Giants in Obstetrics and Gynecology Series: a profile of Christopher Redman, MB, BChir, MRCP, FRCP

Roberto Romero, MD, DMedSci, Editor-in-Chief for Obstetrics

Dr Christopher Redman has made important contributions to the field of obstetrics through his work dedicated to understanding the mechanisms of disease in preeclampsia, placental physiology, and immunology of the maternal-fetal interface and for his invention of the first computerized system of antepartum fetal heart rate analysis, widely used in Europe, Asia, and Australia. For these contributions, Chris is being recognized as a "Giant in Obstetrics and Gynecology."

Dr Christopher Redman

Education at Cambridge and Oxford

Chris was born in 1941 in South Africa. His father, an astronomer, worked at the Oxford University Radcliffe Observatory based in Pretoria. At the end of World War II, Chris's father became Director of the University of Cambridge Observatories, and the family moved to the United Kingdom. Growing up in Cambridge, Chris attended what he described as a "typical English grammar school."

In 1960, Chris enrolled in Cambridge University, choosing to study the natural sciences with an emphasis on mathematics, physics, and chemistry. He drifted toward the study of biochemistry, however, feeling energized by the subject and by the interest and liveliness of his teachers and fellow students. At the time Chris decided to go into medicine, Cambridge did not offer clinical training, and Chris completed this portion of his degree at Oxford's Clinical Medical School.

Chris's first position after medical school was at Johns Hopkins University in Baltimore, Maryland, as a Fellow and an Intern in the Department of Pathology. He then returned to England and completed a medical internship at the Radcliffe Infirmary in Oxford, and subsequently became a surgical intern in the Department of Pediatrics at Children's Hospital in Sheffield. In 1970, he joined Oxford's Regius Department of Medicine, led by Professor Sir Richard Doll, who is credited for discovering the relationship between smoking and lung cancer.

A randomized clinical trial to treat pregnant patients with chronic hypertension

After joining the Department of Medicine at Oxford, one of Chris's first assignments was to organize a randomized clinical trial on the efficacy of α-methyldopa for the early treatment of mild to moderate chronic hypertension in pregnancy. After five years, the study concluded that the administration of α-methyldopa reduced the frequency of severe hypertension during pregnancy and in labor[1] (Figure 1) and was associated with a reduced number of pregnancy losses; however, this could not be attributed to a reduction in the rate of preeclampsia.[2] At the time, there was concern that antihypertensive agents may decrease placental perfusion; therefore, the research team assessed birth weight and found that it was unaffected by the administration of α-methyldopa. Children were followed until the age of seven, and follow-up demonstrated that there were no adverse effects to those exposed to the antihypertensive agent in utero.[3]

During our conversation, Chris reflected on the challenges of undertaking this randomized clinical trial. There was no budget and no research ethics committee, and clinicians had an inadequate understanding of the importance of random allocation in clinical trials. Chris told me that some physicians consented that their patients could be asked to participate in the trial, as long as they were randomized to the active group (antihypertensive agent) rather than the control group.

Chris was often consulted about the treatment of patients with severe preeclampsia. His colleagues in obstetrics thought that the administration of powerful antihypertensive agents would be effective in treating preeclampsia. However, Chris quickly realized that antihypertensive agents did not modify the inexorable course of preeclampsia nor prevent the disorder in patients with preexisting chronic hypertension. He searched the literature for answers, but the lack of research, coupled with his desire to understand the differences between women with and without preeclampsia, and how this information could be used, led Chris to his career-long study of the disease.

"Little did I know that the next 45 years of my life were settled at that time," Chris quipped.

The involvement of platelets in preeclampsia

During the trial of α-methyldopa, Chris observed that some women had lower platelet counts and that this decrease often

From the Perinatology Research Branch, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, U.S. Department of Health and Human Services, Bethesda, MD and Detroit, MI.

Received March 21, 2019; accepted March 21, 2019.

