

THE YEAR BOOK of OBSTETRICS and GYNECOLOGY

(1959-1960 YEAR BOOK Series)

EDITED BY

J. P. GREENHILL, B.S., M.D., F.A.C.S., F.I.C.S. (Honorary)

Professor of Gynecology, Cook County Graduate School of Medicine; Attending Gynecologist, Cook County Hospital; Senior Attending Obstetrician and Gynecologist, Michael Reese Hospital; Associate Staff, Chicago Lying-in-Hospital; Author of Office Gynecology, Surgical Gynecology, Obstetrics and Obstetrics in General Practice

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THE PRACTICAL MEDICINE YEAR BOOKS

This volume is one of the 15 comprising the Practical Medicine Series of Year Books founded in 1900 by G. P. Head, M.D., and C. J. Head, and published continuously since then. The complete list follows:

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OBSTETRICS

PREGNANCY

PHYSIOLOGY

The 100-Day Basal Body Temperature Graph in Early Pregnancy. Alan Grant and W. G. McBride¹ (Women's Hosp., Sydney) note that there is biphasic variation in the basal temperature of normal women between one menstrual period and the next, so the temperature is higher after ovulation than before. Patients who have a good basal body temperature graph for 80-100 days after onset of pregnancy rarely abort, whereas those who have erratic temperature levels often miscarry.

A series of women who were subject to recurrent abortions were requested to chart their temperature for 100 days after conception. The late pregnancy salvage rate of those who had a good graph was 89%, of those with a bad graph, 52%. Forty patients who had poor graphs were treated and 23 were available as a control series. When no treatment was given, 35% had live babies, whereas if progestogens were given postconceptionally in an attempt to elevate the temperature to a normal height and shape, 62% produced live babies.

The postconception level of the temperature for the 1st trimester is more likely to be maintained at a satisfactory height if the thermal shift before pregnancy is normally elevated or made normal by repetitive therapy with progestogens administered orally during the premenstrual 10 days. To discover whether this preconception therapy is indicated, premenstrual curettage must have been performed during some previous month and the tissue "dated" by an expert pathologist. During that same month, a basal temperature graph must have been recorded and the results of this double preconception investigation evaluated. Results

⁽¹⁾ M. J. Australia 1:458-460, Apr. 4, 1959.

are better when the preconception progesterone treatment of habitual abortion has been faithfully applied.

Though the objection that some patients carry on to term even if their basal temperature chart is erratic for the 1st trimester is correct, only about one third of such patients procure a live baby, whereas if the temperature graph is normally and evenly elevated during that time, the number of babies obtained rises to almost 90%.

The presence of occasionally normal ovulation among a series of abnormal cycles is one of the main reasons why so many and so varied treatments have been claimed as successful in habitual 1st trimester abortion.

Progesterone-Induced Withdrawal Bleeding as Simple Physiologic Test for Pregnancy. According to Glen E. Hayden2 (Univ. of Chicago), use of progesterone in diagnosis of early pregnancy is predicated on its ability to induce withdrawal bleeding in patients with proliferative or estrogenprepared endometrium. Application of this method to the differentiation of pregnancy from other causes of amenorrhea is necessarily based on the premise that one of the three principal structures-uterus, ovaries or pituitary-may be responsible for the amenorrhea. Menstruation after progesterone therapy in a patient with amenorrhea indicates that the pituitary must be in a more or less normal functional status, since it is producing enough follicle-stimulating hormone to cause the ovary to secrete enough estrogenic hormone. Finally, the endometrium must be capable of responding and developing to the point of proliferative endometrium. Hence, the patient has a comparatively normal genitoendocrine system. In the absence of proliferative endometrium, as with decidua or the undeveloped endometrium of premenarche or the atrophy of the menopause, no withdrawal bleeding will occur.

Hayden selected 120 patients, aged 18-35, on the basis of previously regular menstrual periods and the distinct possibility that a conception had occurred. They were instructed to report any unusual bleeding and to bring in any clots or tissue passed. All the patients were amenorrheic for 35-70 days from the 1st day of the last menstrual period. The medication was given to 102 patients according to one of the fol-

⁽²⁾ Am. J. Obst. & Gynec. 76:271-278, August, 1958.

lowing modes: (1) anhydrohydroxyprogesterone orally, 200-400 mg./day for 4-5 days; (2) progesterone USP vaginally, 75-250 mg./day for 4-5 days; (3) 17\alpha-hydroxyprogesterone caproate intramuscularly, 125-500 mg./day for 2-5 days.

