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EXPERIENCES WITH ACTH AND EOSINOPHIL COUNTS IN NORMAL PREGNANCY AND TOXEMIA*

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WITH the surprising and increasing range of usefulness of ACTH and cortisone it is natural that the effect of these drugs should be investigated in pre-eclampsia. Cases of normal pregnancy, pre-eclampsia, and chronic hypertensive disease with superimposed pre-eclampsia have been treated with ACTH and the results will be recorded here. The recognition of the value of counts of circulating eosinophils, and alterations caused by various agents, as an index of pituitary-adrenocortical function, provides a new tool for the study of normal pregnancy and pre-eclampsia. Observations on eosinophil counts in nonpregnant, normal pregnant, and toxemic women will be recorded.

The adrenal cortex is increased in size in pregnancy. It has long been suspected of playing some role in pre-eclampsia. Extensive changes have been found in the gland after deaths from eclampsia. Selye[1] and others[2, 3] have suggested eclampsia may belong in the group called diseases of adaption. This would be characterized in part by hyperactivity of the pituitary and adrenal cortex. Hofbauer[4] emphasized the importance of a disturbed hormonal balance in the etiology of toxemia, in particular an increased activity of the pituitary, adrenal cortex, and accessory adrenal medullary tissue in the cervical ganglions. Sodium and chloride retention, increased urinary 17-ketosteroids and uric acid excretion, and a supposed pronounced eosinopenia were cited as evidence of activation of the pituitary adrenocorticotropic secretion The positive water and sodium balance of pre-eclampsia points to the adrenal cortex with its important regulatory action.

I. Eosinophil Counts

Eosinophil counts were made as described by Roche[5] and associates with the use of a wet technique with a modification of Randolph's eosinophil stain.[6] A white cell pipette and special counting chamber were used. Counts are expressed in number of cells per cubic millimeter. The average eosinophil count in the peripheral blood is in the order of 150 to 200 with a wide normal range. Coppinger and Goldner[7] found counts in preoperative patients ran from 11 to 718. Rath and associates[8] reported eosinophil counts in pregnancy ranged from 6 to 545. The mean counts by month were from 126 to 167.

Patients tested in this investigation were usually in hospital at bed rest and fasting. The mean counts in 13 nonpregnant control women, 41 women with normal pregnancies, 20 with pre-eclampsia, and 8 women with chronic

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hypertensive disease and superimposed pre-eclampsia are shown in Table I The means in this group, and in all other groups studied here, were analyzed by Student's t test. There was no significant difference in any of this group. There was a greater variability in the pre-eclamptic patients. Fourteen normal and 10 pre-eclamptic postpartum women tested on usually the first or second postpartum day were essentially alike.

TABLE I. EOSINOPHIL COUNTS IN NONPREGNANT, PREGNANT, AND TOXEMIC WOMEN

	NO PATIENTS	MEAN	STANDARD DEVIATION
Nonpregnant control	13	147.1	± 69.0
Normal pregnancy	41	113.1	± 77.0
Pre-eclampsia	20	129.0	±144.0
Pre-eclampsia and chronic hypertension	8	151.9	± 91.9
Postpartum normal	14	125.3	±109.4
Postpartum pre-eclampsia	10	173.9	±168.1

Four-Hour Epinephrine Test.—Under the influence of certain stimuli (stress, operations, labor, epinephrine) the anterior pituitary causes the adrenal cortex to produce more of its hormones. With this adrenocortical activity there appears a significant percentage decrease in circulating eosinophils. In the presence of a deranged or damaged anterior pituitary-adrenocortical system this fall in eosinophils will not occur. Isolated eosinophil counts are of little value because of the wide range in the counts in normal persons; the decrease, or absence of decrease, following attempt to stimulate the adrenal cortex is the important observation. The work of Long and others[9, 10, 11] demonstrated that epinephrine could stimulate an intact pituitary-adrenocortical system and established the value of the four-hour test, counts before stimulation and four hours later, in testing for dysfunction in this system. A fall of greater than 50 per cent is expected in a normal person. By-passing the pituitary, the adrenocorticotropic hormone (ACTH) can be given and in the presence of a normally functioning adrenal cortex the same change in eosinophils occurs.