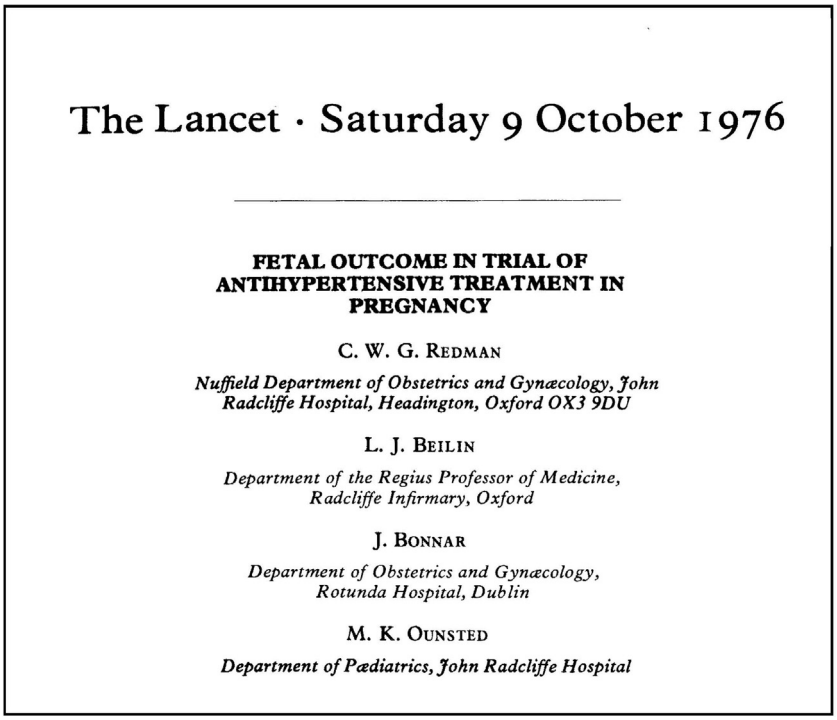
The author reports no conflicts of interest.

This research was supported, in part, by the Perinatology Research Branch, Division of Obstetrics and Maternal-Fetal Medicine, Division of Intramural Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, U.S. Department of Health and Human Services (NICHD/NIH/DHHS).

Corresponding author: Roberto Romero, MD, DMedSci. rr.ajoged@gmail.com

0002-9378/$36.00
Published by Elsevier Inc.
https://doi.org/10.1016/j.ajog.2019.03.020

FIGURE 1
α-Methyldopa reduces frequency of severe hypertension during pregnancy and in labor



The Lancet · Saturday 9 October 1976

FETAL OUTCOME IN TRIAL OF ANTIHYPERTENSIVE TREATMENT IN PREGNANCY

C. W. G. REDMAN

Nuffield Department of Obstetrics and Gynæcology, John Radcliffe Hospital, Headington, Oxford OX3 9DU

L. J. BEILIN

Department of the Regius Professor of Medicine, Radcliffe Infirmary, Oxford

J. BONNAR

Department of Obstetrics and Gynæcology, Rotunda Hospital, Dublin

M. K. OUNSTED

Department of Pædiatrics, John Radcliffe Hospital

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occurred prior to the diagnosis of preeclampsia.[4] This observation has proved to be important, given that patients with preeclampsia and thrombocytopenia have worse pregnancy outcomes than those with a normal platelet count.[5] Indeed, a subset of patients who have hemolysis, a low platelet count, and elevated liver enzymes is now recognized as having a distinct condition called HELLP syndrome.[6] The current use of aspirin to prevent preeclampsia[7-13] was based on the observation that platelets play a role in the pathogenesis of disease.[14,15]

An elevation of serum uric acid and subsequent fetal death in patients with hypertension in pregnancy

Chris noticed that one patient in the α-methyldopa trial experienced a sudden increase in uric acid, with the level doubling over 10 days. The patient then developed preeclampsia and required a preterm delivery. Dr Leon Chesley had also observed this phenomenon and published his report in *AJOG* in 1950.[16] Chris explored the issue further and ran subsequent studies, determining that an increase in plasma uric acid concentrations, in the context of gestational hypertension, was associated with fetal death and adverse pregnancy outcome.[17,18] The relationship between uric acid concentrations and adverse pregnancy outcome in preeclampsia has been confirmed over several decades.[19]

Developing an interest in the human placenta

Although the role of the placenta in preeclampsia had been well established for decades, Chris became interested in the parallels between transplantation and placentation, and how the semi-allograft was tolerated.

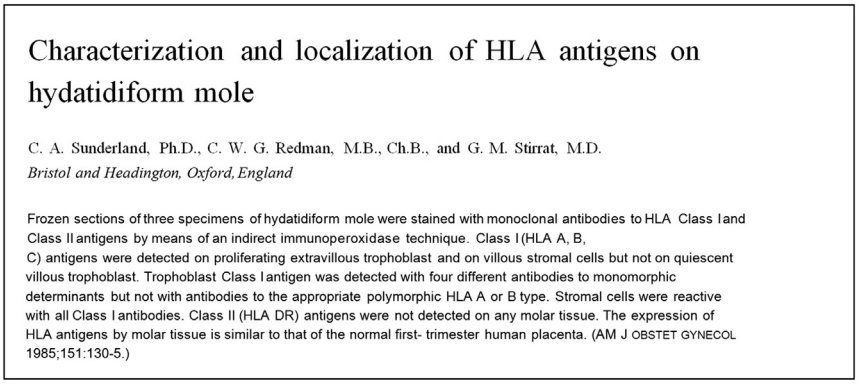
One of the paradigms at the time was that the syncytiotrophoblast covering the villous tree, in direct contact with the maternal circulation, did not express Class I or Class II major histocompatibility complex antigens. Chris collaborated with immunologists to study the differential expression of major histocompatibility antigens in the different forms of trophoblast in patients with normal pregnancy as well as the hydatidiform mole, discovering that trophoblast expresses nonclassical human leukocyte antigen (HLA) (Figure 2).[20]

