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President—V. B. GREEN-ARMYTAGE, F.R.C.O.G., M.D., F.R.C.P.

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Observations on the Human Placenta

By W. J. HAMILTON, M.D., D.Sc., F.R.S.E.
Anatomy Department, Charing Cross Hospital Medical School

and J. D. BOYD, M.A., M.Sc., M.D.
Anatomy Department, London Hospital Medical College

THE increase in our knowledge of the early stages in human development and implantation which has been made in the past ten years provides a suitable basis for the study of the developing and of the mature and fully functioning placenta. This increase has been due chiefly to the contributions of Hertig and Rock (1941, 1945, 1949) though other investigators (*see* Hamilton, Boyd and Mossman, 1945, and Hamilton and Boyd, 1950, for literature) have given less significant, but confirmatory, descriptions. Advances in knowledge of the later stages of human placentation have, however, not kept pace with the contributions to knowledge of early development and there is still wide disagreement and considerable doubt about a number of fundamental points in the structure of the fully established placenta.

Considering that the time was ripe for a re-assessment of the basic structure of the placenta the authors, during the past few years, have collected material from over 100 dated pregnancies including 21 placentæ still *in situ*. The preliminary study of this material has demonstrated the importance of such *in situ* specimens if a correct interpretation of placental structure and function is to be attempted. Indeed many of the doubtful and incorrect accounts of the basic structure of the placenta are, in our opinion, due to the restriction of its study to post-partum specimens. It must be pointed out that the study of *in situ* placentæ is rendered difficult by the infrequency with which such specimens are obtained and by the special problems presented in the serial sectioning of such large and technically refractory material. Nevertheless among the available material there is a number of well-fixed *in situ* specimens and, as the illustrations will show, it has been possible to section them successfully in extensive series.

It has, however, been thought that by presenting, however briefly, some aspects of the results so far obtained certain fundamental misconceptions in the literature will be indicated and the extensive gaps in our knowledge revealed. The points to which special attention has been directed are (1) the arrangement, nature and manner of growth of the placental villi, including their relationships with each other and with the basal plate (area of attachment of the placenta to the decidua); (2) the relationship of the maternal blood vessels to the intervillous space and the nature of this space; (3) the changes in the decidua during pregnancy and the alterations in its structure with increasing placental size; (4) the growth of the placenta; and (5) the nature of the placental membrane. Observations have also been made on the histo-chemistry of the placenta and decidua, following the lead given by Wislocki and his collaborators (1943, 1948*a*, 1948*b*), but it is not intended to consider these observations, except incidentally, in the present communication.

(1) *Arrangement and nature of the placental villi.*—Currently there are three quite different concepts of the relationship of the chorionic villi to each other and to the basal plate. The first, and earliest, is that which considers the fundamental structure of the human placenta to consist of frond-like villi arising from the chorionic plate. The villi, on this view, are believed for the most part to float freely in the intervillous space. Some of them, however,

are considered to reach and fuse with the basal plate and thus to become intercalated into the "trophoblastic shell". Most of the villi are thought of as floating in the intervillous space like water weeds in an aquarium (Stieve, 1948). The second interpretation is that associated with the name of Spanner (1935): this investigator considered that all the villi extend from the chorionic plate to the basal plate whence, after fusing with the "trophoblastic shell", they bend back into the intervillous space and hang freely like the branches of a weeping-willow tree (Stieve, 1948). This concept of Spanner's has been widely accepted. The third concept of the villi, advocated very strongly by Stieve in a number of communications (1940*a*, 1942, 1948) considers that the placenta is fundamentally labyrinthine in structure and that the ultimate branches of the "villi" fuse with each other to form a tri-dimensional lattice work. Our material, and more particularly our sections of placentæ *in situ*, lends support, though in a limited sense, to the Stieve concept. Many villi can be seen to join by way of their lateral branches. We have not, however, been able to persuade ourselves that these fusions of the "fringing villi" (Stieve's "Gitterzotten") are regularly more than fusions of their syncytial covering although there is some evidence for occasional junctions by way of the connective tissue cores and even by their contained fœtal blood vessels. The arrangement, however, is such that the intervillous space is much more like a labyrinth, or the interstices of a sponge, than the widely opened space required by the first two interpretations. It can be pointed out that the method of early development of the intervillous space, by the flowing together of the lacunæ in the syncytio-trophoblast, supports an interpretation of the space along the lines indicated by Stieve rather than an explanation that envisages the space as a cavity into which the villi secondarily extend.