Twelve nonpregnant, 12 normal pregnant, and 10 pre-eclamptic women were given subcutaneous injections of 0.3 mg. of epinephrine, with eosinophil counts taken before injection and four hours later. The patients were in hospital at bed rest and an interval of over three hours without food preceded the second count. There were no significant differences in the mean percentage changes in the three groups (Table II) Again there was a greater variability in the pre-eclampties. Thirteen normal and 9 pre-eclamptic postpartum patients were tested and there was a diminished response in both classes

TABLE II. EPINEPHRINE FOUR-HOUR TEST

	NO. PATIENTS	MEAN PERCENTAGE CHANGE EOSINOPHILS	STANDARD DEVIATION
Nonpregnant control	12	-54.2%	±18.5
Normal pregnancy	12	-58.2%	±18.6
Pre-eclampsia	10	-56.6%	±36.4
Postpartum normal	13	-20.8%	±59.2
Postpartum pre-eclampsia	9	-37.7%	±29.7

Eclampsia.—It has been reported that eosinophils disappear from the peripheral circulation in eclampsia.[12] One eclamptic patient, incidentally with quintuplets, tested three hours after convulsion, had a level of 213 eosinophils per cubic millimeter. Eighteen hours later it was 481 and a week later it was 131. This patient had no allergic disease. A second eclamptic patient, tested seven hours after a convulsion, was found to have a count of 0; 30 hours after the convulsion it was 75. A third eclamptic patient had a level of 25 when tested twenty-four hours after a convulsion. A fourth was tested 4½ hours after convulsion and the count was 0. Furthermore, 5 women with what would often be termed "severe pre-eclampsia" were tested and no remarkable counts resulted. Two of these women were later tested in labor and showed the reduction in count reported elsewhere, and observed by the author, in normal women in labor.

No unusual counts were noted in cord blood specimens or in the presence of hyperemesis gravidarum, diabetes, or a dead fetus. One pre-eclamptic patient with abruptio showed a near absence of eosinophils, 6, but another woman with the same diagnosis had 63. The result in an epinephrine test on a case of hyperemesis was –79 per cent.

The four-hour ACTH test (25 mg.) was used on 4 pre-eclamptic patients, 1 normal pregnant woman, and 2 postpartum pre-eclamptics. The response was in general subnormal in all groups. This can be explored further when ACTH is cheaper.

II. ACTH

At the time of this writing no reports are available on the use of pituitary adrenocorticotropic hormone (ACTH) in pregnancy or its complications. The use of ACTH seems illogical because of its occasional exhibition of sodium-retaining properties. However, because of its diverse pharmacological and physiological actions and its unanticipated usefulness in many disease syndromes it certainly deserves a trial in pre-eclampsia. If toxemia of late pregnancy is a disease in which hyperactivity of the pituitary-adrenocortical system is a prominent feature, as mentioned earlier in reports, ACTH would be expected to make this complication worse.

The effect of ACTH and cortisone in certain other conditions are of interest. Forsham and associates[13] reported considerable fluid retention when normal patients received 10 mg. of ACTH every six hours for a period of four to six days. In nephrosis ACTH has had a variable effect. Diuresis and water retention have both been observed in different patients during therapy as well as a diuresis following cessation of therapy. Rapid decrease in albuminuria and improved kidney function have been noted.[14] This variability in response is not unexpected as cortical steroids have been known to cause either water retention or loss. The complex picture of adrenal cortex and water metabolism has been thoroughly reviewed by Gaunt and co-workers.[15] ACTH and cortisone have caused both edema and diuresis in arthritics.[16] In glomerulonephritis, cortisone caused water retention, followed by a saline diuresis.[17]