Subsequently, the immune interactions between the mother and fetus became a major line of investigation for his team at Oxford. His collaborations with Professor Ashley Moffett at Cambridge University, who was interested in the HLA-C-KIR receptor interactions, were a major contribution to the understanding of adverse pregnancy outcome and obstetric syndromes associated with abnormal maternal-fetal immune interactions.[21,22]

Placental production of microparticles deported into maternal circulation

While recounting this story, Chris recalled a major breakthrough in the field when, in 1989, Dr James Roberts, at the

FIGURE 2
Expression of HLA antigens on molar tissue is similar to that of first-trimester placenta



Characterization and localization of HLA antigens on hydatidiform mole

C. A. Sunderland, Ph.D., C. W. G. Redman, M.B., Ch.B., and G. M. Stirrat, M.D.
Bristol and Headington, Oxford, England

Frozen sections of three specimens of hydatidiform mole were stained with monoclonal antibodies to HLA Class I and Class II antigens by means of an indirect immunoperoxidase technique. Class I (HLA A, B, C) antigens were detected on proliferating extravillous trophoblast and on villous stromal cells but not on quiescent villous trophoblast. Trophoblast Class I antigen was detected with four different antibodies to monomorphic determinants but not with antibodies to the appropriate polymorphic HLA A or B type. Stromal cells were reactive with all Class I antibodies. Class II (HLA DR) antigens were not detected on any molar tissue. The expression of HLA antigens by molar tissue is similar to that of the normal first- trimester human placenta. (AM J OBSTET GYNECOL 1985;151:130-5.)

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Department of Obstetrics and Gynecology at the University of California, San Francisco, published evidence in *AJOG* that preeclampsia could be considered an endothelial cell disorder.[23] In that paper, which became a citation classic, Jim proposed that preeclampsia could be caused by a factor, toxic to endothelial cells, released by the placenta and found in the maternal circulation of patients with preeclampsia.

Given this set of observations, Chris reasoned that if the placenta was the source, then the factor would be found in the part of the placenta that is in direct contact with maternal blood—the placental syncytial surface microvilli. Seeking an antiendothelial protein, Chris studied the microvilli and their interactions with cultured endothelial cells. The results were remarkable.

Chris vividly remembers the day when clinician-scientist Dr Alexander Smárason came "dashing down the corridor, overwhelmed with excitement, saying 'Just look at this, just look at this!'" Alexander was carrying the endothelial cultures he had incubated with vesicles from normal placentas, and the endothelial cells were damaged. The morphology and behavior of the cells changed, revealing very profound anti-endothelial cell activity.[24,25] The next task was to determine whether the preparation that they used ex vivo had an in vivo correlate, and their work led to a number of studies that reported how those vesicles could be found in the blood of pregnant women.[26]

The discovery that pregnancy is characterized by physiologic intravascular inflammation

A fundamental question was the link between placental microparticles and endothelial cell dysfunction in preeclampsia. Using flow cytometry to study circulating monocytes and granulocytes, Chris decided to study the immunophenotype and functional properties of these cells, which are part of the innate immune system, rather than lymphocytes, which are components of adaptive immunity.

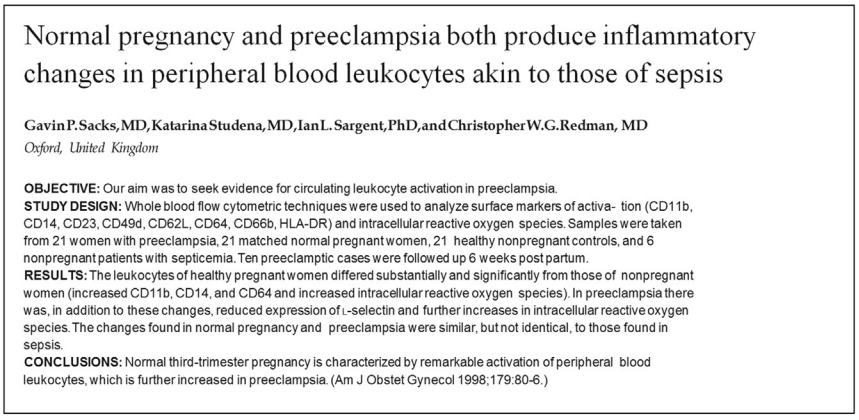
Having noted that endothelial cells are also part of the inflammatory system, Chris and his team discovered that normal pregnancies are characterized by a state of intravascular inflammation, which was exaggerated in preeclampsia.[27] The investigation into intravascular inflammation began in earnest when Chris asked Dr Gavin Sacks, a proficient clinician completing his doctorate, to study monocytes. Unhappy with his assignment, Gavin grumbled about being put on "these dead-end cells," but Chris convinced him to stick with it, correctly predicting Gavin would discover that the phagocytic white blood cells are not "dead-end" cells.