(2) *The relationship of the maternal arteries and veins to the intervillous space.*—Here, again, there is a wide diversity of opinion. Until the contribution by Spanner (1935) it was generally accepted that the uterine arteries opened into the intervillous space principally in the neighbourhood of the margins of the septa which divide the placenta into cotyledons. This view was due principally to the descriptions given by Bumm (1893) who thought, indeed, that most of the terminal uterine arteries opened into the intervillous space quite far down in the septa, and remote from the basal plate. On the other hand the uterine veins were considered to open out of the intervillous space through openings in the basal plate in the interseptal zones. In this way the flow of maternal blood in the intervillous space was described as being from the lower (chorionic) ends of the septa to the basal plate. This description has been widely accepted but critics have not been lacking and, as early as 1901, Webster wrote that Bumm's "beautifully figured artery coiling outward in a decidual hillock, and then sending jets of red paint outward among the villi must be regarded only as a pretty fancy".

Spanner gave quite a different description. Observations on injected uteri led him to consider that the uterine arteries open through the basal plate in the inter-cotyledonary areas. From here the maternal blood then passes down through the intervillous space around the villi and on reaching the region of the chorionic plate is directed towards the periphery where it drains into a marginal venous sinus which, in turn, discharges into the uterine veins. This account has also been widely accepted in the literature. It has the attractive feature of appearing to explain the method of blood circulation in the intervillous space. When added to Spanner's account of the villi the final arrangement is such that the flows of the maternal and fœtal bloods are in mutually advantageous directions from the point of view of exchange. In our material, however, there is no macroscopic or microscopic evidence for the existence of Spanner's marginal sinus (Figs. 1, 2, 3 and 4). The material is now considerable and in extensive serial sections. It seems to us unlikely that the marginal sinus is a feature of the normal placenta. Indeed we are forced from a study of our material to accept as essentially accurate Stieve's severe strictures on this aspect of Spanner's work. Further, our sections show numerous openings of maternal veins all over the basal surface of the placenta (Fig. 5). The veins are of varying sizes at their points of exit from the intervillous space but are occasionally so large (Fig. 6) that quite extensive portions of the terminal villi may "herniate" into them. These villi then have the curious appearance, in isolated sections, of lying free on the uterine side of the basal plate, in the lumen of a component of the uterine decidual venous plexus (Fig. 7). When the specimens are examined in serial sections, however, such "herniated" villi can always be traced back to the intervillous space through the mouth of a vein in the basal plate. Our view of the connexions between maternal vessels and the intervillous space is, therefore, not revolutionary, indeed in a sense, it is reactionary, for, in essentials, it goes back to Farre (1859) and, even earlier, Goodsir (1845) had figured the fundamental arrangement correctly. It is, that the arteries and veins open into or out of the intervillous space more or less regularly over the whole surface of the basal plate. The openings of the arteries are, possibly, concentrated to some extent around the bases of the inter-cotyledonary septa but the veins appear to be quite randomly distributed save near the margin where they are, perhaps, a little more numerous. This view of the