After this procedure, withdrawal bleeding did or did not ensue within 14 days. The accuracy of progesterone-induced withdrawal bleeding as a simple physiologic but nonspecific test for pregnancy or secondary amenorrhea was 100%. The greatest advantage of this method is that no laboratory equipment, animals or specimens are needed. The oral or vaginal mode of administration is preferred to the intramuscular, since with the former, onset of bleeding occurred between the 3d and 7th day in 85% of the patients. In addition, there is no need for office visits.

No alteration in the course of a gestation was noted with either standard or excessively large dosage. No abortion could be attributed to use of the progesterone. In secondary amenorrhea, the progesterone test was not only accurate diagnostically but useful therapeutically, since in 72% of the nonpregnant patients the menstrual cycles were restored to normal regularity.

Menon and Isaiah (J. Obst. & Gynaec. Brit. Emp. 9:97, 1958) say that the male frog test, using urine concentrate, gives the most accurate results. Among 1,183 tests using male frogs there was not a single false positive test. As far as Madras, India, is concerned, there is no seasonal variation in the degree of accuracy of the male frog test. The mortality among frogs is least when urine concentrate or serum is used. Ordinarily, a positive response is obtained in nearly 100% of cases within 5 hours. The authors are not impressed with the accuracy of vaginal cytology in the diagnosis of pregnancy.

Joel and Lancet (Obst. & Gynec. 13:51, 1959) found that disturbances in pregnancy which lower the chorionic gonadotropin excretion of the urine immediately show up as a decrease of the ovarian weight and an increase of the uterine weight of juvenile mice. By repeated tests in the same patient, prognosis can be established in 75% and further treatment of threatened abortion obviated. As a pregnancy test the gravimetric method has shown itself to be quite accurate and it can be used in the early weeks when the frog test is deficient. As a biologic test for hydatidiform nole or choriocarcinoma, this method is as useful as the A-Z reaction. In asses of amenorrhea, when pregnancy is excluded, the test can differentiate between ovarian and hypophysial deficiency; in the former type, when folicle-stimulating hormone is increased, the ovarian weights are low and hows any weight increase.—Ed.]

Changes in Mechanical Properties of Cervix under Influence of Pregnancy. Physiologic and histologic study of the cervix indicates that during gestation the properties of cervical tissue change considerably and that at the end of parturi-

tion the tissue rapidly returns to its state before conception. These marked biologic changes would seem to mask any effects due to stress of parturition unless severe stresses were to cause marked changes in the biologic processes of recovery. Because evidence concerning the properties of the cervix, obtainable during clinical conduct of labor, is so indirect, E. C. Halliday, G. van Wyk Jacobs and O. S. Heyns³ devised a direct experimental attack on the stretch-resisting properties of human cervices as a test of validity of the theory. An instrument was designed that would dilate and maintain the cylindric shape of the cervix of a human uterus, at the same time measuring force involved and dilatation produced.

Measurements of cervical resistance to stretch were made on 159 women admitted for curettage under general anesthesia because of inevitable or incomplete abortion. Patients with cervical damage were excluded. The mean value of dilatability and of dilatation rate in two groups of women—those who had not borne children and those who had borne one or more—was practically the same. On this evidence the cervix that has experienced passage of one or more fetal heads has not had its dilatability increased to any degree; i.e., its resistance to dilation has not been reduced. The ease with which the cervix can be dilated is strongly related to the actual degree of dilatation that occurred during abortion. As time passes subsequent to abortion, the ease with which the cervix may be dilated steadily decreases.

The process of recovery of the cervix after abortion might be described in terms of build-up of connective tissue at the expense of muscle, or even as a reduction in vascularity, because vascular elements have a viscous property even though they may not possess the contractility of muscle.

Stephens (Am. J. Obst. & Gynec. 75:1255, 1958) found that routine serial observations of cervical changes throughout pregnancy have proved valuable. These studies along with the usual antepartal observations may be used to predict premature labor. Two anticholinergic drugs have proved effective in delaying imminent premature labor as evaluated in 76 women during 81 pregnancies. Dactil® has been used as a preventive measure with great success and no untoward effects. Dibuline® may be used in extreme conditions to arrest uterine contractions but is limited by the undesirable side effects and parenteral administration. It should be restricted to hospital use.

Verschoof (Nederl. tijdschr. verlosk en gynaec. 58:101, 1958) made fern tests of the cervix in 437 women and found typical features in 24.4%.

⁽³⁾ J. Obst. & Gynaec. Brit. Emp. 65:409-413, June, 1958.

There was no demonstrable correlation between atypical fern reactions and the following factors: (1) imminence of abortion or labor, (2) parity, (3) placental coefficient and (4) fetal sex. An atypical fern test during pregnancy is generally assumed to indicate placental deficiency, but the author's investigation showed that this test during pregnancy has no prognostic significance whatever.—Ed.]