Gavin used flow cytometry,[28,29] a new technique at that time, to study not only normal pregnancy but also patients with preeclampsia. In addition to comparing these groups, Gavin recruited nonpregnant women and, for fullness of documentation, men and women admitted to the intensive care unit for treatment of sepsis. Chris said, "[Gavin] had the real skill of someone who follows his nose. He had the discipline to finish his experiments and write them up cleanly, and he came back with the answers."

Data collected from the additional control groups proved very informative, and two observations were made: 1) monocytes and granulocytes of pregnant women had a phenotype consistent with a state of activation and produced more reactive oxygen radicals, indicating that normal pregnancy was a physiologic state of intravascular inflammation; and 2) the inflammatory process of normal pregnancy was exacerbated in patients with preeclampsia. The data also indicated how intense these changes were relative to those in nonpregnant patients with sepsis. The findings were published in two papers in *AJOG*, which became citation classics.[30,31] These offered a new vista of preeclampsia, which was simultaneously unexpected and exciting (Figures 3 and 4).

In collaboration with Dr Ian Sargent, Professor of Reproductive Science at the University of Oxford, Chris and Gavin reported an increase of microvesicles circulating in pregnant women with preeclampsia.[32,33] The findings demonstrated the presence of the placental toxic factor that had been proposed for decades to be responsible for toxemia of pregnancy. Chris and Ian devoted an enormous amount of time and

FIGURE 3
Normal pregnancy is characterized by changes in peripheral blood leukocytes, marking a generalized inflammatory response that is exaggerated in cases of preeclampsia



Normal pregnancy and preeclampsia both produce inflammatory changes in peripheral blood leukocytes akin to those of sepsis

Gavin P. Sacks, MD, Katarina Studena, MD, Ian L. Sargent, PhD, and Christopher W.G. Redman, MD
Oxford, United Kingdom

OBJECTIVE: Our aim was to seek evidence for circulating leukocyte activation in preeclampsia.
STUDY DESIGN: Whole blood flow cytometric techniques were used to analyze surface markers of activa- tion (CD11b, CD14, CD23, CD49d, CD62L, CD64, CD66b, HLA-DR) and intracellular reactive oxygen species. Samples were taken from 21 women with preeclampsia, 21 matched normal pregnant women, 21 healthy nonpregnant controls, and 6 nonpregnant patients with septicemia. Ten preeclamptic cases were followed up 6 weeks post partum.
RESULTS: The leukocytes of healthy pregnant women differed substantially and significantly from those of nonpregnant women (increased CD11b, CD14, and CD64 and increased intracellular reactive oxygen species). In preeclampsia there was, in addition to these changes, reduced expression of L-selectin and further increases in intracellular reactive oxygen species. The changes found in normal pregnancy and preeclampsia were similar, but not identical, to those found in sepsis.
CONCLUSIONS: Normal third-trimester pregnancy is characterized by remarkable activation of peripheral blood leukocytes, which is further increased in preeclampsia. (Am J Obstet Gynecol 1998;179:80-6.)

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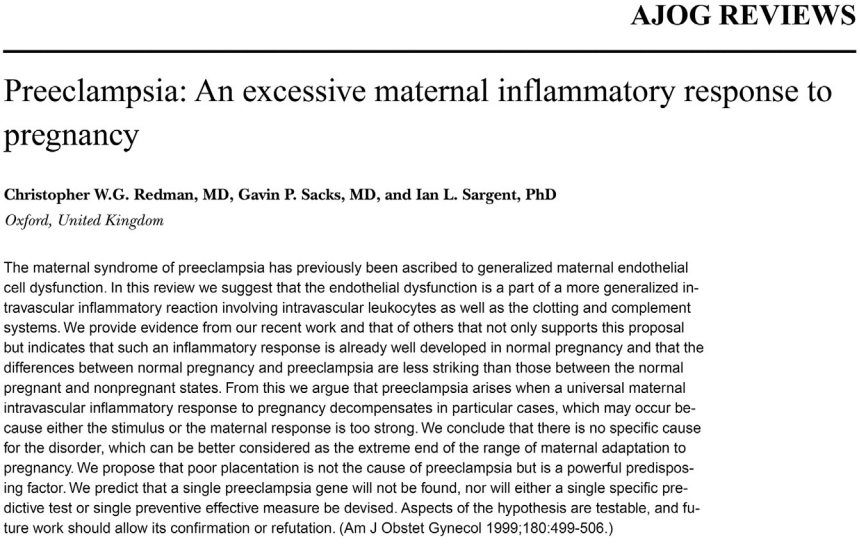
effort to uncover this "factor x". Then-doctoral candidate Marian Knight, who was working with Dr Sargent and is now the Director of the National Perinatal Epidemiology Unit of the United Kingdom, developed and validated an enzyme-linked immunosorbent assay (ELISA) to detect trophoblast particles. Over the course of three years, Dr Knight's assay verified the increase of vesicles in cases of preeclampsia.[34] Although the results were encouraging, further investigation was beyond available technological capabilities at the time. In our conversation, Chris noted that researchers are now revisiting this question with more sophisticated approaches, such as mass spectrometry.