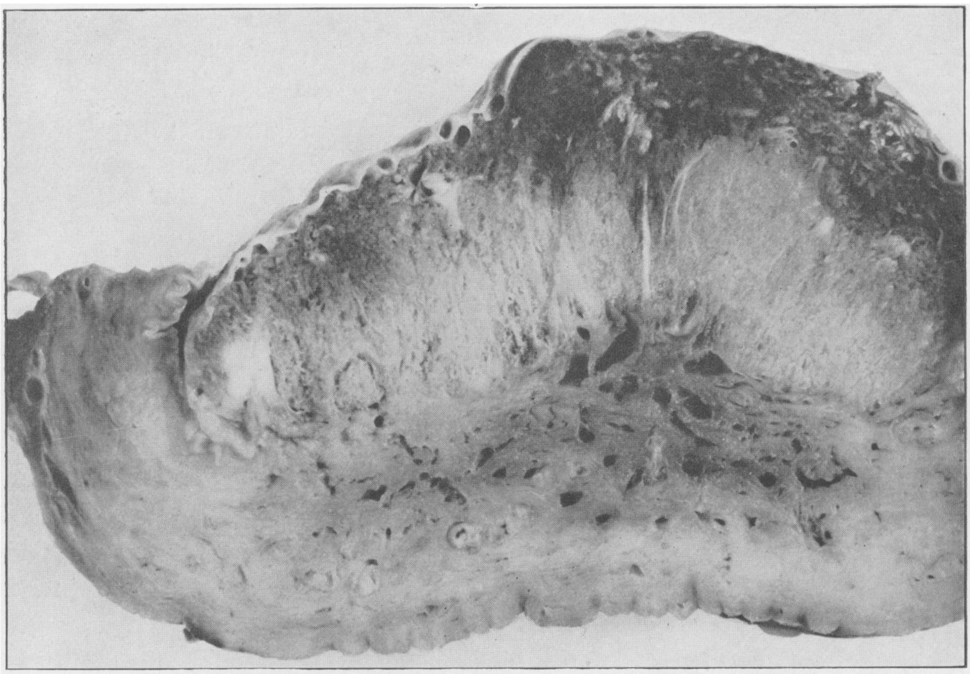

FIG. 1.—Photograph of half placenta *in situ* of specimen H. 219 (fœtus measured 157 mm. C.R.L.). Note marked vascularity of uterine wall opposite central part of basal plate. × 1·4.

FIG. 2.—Photomicrograph of marginal region of placenta *in situ* of specimen H. 212 (fœtus measured 145 mm. C.R.L.). Note the complete absence of a marginal sinus and the looseness of the attenuated decidua over the basal plate. × 4.

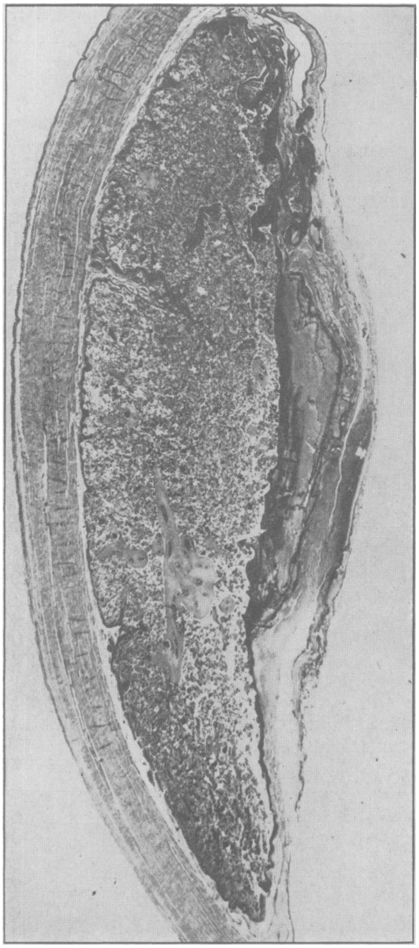

FIG. 3.

FIG. 4.

FIG. 3.—Section of placenta *in situ* of specimen H. 212. There is much fibrinoid deposit in the region of the chorionic plate and absence of the marginal sinus. × 2.