Clinical Trial.—Nine women in the latter weeks of pregnancy were treated with ACTH (Armour). All were hospital patients and generally at bed rest. Intake and output were accurately measured before, during, and for several days after therapy. Weights were recorded at the same time each day. Each patient had a daily fasting blood chemistry performed for glucose, uric acid, and total serum proteins; in some cases chlorides and blood urea nitrogen were also measured. This blood was utilized for a daily eosinophil count. This collection was made one to three hours after the last injection of ACTH. Regular observations of blood pressure were made. There were daily hematocrits and tests for glycosuria. Some patients were on a regular hospital diet

and received no medication. Others were on the toxemia regimen of sedation, ammonium chloride, and low salt diet. All patients received fluids ad lib.

Brief abstracts of case histories in the order in which they were treated follow:

CASE 1.—L. T. Normal primipara. 38 weeks' gestation. 10 mg. ACTH every 6 hours for 7 days. No other medication Regular diet. No evidence water retention Gain ½ pound in the 7 treatment days.

CASE 2.—G. K. Chronic hypertension. Acutely superimposed pre eclampsia at term. Controlled and lost 5 pounds on 2 days of toxemia regimen. Then ACTH 10 mg. every 6 hours added. Loss 4½ pounds in 3 days and went into spontaneous labor.

CASE 3.—D. H. Severe pre-eclampsia at 36 weeks. No improvement on first hospital day. Then ACTH 10 mg. every 6 hours added to toxemia treatment. Albuminuria cleared on third day but blood pressure and edema improved only slightly. Output over 2,000 c.c. every 24 hours. Normal spontaneous labor on seventh hospital day.

CASE 4.—L. W. Normal multipara at 39 weeks. 10 mg. ACTH every 6 hours for 10 days. Loss 6 pounds while receiving ACTH.

CASE 5.—M. B. 37 year-old multipara. Chronic hypertensive disease with acute pre-eclampsia. After 7 days with improvement, ACTH 10 mg. every 6 hours added to toxemia regimen and continued for 9 days. Loss 7 pounds during ACTH therapy and output over 4,000 c.c. each day.

CASE 6.—E L. Chronic hypertension with pre eclampsia. Improved on 2 days' toxemia treatment to which was then added 10 mg. ACTH every 6 hours. In three days of treatment continued to improve losing 4 pounds with an output over 4,000 c.c every 24 hours.

CASE 7.—P. A. Pre-eclampsia. Primipara at 32 weeks. Improved on toxemia regimen. Third hospital day, ACTH 20 mg. every 6 hours and toxemia regimen discontinued. Received 720 mg. over 9 days. Loss only 2 pounds while on ACTH and edema remained unchanged. Output over 4,000 c.c. daily.

CASE 8.—C. P. Pre eclampsia superimposed on chronic hypertensive disease at term. Received 30 mg. ACTH every 6 hours for three doses and went into spontaneous labor.

CASE 9.—G. E. Normal primipara at 39 weeks. 30 mg. ACTH every 6 hours for total 1.04 Gm. on 9 days. No other treatment. Gain 4 pounds. Output usually over 3,000 c.c. each day. No edema. Lost 2 pounds in 2 days after discontinuing treatment.

The pronounced metabolic changes reported by others were not found to occur in pregnant women when treated with ACTH, whether pre-eclampsia was present or not. On doses as small as 10 mg. every 6 hours water retention and a rise in serum uric acid have been reported in normal patients. Blood sugars have been raised and serum proteins have declined More pronounced metabolic shifts and water retention have been noted on dosages of 25 mg. every 6 hours. The smaller doses are effective in many conditions responsive to ACTH, for example, the collagen diseases. This is pointed out as explanation that all patients in this study received ACTH in quantities that are in a usually effective range.