Placental extracellular vesicles

Chris and Ian published a review in *Science* in 2005, summarizing recent and ongoing research efforts to better understand the pathogenesis of preeclampsia.[35] Their paper discussed placental factors of preeclampsia, immunological implications, a new mode of maternal immune recognition of the fetus, and new understandings of placental circulating factors that contribute to preeclampsia.

Researchers had found that not all extracellular vesicles are shed from cellular surfaces; rather, some are secreted from multivesicular bodies inside the cells—moving to the surface of the cell, fusing with the overlying membrane, and releasing

FIGURE 4
Preeclampsia is not a distinct abnormality of pregnancy but an extension of changes induced by pregnancy



AJOG REVIEWS

Preeclampsia: An excessive maternal inflammatory response to pregnancy

Christopher W.G. Redman, MD, Gavin P. Sacks, MD, and Ian L. Sargent, PhD
Oxford, United Kingdom

The maternal syndrome of preeclampsia has previously been ascribed to generalized maternal endothelial cell dysfunction. In this review we suggest that the endothelial dysfunction is a part of a more generalized intravascular inflammatory reaction involving intravascular leukocytes as well as the clotting and complement systems. We provide evidence from our recent work and that of others that not only supports this proposal but indicates that such an inflammatory response is already well developed in normal pregnancy and that the differences between normal pregnancy and preeclampsia are less striking than those between the normal pregnant and nonpregnant states. From this we argue that preeclampsia arises when a universal maternal intravascular inflammatory response to pregnancy decompensates in particular cases, which may occur because either the stimulus or the maternal response is too strong. We conclude that there is no specific cause for the disorder, which can be better considered as the extreme end of the range of maternal adaptation to pregnancy. We propose that poor placentation is not the cause of preeclampsia but is a powerful predisposing factor. We predict that a single preeclampsia gene will not be found, nor will either a single specific predictive test or single preventive effective measure be devised. Aspects of the hypothesis are testable, and future work should allow its confirmation or refutation. (Am J Obstet Gynecol 1999;180:499-506.)

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small microvesicles called exosomes. In 2008, Chris and Ian published a paper that described the interaction of these exosomes with immune and endothelial cells, revealing their effect on systemic inflammation of normal pregnancies and those with preeclampsia.[36]

Chris reflected on the current state of understanding: "The difficulty in today's research is determining how microparticles in preeclampsia actually promote the features of the disease mechanistically, step-by-step. That they are involved is undoubted, how they are involved is still under discussion."

He further explained, "Overall, the microvesicle story reveals a magnificent new signaling system that has to be important in pregnancy—the placenta is not releasing these millions of microvesicles into the maternal circulation for fun. What it is doing is talking to the mother and telling her what to do. What needs to be appreciated is the wonderful elegance of the system and the way it allows the body so many different ways to achieve homeostasis."

Computerized fetal heart rate monitoring and analysis

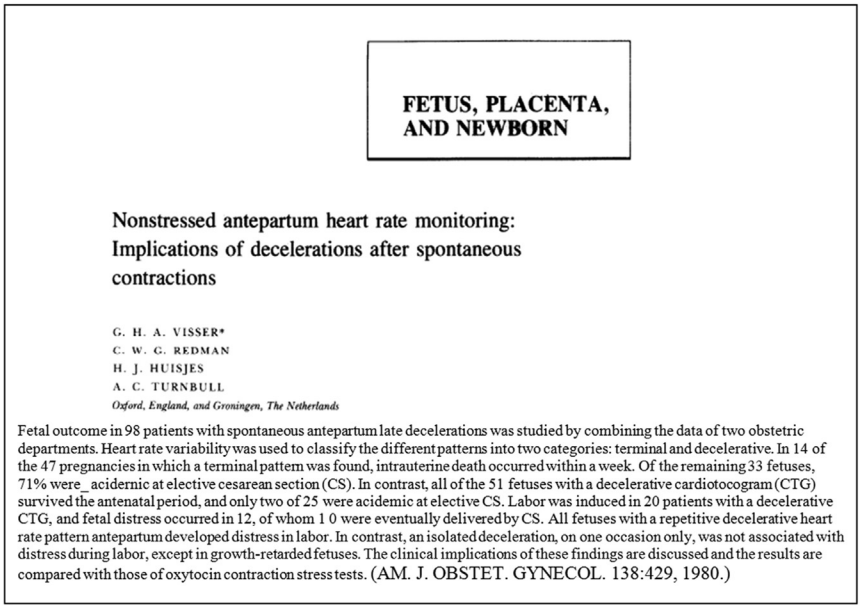
The need for a computerized method for antepartum fetal heart rate monitoring became clear to Chris in the 1970s, when he cared for pregnant women with early-onset preeclampsia. During his first two years of patient care, perinatal outcomes were poor. Familiar with the fetal heart rate monitor used in the Labor and Delivery Unit for intrapartum care, he borrowed one and began antepartum fetal heart rate surveillance, quickly realizing how much could be learned about the fetus and recognizing patterns that preceded fetal death. He realized that fetal heart rate interpretation was subjective and that there was a need for an objective method to assess changes in fetal heart rate, thus began his quest to develop the first computerized system for antepartum cardiotocography.