FIG. 4.—Photomicrograph of marginal region of placenta *in situ* of specimen H. 7 (fœtus measured 240 mm. C.R.L.). Note the absence of a marginal sinus. × 2·5.

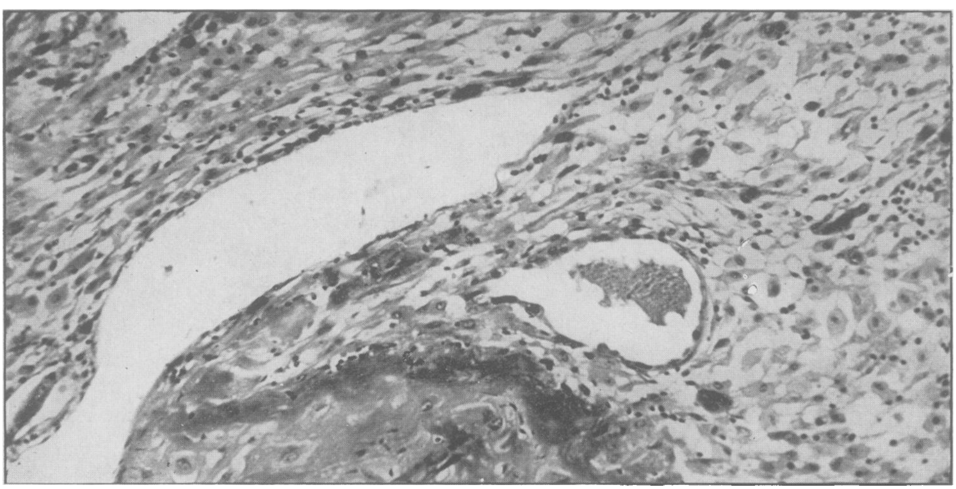

FIG. 5.—Detail of placenta *in situ* of specimen H. 212. The opening of a uterine vein from the intervillous space is shown. The trophoblastic shell can be seen in the lower part of the figure. × 440.

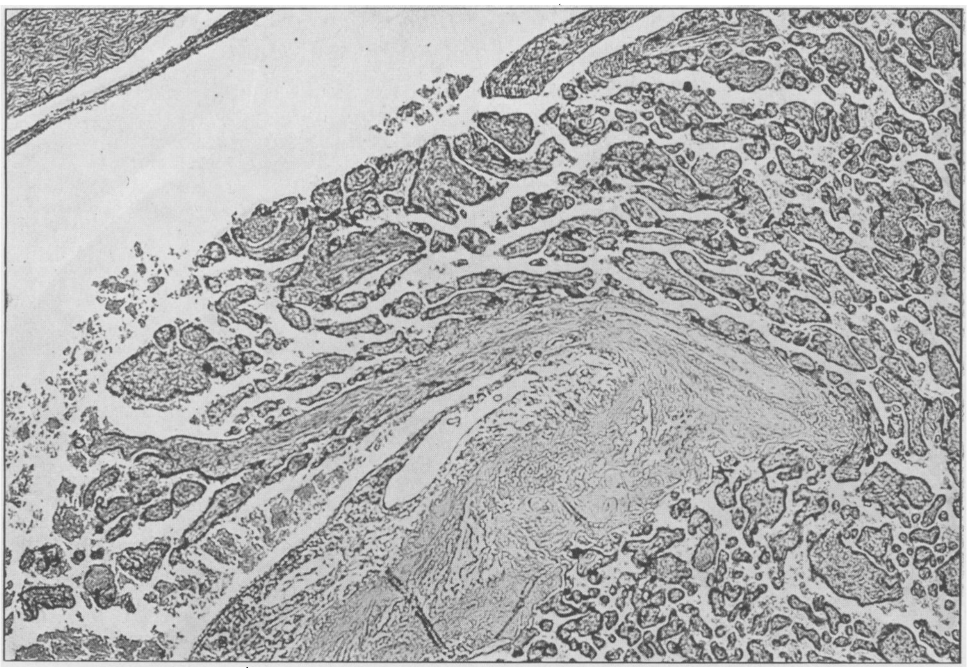

FIG. 6.—Basal plate region of specimen H. 7 (fœtus measured 240 mm. C.R.L.). A large plug of chorionic villi extends through a venous opening in the basal plate into a uterine vein. × 120.