ACTH did not alter the blood uric acid, glucose, or serum protein in any case in the present study. The hematocrits were unchanged. No variations in blood urea nitrogen or chlorides followed Glycosuria did not develop

The reduction in eosinophil counts that others have reported,[13, 18] often to the point of disappearance of these cells from the peripheral blood, did not occur here except in one case (G. E.), the normal patient who received 30 mg. every 6 hours In her case the daily eosinophil count was lowered to 3 to 6 cells per cubic millimeter. In all other cases there was no reduction in eosinophils.

ACTH did not definitely affect, favorably or unfavorably, the clinical course of pre-eclampsia. Patients made the improvement that would usually be expected from bed rest or the toxemia regimen, if used. G. E., the patient who received the greatest amount of the drug, showed mild water retention.

No consistent change in the blood pressure was noted except that in a majority of cases the graded reduction that would be expected from rest in hospital was observed. One patient (D. H.) had an inconsistent slight elevation on the hourly recording that followed administration of the drug.

Two women (M. B. and P. A.) had electrocardiograms before and at the termination of ACTH therapy. There was no evidence of hypopotassemia.

None of the many side effects reported by others occurred. Forsham[15] noted 25 mg. of ACTH caused uterine cramps and 3 women bled who had not menstruated for a year The ACTH may have been a factor in the cases of the 5 women who went into labor while under treatment. At the time, most batches of the drug were reported running 0.02 to 0.04 USP units of oxytocin to 25 mg.

Four of the 9 patients experienced heartburn while receiving ACTH and only then. No other reports of heartburn as a side effect of ACTH therapy have been noted. This reaction should not be surprising in light of the ill effects of ACTH in trials with peptic ulcer[19] and the report of a perforated ulcer during treatment of periarteritis nodosa.[20] The pregnant woman has an inclination to develop heartburn due to the horizontal positioning of the stomach and atonicity of the gut. ACTH in these cases was apparently the extra burden needed to produce this symptom

Comment

The lack of significant differences in eosinophil counts in toxemia and normal pregnancy appears to make this procedure valueless as an indication of the status of pregnant diabetic women as proposed by P. White.[21] The absence of lowered eosinophil counts in toxemia casts some doubt on the presence of increased pituitary adrenocortical stimulation, at least as detectable by this test.

The possibility of pre-eclampsia being a state of depleted adrenal reserve seems ruled out by the normal results found in the four-hour epinephrine test. At the same time it appears that the anterior pituitary has lost none of its power to stimulate the production of corticosteroids. Some of the counts and epinephrine tests were done in the most serious forms of the syndrome. There was no apparent difference in the mild and severe forms. It has been remarked that there was a greater variability in the results in pre-eclampsia. No correlation in clinical course and eosinophil count or the four-hour epinephrine test could be made.

The fact that ACTH failed to produce definite increased water retention in pregnancy and pre-eclampsia, conditions of natural water retention, is particularly interesting. The possibility that pre-eclampsia may be influenced by doses greater than 30 mg. every six hours should be considered. This thought is supported by Thorn's[22] contention that unless a fall in eosinophils follows ACTH therapy no conclusions can be drawn on its therapeutic efficacy. It might be hypothesized that the ACTH administered to these pregnant women depressed the secretion of the pituitary's adrenocortical hormone enough to block expected physiologic reaction.

The failure of response to ACTH may mean that the adrenal gland in pregnancy is already under the stimulation of the patient's endogenous ACTH and not capable of responding to this dose. A concept that the adrenal cortex

is exhausted seems untenable because of the normal response to epinephrine. Daughaday and MacBryde[23] suggested the possibility of an adrenocortical salt hormone that is independent of ACTH.

The lack of water retention following ACTH therapy indicates that excessive adrenocortical stimulation is probably not the cause of positive water balance in pregnancy or pre-eclampsia. Obviously a great deal more study is needed to understand the relationship of the adrenal cortex to pregnancy and toxemia.