In 1977, Chris began collaborating with Professor Geoffrey Dawes, CBE, a well-known fetal physiologist and Director of the Nuffield Institute for Medical Research in Oxford, who was using computerized analysis to study heart rate in fetal lambs.

Chris and Professor Dawes advanced the project successfully and published their results in *AJOG*.[37] By 1980, they had a prototype; by 1982, they tested it on the ward; and by 1990, they produced a workable, reliable, and marketable system that standardized trace interpretations. Oxford Medical Instruments, Ltd agreed to produce the Dawes Redman Computerized Cardiotocography system, and the first models sold in 1991.[38] The equipment is widely used throughout Europe, Asia, and Africa; however, it is not currently available in the United States because of licensing issues (Figures 5 and 6).

The system's algorithm for antepartum assessment, however, was inappropriate for use during labor. Anticipating that this would be the next step, Chris advocated for a central monitoring system at Oxford in 1991 to record all intrapartum tracings and developed a hospital-wide database of fetal outcomes. By 2007, nearly 80,000 records had been archived. Chris was able to employ a research scientist, Dr. Antoniya Georgieva, with expertise in biomedical engineering to examine the intrapartum tracings and to determine whether a similar system could be developed for use during labor using advanced computing techniques.

FIGURE 5
Antepartum heart rate variation analysis improves fetal outcome and reduces rate of false positive tests



FETUS, PLACENTA, AND NEWBORN

Nonstressed antepartum heart rate monitoring: Implications of decelerations after spontaneous contractions

G. H. A. VISSER*
C. W. G. REDMAN
H. J. HUISJES
A. C. TURNBULL
Oxford, England, and Groningen, The Netherlands

Fetal outcome in 98 patients with spontaneous antepartum late decelerations was studied by combining the data of two obstetric departments. Heart rate variability was used to classify the different patterns into two categories: terminal and decelerative. In 14 of the 47 pregnancies in which a terminal pattern was found, intrauterine death occurred within a week. Of the remaining 33 fetuses, 71% were_ acidernic at elective cesarean section (CS). In contrast, all of the 51 fetuses with a decelerative cardiotocogram (CTG) survived the antenatal period, and only two of 25 were acidemic at elective CS. Labor was induced in 20 patients with a decelerative CTG, and fetal distress occurred in 12, of whom 1 0 were eventually delivered by CS. All fetuses with a repetitive decelerative heart rate pattern antepartum developed distress in labor. In contrast, an isolated deceleration, on one occasion only, was not associated with distress during labor, except in growth-retarded fetuses. The clinical implications of these findings are discussed and the results are compared with those of oxytocin contraction stress tests. (AM. J. OBSTET. GYNECOL. 138:429, 1980.)

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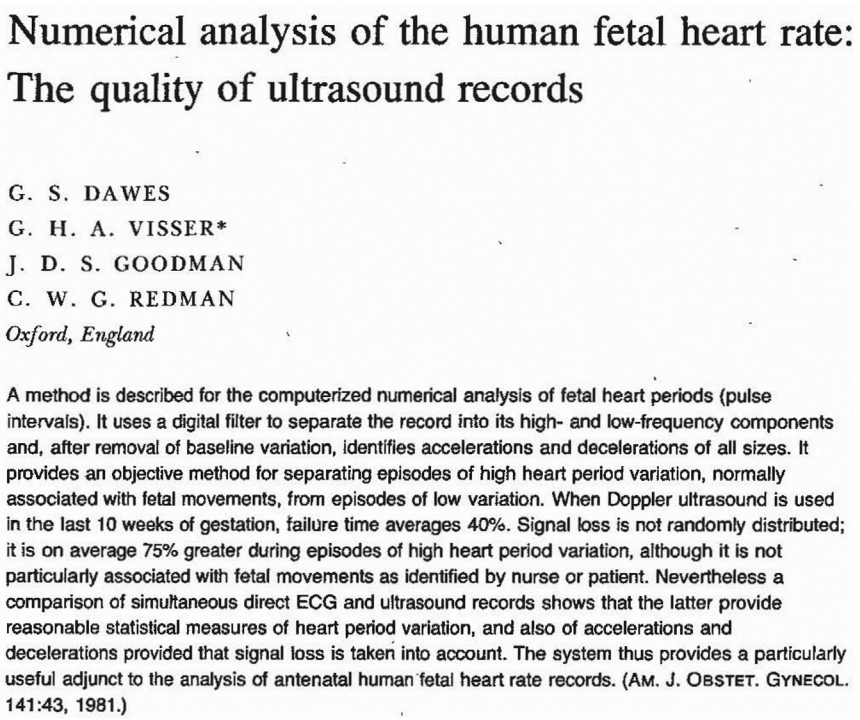
FIGURE 6
Computerized analysis of fetal heart rate patterns provides an objective method for assessing variations