FIG. 7.—Decidua and basal plate of specimen H. 212 (fœtus measured 145 mm. C.R.L.). In the central part of the figure a number of villi can be seen lying in the decidua. They are situated in the lumen of a uterine vein. × 120.

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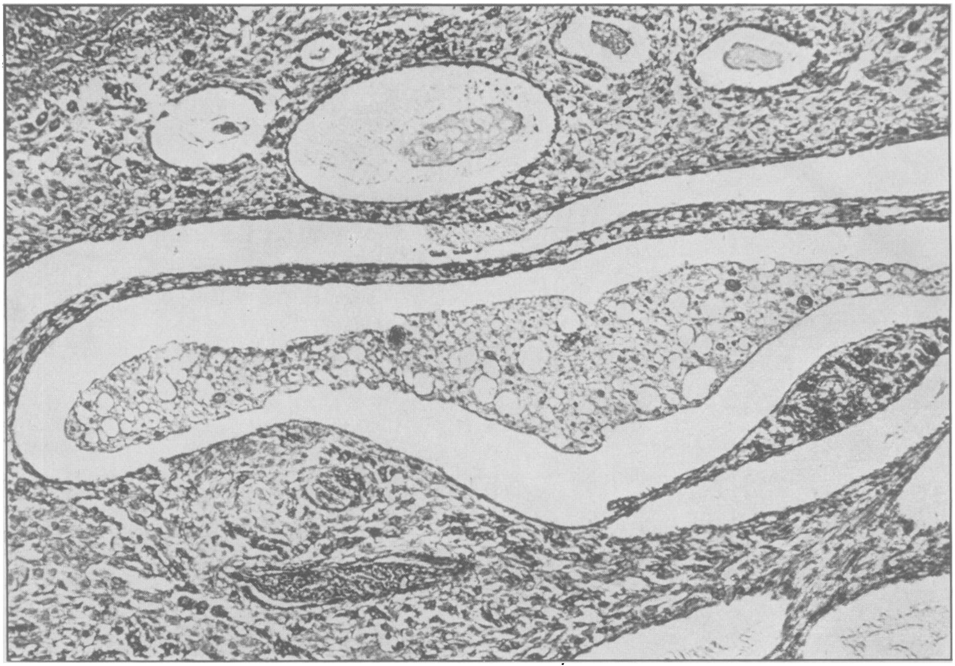

FIG. 8.—Section through decidua and basal plate of specimen H. 212 (fœtus measured 145 mm. C.R.L.). It shows secretion in the glands of the decidua basalis. × 120.