Conclusions

There is no significant difference in the number of eosinophils in the peripheral blood of women who are not pregnant, women who have a normal pregnancy, and patients with pre-eclampsia. There is no evidence of altered anterior pituitary-adrenocortical function in pre-eclampsia or normal pregnancy when evaluated by the four-hour epinephrine test. Disappearance of eosinophils from the circulation occurs in eclampsia but is not a constant phenomenon. ACTH in doses which are usually therapeutic has no definite effect on pre-eclampsia or normal pregnancy. The pregnant woman appears peculiarly resistant to ACTH as she fails to show expected physiological changes.

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RUPTURE OF THE MARGINAL SINUS OF THE PLACENTA

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I BELIEVE rupture of the marginal sinus is a lesion that merits further illumination because it is a frequent cause of maternal hemorrhage and, in a sense, is a new complication of pregnancy. I will try to deve' p the two ideas that rupture of the marginal sinus is far from rare and that it has some of the quality of newness.

I know that many have doubts that there actually exists such a thing as a marginal sinus, let alone a rupture of the marginal sinus. It would be naive to think that any skeptic is going to be convinced this morning but possibly disbelievers and the hitherto disinterested will be persuaded to look for rupture of the marginal sinus. My experience has been that if men will look for rupture of the marginal sinus they will find it. The sinus itself has been described so many times in the literature of anatomy I do not feel that I have to defend its existence.

The reasons we can look upon rupture of this marginal sinus as a new lesion are several. I have learned that in some hospitals it is so new the diagnosis has never been made or, apparently, not even considered. From other hospitals I have news that rupture of the marginal sinus has only recently been sought for the first time and found. From the literature I sense that rupture of the marginal sinus is neglected in many places.

To the best of my knowledge, and of our record librarian's, the diagnosis of rupture of the marginal sinus never appeared on the face sheet of a patient's chart at the Charity Hospital in New Orleans until the second half of 1951. Prior to July, 1951, I had never diagnosed a case of rupture of the marginal sinus nor had I ever searched for one. My attention was called in 1951 to this example of morbid parturition by the publication of Fish and his associates.[1] It seemed to me this might be an important lesion that deserved more attention and better understanding. Therefore this study was undertaken.

Where had rupture of the marginal sinus been meanwhile? Or, better put, where had most of us been in relation to rupture of the marginal sinus? Possibly you have asked yourself, or will ask yourself, this question. If I ever heard of rupture of the marginal sinus before 1951 it must have been in a most unreceptive moment.

The diagnosis of rupture of the marginal sinus has not been acknowledged by a listing in the Standard Nomenclature of Diseases. It can be described

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and coded as, "Placental vessels, hemorrhage, cause undetermined" (79 × -Y00.7), or it could be, "rupture or perforation" (Y00.3), or "rupture" (Y00.5).

History

I have not been able yet to piece together a continuous history of this concept of bleeding from a ruptured marginal sinus. Actually, it is far from being a newly recognized complication of pregnancy. It seems merely to have been overlooked for a few recent decades. The earliest article on rupture of this sinus that I have read is well over a century old. Jacquemier in France wrote about it at least as early as 1839.[2] He thought that rupture of a marginal sinus was frequent in normal pregnancy, in premature separation of the placenta, and in placenta previa. Something Jacquemier said is of interest to us today because it describes the experience I am reporting: "While I was at the Maternité, I examined with great care the placentas of almost all of the women who had had a hemorrhage, either during pregnancy or in labor. I have found in some clear proof that the loss of blood came from the circumference of the placenta without this showing signs of earlier detachment."

In Edinburgh both Duncan[3] and Simpson[4] wrote about it in the 1870's. They understood bleeding from the sinus at the placental margin to be one of the major causes of antepartum hemorrhage. From Paris in 1893 Budin[5] provided drawings that depict exactly what I am talking about this morning. The prominence and the number of the corroborators that these men mention suggest that bleeding from the marginal sinus was a widely used diagnosis.