Numerical analysis of the human fetal heart rate: The quality of ultrasound records

G. S. DAWES
G. H. A. VISSER*
J. D. S. GOODMAN
C. W. G. REDMAN
Oxford, England

A method is described for the computerized numerical analysis of fetal heart periods (pulse intervals). It uses a digital filter to separate the record into its high- and low-frequency components and, after removal of baseline variation, identifies accelerations and decelerations of all sizes. It provides an objective method for separating episodes of high heart period variation, normally associated with fetal movements, from episodes of low variation. When Doppler ultrasound is used in the last 10 weeks of gestation, failure time averages 40%. Signal loss is not randomly distributed; it is on average 75% greater during episodes of high heart period variation, although it is not particularly associated with fetal movements as identified by nurse or patient. Nevertheless a comparison of simultaneous direct ECG and ultrasound records shows that the latter provide reasonable statistical measures of heart period variation, and also of accelerations and decelerations provided that signal loss is taken into account. The system thus provides a particularly useful adjunct to the analysis of antenatal human fetal heart rate records. (AM. J. OBSTET. GYNECOL. 141:43, 1981.)

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Mentors and the scientific culture at Oxford University

Chris told me that his most influential early mentors were Dr Lawrie Beilin and Dr John Bonnar. He described Lawrie as a "remarkable person—very sophisticated, academic, and learned." About Dr Bonnar, Chris said, "John was always extremely generous and encouraging and had enormous energy and enormous interest in aspects of pregnancy that very few other obstetricians and obstetrical surgeons [had] at the time, at least in the UK." Both supported and advised Chris on his research of the early treatment of hypertension in pregnancy.

Another influential mentor was Professor Geoffrey Dawes, who brought to fruition Chris's idea of computerized fetal heart rate analysis. When Geoffrey retired in 1985, he devoted himself even more fully to developing this system, and the two of them communicated and collaborated closely until Geoffrey's death in 1996. Chris considers Geoffrey his most important personal mentor, as they spent so much time together. "For 10 years, we shared this interest and it was really quite remarkable that he in his 70s was teaching me in my 50s," Chris said. "That's not the usual student-mentor relationship, but it worked."

When asked why Oxford is such a magnet for talent, he listed several strengths: large endowments and the strong direction of its medical school; a supportive environment that fosters achievement for researchers who are driven and willing to work hard; and a "superb" library system and collegiate atmosphere. Chris said his motto—look through the university—was useful whenever he encountered research problems. "There's usually somebody in a laboratory who you have never heard of before who is the world's expert. It's very rare that you need to go outside Oxford to get your first advice on a problem." For example, the discovery of nucleic acids in the maternal circulation by Dr Dennis Lo[39] took place at Oxford in collaboration with Chris.

Co-founder of Action on Preeclampsia

Chris co-founded Action on Preeclampsia in 1991, a charity established to improve care, raise public and professional awareness of the disease, and support research. The charity has sponsored runners in the London Marathon, in which Chris himself competed 10 times. Chris estimated that his marathon running raised about £120,000 for John Radcliffe Hospital's Silver Star Unit, helping to secure a second flow cytometer in the early 1990s.

Dance classes, family, and cycling to work

Chris and his wife, Corinna, recently celebrated their 54th wedding anniversary. The couple met during grammar school when their single-sex classes were brought together for ballroom dancing. They became a pair while preparing to depart for their university lives, he to Cambridge for science and she to Oxford for classical studies, and they married in 1964 after a steady four-year courtship. Today, they assemble annually

with their five children and 13 grandchildren to celebrate a week together at a unique site in northwest England. Chris chose the location specifically because the house has a table long enough for the whole family to sit around and enjoy a meal together.