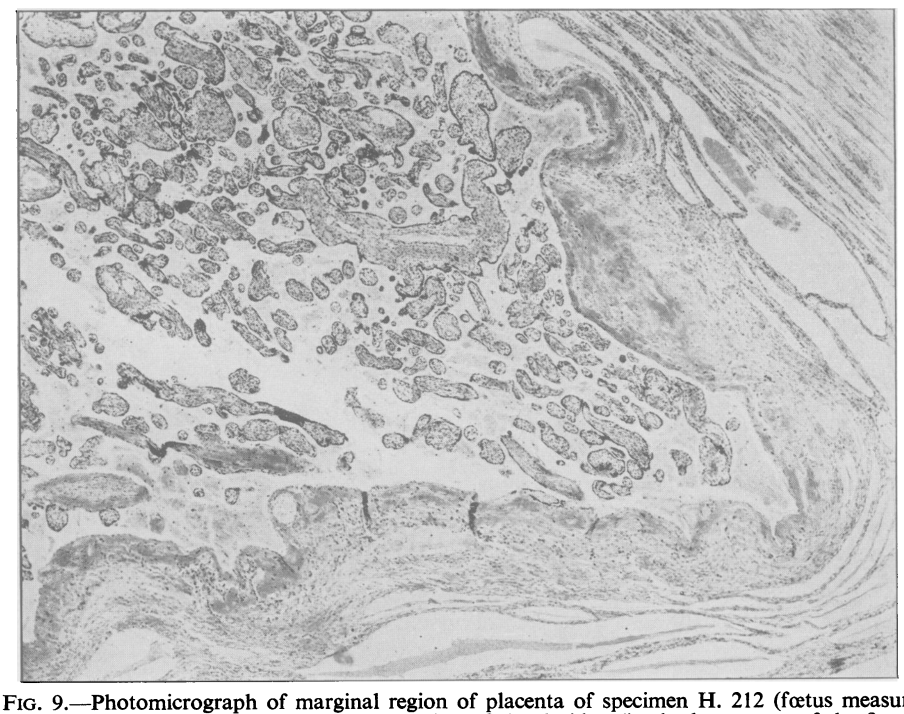

FIG. 9.—Photomicrograph of marginal region of placenta of specimen H. 212 (fœtus measured 145 mm. C.R.L.). It shows sub-chorial extension of the decidua (in the lower part of the figure). Note absence of marginal sinus. × 120.

method whereby the maternal arteries and veins are connected with the intervillous space has the disadvantage of leaving unexplained the free circulation of blood in this space. It has not the functional appeal of the interpretations of either Bumm or Spanner. This disadvantage is much more than compensated for by the fact that it corresponds with what is actually found in well-fixed sections of placentæ *in situ*. The need for a functional explanation of the circulation in the intervillous space is hardly met by postulating an arrangement of the vessels which however useful in explaining the flow has actually no basis in anatomical fact!

(3) *Changes in the decidua during pregnancy*.—A striking feature of the sections of placentæ *in situ* during the stage of functional maturity (say from the fourth month to term) is the extraordinary "looseness" of the decidual tissues between the basal plate and the uterine musculature. In this position the decidua consists of a very dense venous plexus and of dilated and distorted uterine glands with extremely thinned walls. There is little cellular material lying between the veins and the glands but terminal branches of the uterine arteries traverse the interstices to reach the basal plate. The appearances are such as to raise the question of the mechanism whereby the placenta is held in position. The uterine glands preserve secretion in their lumina until quite late and long after the flattened cells of the glandular walls can be considered as capable of active secretory processes (Fig. 8). Many of the glands can be followed into the bases of the inter-cotyledonary septa where they end blindly. At the margins of the placenta the decidual tissue becomes more compact. It always shows, though to a variable extent, a sub-chorial extension. This sub-chorial extension of the decidua is, in our opinion, a result of the lateral extension of the placental margin during its growth (Fig. 9).

(4) *Growth of the placenta*.—Our observations on the growth of the placenta confirm in general the opinion held by Stieve (1940*b*) and are contrary to the views expressed by Spanner and others. According to Spanner's conception, the placenta does not grow in circumference during the second half of pregnancy, but only in thickness. Our specimens show, as did those of Stieve, that the placenta continues to grow in circumference throughout pregnancy. This increase in diameter is brought about in part, at least, by growth at its edge. But more data are required before interstitial growth can be excluded. Unlike Stieve we have found that, within narrow limits, the placenta does increase in thickness during the second half of pregnancy. The greatest increase in thickness, however, occurs from the fourth to the seventh month.