What has happened to rupture of the marginal sinus in the intervening years I can only guess. Possibly the men whose textbooks and schools dominated American obstetrics in the first half of this century slighted it because they were more intrigued by abruptio and placenta previa. Some of our textbooks and the current literature convey the idea that the two most common causes of bleeding in the last trimester or semester of pregnancy are placenta previa and abruptio. We can have reason to suspect that this is entirely wrong. They may be the most important because they are the most dangerous, but I do not think they are the most frequent. A solid argument can be built for the claim that there are more common varieties of bleeding in this part of pregnancy and one of them is rupture of the marginal sinus. There is also a substantial group in which the cause of bleeding is never accurately identified

Anatomy of the Marginal Sinus

The marginal sinus of the placenta is a system of veinlike channels of great delicacy and thinness. These sinuses lie in the decidual tissue at the edge of the placenta and they discontinuously encircle the placenta. The name "circular sinus" has also been used The lengths and diameters of the sinuses vary The caliber is in the order of 2 to 5 mm. I have seen a sinus filled or, better perhaps, ruptured, and replaced by a finger of clotted blood that measured 2 cm in diameter.

With experience you can identify the marginal sinus rapidly by incising into the placenta's margin. Perforations into the sinuses can be disclosed by peeling back the membranes at their placental attachment and wiping clean the edge of the placenta. I know that many have looked for the marginal sinus and have been disappointed. Some were mistakenly seeking an unbroken, uniform vessel that made a circle around the placenta. Actually the sinuses have no obvious intercommunications as viewed under the conditions imposed upon us, i.e., inspection of the maternal surface of the placenta, out of the

uterus and in our hands. Another reason for failure to recognize the marginal sinus is that when the fresh specimen is held in the hands with the maternal surface uppermost, the blood, still liquid, escapes from the sinuses, if it has not already done so; the walls of the sinuses collapse and their flaccidity makes it difficult to identify them. Parts of the marginal sinus may be left behind in the decidua at the time of the placental separation.

For class demonstration of the marginal sinus take two or three normal placentas and let them lie overnight in a refrigerator, not a freezer. Blood in the marginal sinuses at first is liquid and will remain in that state for some time. The next day, in the portions where the blood has not drained away, the sinus cavities can be identified by the casts of coagulated blood they contain.

These sinuses contain venous maternal blood and are part of the placental-uterine plexus that forms the maternal blood-collecting system. From these sinuses the blood passes to other decidual vessels, to the uterine veins, and hence into the mother's general circulation. Recent experimental work has confirmed that the blood in the marginal sinus is maternal blood.[6] In 1873 Turner,[7] in an exposition on the circulation of maternal blood in the placenta, could cite a formidable list of corroborators. He named the circular sinus as part of that circulatory system.

Observations at the Charity Hospital

My own attempt to learn something about rupture of the marginal sinus covers three periods and two slightly different approaches. The first portion of these observations began July 1, 1951, with the collection and examination of as large a number of placentas as possible from the women with antepartum hemorrhage on the obstetric unit of the Tulane Service of the Charity Hospital at New Orleans. The study continued for one year and by a wide margin lacked being a continuous series of cases. In that fiscal year there were 4,103 deliveries on the Tulane Service. I identified 16 cases of hemorrhage as being due to rupture of the marginal sinus. These cases will be combined with others in my description of the syndrome.

In the first and third quarters of this year (1954) we were successful in gathering and categorizing by cause of bleeding the placentas from every case with antepartum bleeding on the Tulane Obstetric Service at the same hospital. Because there were 2,251 deliveries in those 6 months we can get some notion as to the frequency of the various causes of bleeding. The use of this number of patients might introduce some sampling errors so I do not claim that my incidences are any more than notions. I think they do hint that rupture of the marginal sinus is something big enough for us to give more thought to it.

During the intervals between the studies the diagnosis of rupture of the marginal sinus was made a number of times by the residents. These cases are not available for inclusion in this report.