Deciduosis of Uterine Cervix: Clinical and Colposcopic Aspects. J. Bret, F. Coupez and J. De Brux⁴ (Paris) observed 14 cases during the past 2 years. Routine search for cervical cancer during pregnancy renewed interest in this condition by showing that it is more frequent than previously believed and by posing the problem of its differential diagnosis. In deciduosis, the cervix exhibits cells similar to those in uterine decidua during pregnancy. After fertilization of the ovum and implantation in the uterine mucosa, the latter is thickened; its epithelium appears to be flattened and to lose its vibratory cilia while the subjacent conjunctiva undergoes decidual change.

It is inappropriate to speak of functional signs of deciduosis; leukorrhea and reddish secretion are due to gravid ectropion accompanying certain types rather than to the deciduosis itself. Examination of the cervix with the speculum is deceiving. All lesions hitherto described as deciduosis were simply lesions of gravid ectropions more or less altered by infection.

The authors' cases were all discovered during search for dysplasias and cancer during pregnancy in women whose cytologic findings aroused suspicion or in whom the cervix was macroscopically abnormal. Some cases of deciduosis with no cytologic signs or changes revealed by speculum examination may thus have been overlooked.

Deciduosis of the cervix is of interest principally because of its differentiation from beginning cervical cancer. Although clinical deciduosis with hemorrhage is not difficult to differentiate from cancer, certain exocervical types have a cytologic similarity and pose diagnostic difficulties with gravid dysplasias or carcinoma in situ. If such difficulty exists, colposcopy and local biopsy must be combined to elucidate the source of the abnormal cells. These permit marking of a submalpighian deciduosis which is easily checked histologically; they easily localize plaques of dysplasia and confirm the microscopic diagnosis.

⁽⁴⁾ Gynéc et obst. 58:199-207, Apr.-May, 1959.

The course of deciduosis is benign, with spontaneous cure, and it is usually asymptomatic. Locations are variable, but the submalpighian exocervical type appears to be most frequent. It can be recognized by colposcopic examination.

Serial Studies of Serum Lipids in Normal Human Pregnancy were made by Russell R. de Alvarez, Donald F. Gaiser, Donna M. Simkins, Elizabeth K. Smith and Gloria E. Bratvold⁵ (Univ. of Washington), with the technical assistance of Jean B. Forsander, Janice E. Ekholm and Ruth Portman. Recently, attention has been focused on the production of arterial and arteriolar thickening, deposition of atheromatous plaques in vessels and eventual production of hypertension. These features have further attracted attention in attempts to establish possible relation between cholesterol metabolism and ultimate development of atherosclerosis. Increase in circulating lipids occurs during pregnancy.

To establish baseline values, changes in total lipid; total serum, ester and free cholesterol; phospholipid; and lipid phosphorus values during normal pregnancy were studied. The 25 pregnant patients studied came from about the same nonindigent economic and social level, and all received the same antepartum advice and care. All pregnancies were normal, and no patient was included if any abnormality developed during pregnancy. In 10 patients, all lipid studies and determinations were made serially at about monthly intervals throughout pregnancy. In 15, "spot" determinations were made at varying times during pregnancy.

During early pregnancy, values for total, ester and free cholesterol; lipid phosphorus; phospholipids; and total lipids did not differ significantly from those for normal non-pregnant controls. Though the trend of free cholesterol values decreased during early pregnancy, the differences were not statistically significant when compared with control values. All values increased as pregnancy approached term, with return to normal for most fractions by the 6th post-partum week; total lipids and lipoproteins were the principal exceptions.

Whereas estrogen reportedly effects an increase in alpha lipoprotein, pregnancy produces an increase in beta lipoprotein values. Changes in the blood lipid values during preg-

⁽⁵⁾ Am. J. Obst. & Gynec. 77:743-759, April, 1959.

nancy cannot be accounted for by increase in estrogen alone or increase in adrenal steroids alone.

Can Dietary Protein Deficiency Be Assessed Biochemically? Study of 54 Obstetric Patients is presented by S. C. Werch, G. T. Lewis and J. H. Ferguson⁶ (Univ. of Miami). The concept of increased protein need by pregnant women is generally accepted. Growth of the uterus and fitus, increased blood volume, development of breasts and increased metabolism make demands that explain increased protein requirements. That pregnant women may reveal dietary protein deficiency more consistently than nonpregnant women should prove even more true for those who do not digest or absorb well the protein in the diet. For these reasons, pregnant women were chosen for study.