(5) *Placental membrane*.—In the human placenta this term is used to designate the full thickness of the fœtal tissue which separates the maternal blood in the intervillous space from the fœtal blood in the capillaries of the villi. This "membrane" has been shown by many investigators to be a structure of unusual complexity and not a simple semi-permeable membrane. It is not our intention to give an account of its structure in the different vertebrate groups, but to refer briefly to the membrane in the human placenta.

During the course of gestation, the membrane varies greatly in its thickness. In the early period of development it is much thicker than in the last half of pregnancy. When the blood capillaries first make their appearance in the villi, the fœtal blood is separated from the maternal blood by the endothelium of the fœtal capillary, the surrounding mesenchyme and the two layers of trophoblast. By the fourth month of pregnancy, the cyto-trophoblast on the villi begins to disappear and is completely lost by the fifth month. From this time until term, the placental membrane consists of the endothelial lining of the fœtal capillary, a very attenuated layer of mesenchyme and syncytio-trophoblast. We have not observed any marked difference in the thickness of the placental membrane during the last half of pregnancy. The membrane varies in thickness in different regions of a given placenta but it may be as thin at the fifth month as at the ninth month.

The efficiency of the membrane is not necessarily related to its thinness. As Wislocki has stressed, if the membrane has secretory activities, the relative thickness is unimportant.

Flexner and his colleagues (1948) have shown that there is considerable increase in the permeability of the placental membrane to radioactive sodium as gestation proceeds. The peak of transfer is at the 36th week when it is seventy times greater than at the 9th week. This peak is followed by a rapid decline in the last weeks of pregnancy due, amongst other things, to the ageing of the placenta associated with retrogressive changes in the fœtal blood vessels, or to the deposition of fibrin. Hellman *et al.* (1948) found a fivefold increase in the transfer rate of heavy water per unit of placenta from the 14th week until full term. The transfer coefficient for water is five times that of sodium from the 12th to 35th week. This difference may be due to the secretory activity of the membrane or to its physical characteristics or, owing to the growth of the whole placenta, to the increased surface area of the placental membrane. It may be that a further factor is the pressure in the fœtal circulation. This gradually increases as pregnancy advances. The higher head of pressure may influence the permeability.

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The Surgical Menopause Following Hysterectomy: A Study of 332 Cases. [*Abstract*]

By N. A. RICHARDS, M.B., B.S., M.R.C.O.G.

MANY investigators have come to the conclusion that hysterectomy hastens the onset of the climacteric. A survey of the literature, however, reveals that, for the last fifty years, two groups of gynæcologists have held opposite opinions on whether conservation of one or both healthy ovaries delays the onset of the menopausal syndrome, or lessens the severity of the associated symptoms.

This is a brief account of an investigation which Dr. P. M. F. Bishop, Mr. William Kenny and I have carried out in an attempt to obtain some information on this problem. The records at Chelsea Hospital for Women were searched for public ward patients up to the age of 45 on whom hysterectomy had been performed between the years of 1944 and 1948 inclusive and 332 of these patients were personally interviewed and examined.

It was decided to include in our series women up to the age of 45 at the time of operation, so that the best use could be made of the clinical material available and, in the final analysis, patients who were having hot flushes before operation were discarded (20 cases).

In assessing each case particular attention was paid to the incidence, frequency and severity of hot flushes following hysterectomy. It was considered that, with all subjective symptoms except hot flushes, it would be difficult to establish a menopausal relationship as they are so commonly associated with functional neuroses.

It was decided to consider that hot flushes which occurred within two years of hysterectomy were due to operative interference. This was not, however, an invariable rule and each case was assessed impartially and with considerable care.

The effects of hysterectomy with ovarian conservation, with unilateral oophorectomy and with bilateral oophorectomy are shown in Table I.

TABLE I.—INCIDENCE OF HOT FLUSHES

Operation	No. of cases	Incidence of hot flushes Number	%
Hysterectomy with ovarian conservation ..	204	55	27
Hysterectomy with unilateral oophorectomy	66	34	52
Hysterectomy with bilateral oophorectomy	42	41	98