I made my criteria for the diagnosis rather severe to encourage objectivity and to avoid errors inherent in any effort to find a place for a new or neglected subject. The sine qua non for diagnosis was the immediate postpartum exhibition at the margin of the placenta of a clot that was continuous with clotted blood in the marginal sinus. This is a stringent requirement and certainly some cases were discarded into the group in which no diagnosis could be made because the clot at the placental margin was dislodged in passage through the cervix, vagina, and the obstetrician's hands. The clot at the margin is usually not large and does not give the impression that it has interposed itself between

the placenta and the uterus. I would guess that the clot at the margin averages between 50 and 100 c.c. The clotted blood in the sinus is not difficult to find because this cylinder of blood is usually thick, appearing to burst from its confines. Conceivably there are cases in which the blood did not clot and which therefore are not included.

Table I shows the causes of bleeding in the 97 cases of uterine antepartum bleeding on the Tulane Obstetric Service of Charity Hospital in the first and third quarters of 1954. There were 2,251 women delivered on the unit in those six months. In that period there were 33 cases of rupture of the marginal sinus, a ratio of one to 68 cases. There were only 6 cases of placenta previa and 13 cases of abruptio. The cause of bleeding could not be positively determined in 30 cases. Cervicitis, low-lying placenta, and a circumvallate placenta were less frequent causes of bleeding.

TABLE I. CAUSES OF HEMORRHAGE, 97 CASES IN 2,251 DELIVERIES

Rupture of the marginal sinus	33 cases
Cause undetermined	30 cases
Abruptio	13 cases
Cervicitis	10 cases
Placenta previa	6 cases
Low-lying placenta	4 cases
Circumvallate placenta	1 case

I should define the qualifications that were needed for a case to be considered one of antepartum hemorrhage. Rather than base it on an estimation of the amount of blood seen, on which two persons rarely agree, I have included all cases in which there was enough blood loss that the patient's blood was typed and cross-matched, the facilities for cesarean section alerted, and then a vaginal examination performed. The qualification of preparedness for operation eliminates several cases of abortion, one of them a missed abortion. A case of bleeding from condylomas in the vagina is also excluded

In each case of rupture of the marginal sinus the diagnosis of placenta previa had been ruled out by failure to palpate a placenta on vaginal examination. Abruptio was dismissed as a diagnosis when neither the placenta nor the clinical picture was considered diagnostic by the staff.

These inflexible criteria serve to prevent rupture of the marginal sinus at this time from being a diagnosis of exclusion or elimination. Such a diagnosis would be a bad start for our comprehension of a lesion that may be entering a renaissance.

Rupture of the Marginal Sinus

When you pick up the placentas and handle them to become better acquainted with the marginal sinus you will see that its delicacy and peripheral position make it vulnerable. It is easy to imagine that with the changes that went on directly under it there could have been a disturbance, a tearing, that permitted blood to escape The changes in the uterus that could effect this were the uterine contractions, formation of the lower uterine segment, effacement, and dilatation With slight traction on the membranes you can tear open some sinuses. This can be visualized in the photograph, Fig. 1. There is a possibility that inside the uterus the fetal surfaces make a traction in the direction of the cervical os. To these changes and stresses it appears that the edge of the placenta that is closest to the cervical os would be the most exposed and some data that support this conjecture will be presented

Because that which transpired does so under cover, we will for the time being have to assume that blood escapes from the marginal sinus, dissects

between the membranes and the uterus, and makes its way to the cervix. I think that we have collected enough indirect evidence that just that happens. It is not taking any more liberties with our imagination than we do with abruptio. We have seen the end results of abruptio but exactly how it transpired is a surmise. In some specimens I have seen a track the blood made on the chorion as it made its way from the sinus rupture to the opening in the membranes (and the cervical os).