Each patient was questioned by three interviewers, and estimates of the protein content of the diet were made. Digestibility of proteins, determined by the method of preparation, and absorption, determined by state of t'e bowel, were also assessed. Nine per cent of the women had a diet with a protein content of about 40 Gm. or under (poor); 67%, 40-60 Gm. (fair); and 24%, 60-80 Gm. (good). Thus, no patient had a diet with a protein content that fulfilled the recommendation by the Food and Nutrition Board of the National Research Council of 85 Gm./day for pregnant women, and only about a fourth approached this recommendation.

The low values of the biochemical profiles appeared to correlate with a protein-deficient diet. Until a better method is introduced, careful correlation of the findings of a dietary interview with a chemical profile, including blood albumin, amylase and pseudocholinesterase determinations and the albumin-globulin ratio, is suggested for detection of possible protein deficiency.

Pasamanick and Knobloch (Obst. & Gynec. 12:110, 1958) say that on the basis of their data it appears highly likely that inadequate maternal diet, particularly during the early months of pregnancy, as a result of summer heat might result in fetal cerebral anoxia-producing complications of pregnancy that in turn might account for a significant increase inmental deficiency and possibly other constituents of a continuum of reproductive casualities. Preventive measures of adequate dietary supervision and administration appear to be indicated.

Nesbitt and Chow (Obst. & Gynec. Surv. 13:461, 1958) say that normal pregnancy appears to increase the requirements for vitamin B₁₂. As

⁽⁶⁾ Obst. & Gynec. 11:676-679, June, 1958.

yet, pregnancy is the only known method of increasing vitamin B12 absorption in the adult. Despite increased vitamin B12 absorption and decreased excretion, the B12 serum level of the maternal blood is considerably lower than that of nonpregnant women of comparable age and much lower than that of the fetal cord blood. The fetus is the main beneficiary of the increased B12 absorption rate in pregnancy. Because the fetuses draw from the mother during the gestation period and supply their needs in the early months of pregnancy, the maternal B₁₂ serum level decreases progressively throughout the course of pregnancy. This reduction in serum B₁₂ indicates a depletion of B₁₂ reserve. Serum B₁₂ levels may be maintained throughout the course of pregnancy provided the administered dose is large enough. The critical dose would appear to be about 100 µg. although only a small portion of this dose is absorbed. It is reasonable to assume that a mild degree of vitamin B12 deficiency may exist at least toward the end of pregnancy in most patients. Although lowered or depleted stores of vitamin B₁₂ seldom produce clinical manifestations in the mother, it is impossible to predict at present what subtle influence low serum B12 levels of the mother may have on her fetus. Nesbitt and Chow believe that low vitamin B_{12} serum levels in the mother at the time of delivery justify the routine supplementation of the prenatal diet with B_{12} . The B_{12} content in the colostrum and in the milk, which normally decreases after the first several weeks of lactation, can be increased by the oral administration of the vitamins in the mother, particularly in combination with cobalt.

Prystowsky and associates (Am. J. Obst. & Gynec. 77:1, 1959) determined the vitamin B₁₂ level, B₁₂ binding capacity and transaminase content of the serum and the glutathione content of the erythrocytes of fetal and maternal blood and compared the levels obtained with those in a series of nonpregnant subjects. The maternal levels of these substances were lower than those in fetal blood and in nonpregnant women. The only exception was the B₁₂ binding substance, in which the relationship was

reversed.

Chow and associates (ibid. 76:91, 1958) found that the vitamin-mineral preparation containing D-sorbitol is a particularly effective method of administering vitamin B₁₂. Although it is an oral preparation, it is capable of increasing serum B₁₂ levels to an extent comparable to those obtained with intramuscular injections of the vitamin.

Kalter (Pediatrics 23 (pt. 2):222, 1959) says that if lack of riboflavin has such variable and widespread consequences in the four strains of mice which he studied, it can be presumed that the range of possible teratogenic effects of riboflavin deficiency in other strains may be vastly greater than this and the variabilities and differences described for mice can be only a crude approximation of the complexity of the response to a similar situation that is potential in a species so unimaginably heterogeneous genetically as man.—Ed.]

Phosphorus-Free Calcium Supplements in Pregnancy. A test group of 36 women between the 21st and 31st weeks of pregnancy was placed on three 3-week courses of calcium lactate, calcium citrate and calcium carbonate used with varying rotation. Initially and after each 3-week course, ionic calcium and phosphorus and their ratios were calculated.

Jerome J. Hoffman and George Blinick⁷ (Beth Israel Hosp., New York) found that during the 9-week period,

⁽⁷⁾ Obst. & Gynec. 12:694-698, December, 1958.