio (N/L ratio) are indicators of the degree of preparedness of the foetus at birth and allow prediction of the individual's chances of survival.
- The ability of the adrenal cortex to respond to an individual's increased endogenous ACTH is strongly related to its ability to survive in the extrauterine environment (Silver *et al.* 1984).
- The renin-angiotensin-aldosterone system (RAAS) plays a regulatory role on cardiovascular homeostasis during the perinatal period of the foal, as in other species (Broughton Pipkin *et al.* 1982).
- A positive correlation exists between endogenous glucose and insulin concentration at all ages but the response of pancreatic beta cells and the concentrations of glucose that are able to induce insulin discharge vary with age (Fowden *et al.* 1982).
- The spinal cord is neurochemically more mature in horses than in cows, sheep and pigs. Results in premature foals do not show lipid abnormalities that might suggest myelin immaturity or degeneration (Sweasey *et al.* 1982).
- The lungs of the equine foetus mature early and in the last trimester of gestation a mature architecture of the blood vessels and trabeculae can already be seen (Barnard *et al.* 1982). In dysmature foals, a lower collagen content is observed, probably as a result of collagen and cross-linking abnormalities. It is suggested that these structural abnormalities in the lungs may be the cause of haemorrhages in the central nervous system.

After this intense period of scientific production, which enabled the concept of 'readiness for birth' to be defined (Rossdale and Silver, 1982), the pony herd was maintained for another ten years and enabled such clinically relevant concepts as the phenomena of foetal and post-natal maturation to be explored further (Ousey *et al.* 1998 ; Ousey *et al.* 2000 ; Ousey *et al.* 2011).
Finally, Peter Rossdale was one of the first to understand the relevance to equine medicine (Rossdale and Ousey, 2003) of David Barker and Nick Hales' findings in the 1990s on the Developmental Origins of Health and Disease (DOHaD) (Barker, 1998).

TRAINING AND DISSEMINATION OF VETERINARY INFORMATION

"The educated man is the one who continues to learn" was one of Peter Rossdale's mottos as he became a founder member of the British Equine Veterinary Association (BEVA, https://www.beva.org.uk/) in 1961 and of ISER (International Symposia for Equine Reproduction, https://www.iser-online.org/) in 1973. In addition to his work as a clinician and researcher, he was the Editor for over 30 years (1980 - 2010) of Equine veterinary Journal (EVJ), before becoming Editor Emeritus for life. The journal, initially published by BVA publishing Services, was soon taken over by his own publishing company R&W until the late 1980s when EVJ Ltd (Equine Veterinary Journal Limited), owned by BEVA, took over. EVJ became the official publication for BEVA members. Peter's constant drive to improve the quality standards of clinical medicine led him to successfully publish peer-reviewed papers from 1975 onwards, covering all aspects of equine veterinary science. To meet the ever-increasing demand for publications, the Journal increased in size and number of volumes from around 80 articles in the 1980s to over 130 in 2010. The journal became one of the leading journals in equine veterinary science and remained at the top of the veterinary science citation index (Impact Factor of 2.888 in 2020). Peter demonstrated his awareness of the major changes in the veterinary profession brought about by specialisation by publishing theme-specific EVJ supplements and special issues of the journal dealing in depth with a single topic as early as 1983. At nearly 80 years of age, it was Peter who encouraged and supported the online publication of EVJ (Blikslager *et al.* 2011; Silver *et al.* 2011; Marr and Mair, 2022). On his initiative, a second journal, dedicated to the continuing education of veterinarians, was created in collaboration with Lawrence Gerring and Jan Wade who initially became co-editors. In 1986, the first issue of Equine veterinary Education (EVE) was published. This journal was also very successful, both in terms of the number of contributors, which increased exponentially, and the enthusiasm of its readers. The success of this new venture is crowned by an agreement with the American Association of Equine Practitioners (AAEP) and from 1999 onwards each issue has been reprinted in the USA and distributed to AAEP members. EVE is one of the most important educational journals for English-speaking practitioners of equine medicine. Last but not least, Peter Rossdale organised numerous congresses, particularly in the field of perinatology, including many workshop meetings funded by the Havermeyer Foundation (http://www.havemeyerfoundation.org/), which bring together clinicians and researchers, both veterinary and medical.

CONCLUSION

Peter Rossdale's scientific interests were not limited to reproductive biology and the foal. He also published widely in other areas, for example on the management problems of breeding mares, young horses in training, infectious diseases, heart disease, nutrition and clinical examinations of young horses for sale. Peter Rossdale contributed to countless conferences around the world, always generous in sharing his knowledge and expertise with all who were interested. This earned him the admiration and respect of the entire veterinary and academic community, including honorary degrees from the Universities of Edinburgh, Bern and Sydney. Among other honours he was awarded a Fellowship of the Australian College of Veterinary Scientists in 1975 and Honorary Life Membership of the British Equine Veterinary Association in 1978. The University of

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Cambridge awarded him a Doctor of Philosophy (PhD) on the basis of his published work in the field of perinatology and reproductive biology, a rare honour for a clinician. He received numerous awards during his career including the John Henry Steel Memorial Prize, the William Hunting Prize, the Tierklinik Hochmoor International Prize, the Dalrymple Champneys Prize and Cup, the Duke of Devonshire Award for his contribution to the British equine breeding industry and the BEVA Equine Welfare Award. Peter Rossdale is immortalised in the University of Kentucky's Equine Research Hall of Fame. In 1998 he was awarded an OBE by Queen Elizabeth II (Order of the British Empire) for services to equine veterinary science. His dedication, his observational skills, his insatiable curiosity, his ability to connect and unite, to create links and to collaborate, and his humour made him an exceptional character, as his colleagues Anthony Blickslager, Rob Christley, Leo Jeffcott, Ian Silver and René van Weeren have written: "Peter Rossdale is the most remarkable colleague with unbounded vision and energy - he is an organiser and entrepreneur par excellence, a great scientist and researcher, a prestigious author and an extraordinary veterinarian. These characteristics together with his remarkable modesty, a great sense of humour and a philosophical view of the world, has made it more than a privilege to work with him" (Blickslager *et al.* 2011). He has also been an inspiration to countless young veterinarians and a mentor to the three authors of this article.

All practising equine veterinarians can feel indebted and grateful to Peter Rossdale who, as early as the 1960s, not only recognised that the practice of veterinary medicine must be based on science on a daily basis, but above all to his immense legacy of knowledge to the veterinary community on which much of that science is based. The two journals, EVJ and EVE, in whose development he played a pivotal role will continue to improve the knowledge of veterinarians and thereby the condition of equine patients, one of Peter Rossdale's greatest wishes.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

ETHICS COMMITTEE

The drafting of this document did not require the involvement of an ethics committee.

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