An eclectic reader of fiction, Chris has embraced the transition in reading from paper books to a Kindle, where he can have a large selection without creating a mess at home. He enjoys classic films, particularly from directors such as Sir Alfred Hitchcock and Federico Fellini, although now, he said, his grandchildren choose his movies (eg, the Paddington Bear series). In his free time, Chris enjoys hillwalking, an activity well-catered for in the United Kingdom, he noted, as well as gardening, dining in good restaurants, indulging in fine wines, and riding his bicycle back and forth to his office.

"It's remarkable what thinking you can do on your bicycle as you pedal along to work," he said.

Thoughts about the placenta

"I had not intended to be interested in the placenta; it was an unexpected line of investigation that became inevitable as the way to understand how preeclampsia developed," Chris recalled. "The more I learned about the placenta, the more perplexing it was and the more interesting it became."

He now considers the placenta to be the second-most interesting human organ, after the brain. Chris described the placenta as "a remarkable tissue—half fetal, half maternal, not yet innervated—that produces many of the hormones that the rest of the body produces, and lots of other things that are very specific to its own functions, and it's a throwaway organ. After nine months, its job is done and it goes. And with it goes the complete history of the pregnancy wrapped up inside it."

Growing knowledge about the role of trophoblast has revealed the existence of a complex signaling system between the placenta and the mother that "now needs to be un-coded," Chris told me. In learning more about the intrauterine dialogue, "we will find causes of both health and disease," he said. It is now understood that future health in adulthood begins with what happens before and immediately after birth. To that end, Chris said, "the placenta is at the epicenter of our health all through our lives, so it's worth the effort."

Reflections on academic medicine and research

To enjoy and succeed in academic medicine, Chris believes that one must be curious about why problems develop and must be committed to a research life that can be extremely rewarding but also often unexciting and disappointing.

"There are the 'eureka' moments that pop up unexpectedly, which suddenly throw an intense new light on projects that have puzzled you for a very long time," he said. "You have to encounter just one eureka moment to be hooked forever, because then of course you want another one and another one."

One must also enjoy writing about research results as much as conducting the research itself. Chris learned about writing early on in his career, after his paper on α-methyldopa for hypertension in pregnancy was rejected by the *British Medical Journal*. The Editor wrote him a personal letter that ended with this caveat: "May I say that this has been the worst written paper that I have read in my position as editor," Chris recalled. To improve, Chris bought and studied a copy of *Fowler's Dictionary of Modern English Usage*. He rewrote his paper using the "clear, simple, grammatical English" prescribed in the book and submitted it to *The Lancet*, where it was published in 1976.

His first rejection carried a very important lesson for Chris, and he imparted that hard-earned wisdom to his colleagues and students. He routinely took a heavy pen to his students' papers and advised them "the simpler you can write, the better." The same lesson is applicable to oral presentations, he said, where a major problem is trying to say too much in too little time. Chris's advice: "Keep it simple. Don't try and say anything more than you need to say to reach the conclusions that you want to make."

During our conversation, Chris emphasized that it is an exciting time to enter the field, echoing what other "Giants" have said about their specialties. "Now is the most beautiful moment to go into preeclampsia research. There have been so many advances in scientific knowledge over the past 10 years that are just waiting to be applied," he said. "Answers are going to come tumbling out over the next generation."

Legacy

Chris's work has broadened the conversation about preeclampsia and placenta research, setting the stage for future generations of researchers and clinicians. His work laid the foundation for major research projects being undertaken today. For example, the NIH Human Placenta Project, an initiative of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, aims to create new tools to study the placenta in real time to learn how it develops and functions throughout pregnancy.[40]

For his many contributions to the understanding of preeclampsia, placental physiology, and pathophysiology of pregnancy, and for his work in antepartum fetal heart rate monitoring, the *American Journal of Obstetrics & Gynecology* recognizes Dr Chris Redman as a "Giant in Obstetrics and Gynecology."

ACKNOWLEDGMENTS

This profile is based on a conversation with Dr Christopher Redman in November 2018. I would like to thank Christine Kilgore, Rebecca Hudson, Andrea Bernard, and Maureen McGerty for their contributions to this profile.

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SUPPLEMENTAL FIGURE 1

Chris receives a plaque for being recognized as a "Giant in Obstetrics and Gynecology" from Dr Roberto Romero, Chief of the Perinatology Research Branch

Romero. A profile of Christopher Redman. Am J Obstet Gynecol 2019.

SUPPLEMENTAL FIGURE 3

Chris with Dr Sonia S. Hassan, Dr Annetine Staff from the University of Oslo, Dr Romero from the Perinatology Research Branch, and Dr Chaur-Dong Hsu from Wayne State University School of Medicine

Romero. A profile of Christopher Redman. Am J Obstet Gynecol 2019.

SUPPLEMENTAL FIGURE 2

Chris visiting the Perinatology Research Branch of NICHD/NIH in Detroit, MI

Romero. A profile of Christopher Redman. Am J Obstet Gynecol 2019.