The 49 cases of rupture of the marginal sinus that I have collected hardly give me the temerity at this date to state what the clinical picture of the syndrome is. Not many cases have been analyzed in the literature. There has been only one larger series of cases than mine and that contained but one more case. As I relate a description of my patients and what happened to them I unfortunately see no clues to a predelivery diagnosis of rupture of the marginal sinus. There were no trends discernible in the age or race of the patients. When more cases are collected this may turn out to be a complication of multiparity. Only 8 of the patients were pregnant for the first time and 37 per cent had been pregnant five or more times. The median length of gestation for these cases was 36 weeks. All except 5 women were delivered within two days of the onset of bleeding, so recurrent hemorrhage may not be a prominent feature.

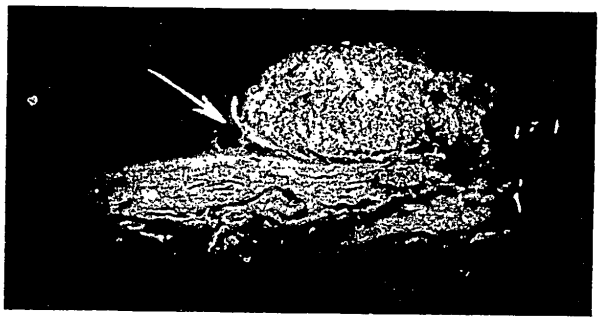

FIG. 1. Uterus with placenta in situ, showing marginal sinus. Eighth month of pregnancy. (Courtesy Dr. Harold Cummins, Department of Anatomy, Tulane University.)

Only 7, or 14 per cent, of these women with rupture of the marginal sinus had toxemia. On the same service it has recently been tabulated that in a period of one year 19 per cent of the patients had hypertensive albuminuric disorders of pregnancy. Thus at present it does not appear that rupture of the marginal sinus will be an added burden for toxemic women.

In all cases the bleeding was painless. Increase in uterine tone and tenderness to abdominal palpation were never demonstrated but it does not seem to be beyond the realm of possibility that a collection of clotted blood at a placental margin and between the membranes and the uterus will at some time cause pain. If someone starts putting leading questions to these patients we will presently have recorded that some of these patients have pain or tenderness. This type of history taking has often led to a diagnosis of abruptio where no abruptio existed.

In relation to labor, the bleeding appears to be anything but a late occurrence. In 31 of these 49 cases the bleeding began either shortly before labor, at the onset of labor, or early in the first stage of labor. Bleeding began in the second stage of labor in only 5 cases.

The form in which the blood appeared was in all the forms that blood can take. Bright red bleeding predominated. Clots and dark red blood were also recorded. Blood in different physical forms was often seen in the same patient.

No patient showed general signs of acute blood loss. In 5 instances it was believed the patient had lost over 500 c.c. In only 9 of the 49 women was the estimated blood loss less than 100 c.c.

The effect of rupture of the membranes is of interest in every type of last-trimester bleeding. I cannot say whether artificial rupture of the membranes will dependably control this bleeding because it has not been tried often enough. In 8 cases the membranes were already ruptured when the bleeding began. The height of the placenta in the uterus would seem to make tamponade less likely than in marginal placenta previa.

Rupture of the marginal sinus gives promise of being less hazardous for the fetus than abruptio and placenta previa. This should not be surprising because the blood that is lost is maternal blood, characteristically is not great in quantity, and would not profoundly disturb the placentouterine union. One of my babies was a 26-week stillborn but the others did not give a distinct impression that as a group they were handicapped by the rupture of the marginal sinus. I have data only on the immediate postnatal state of the babies.

Thirty-six per cent of the babies in my series were premature by weight (2,500 grams or less). As the premature rate at the Charity Hospital is about 14 per cent there may be a significant relationship between rupture of the marginal sinus and premature birth.

I have no indication that any other pathologic condition occurs with any frequency in association with rupture of the marginal sinus. There have been no cases of hypofibrinogenemia. The third stage of labor appeared unaffected At another state charity hospital two of our residents operated on a woman because of a diagnosis of abruptio. Later they decided that the true diagnosis was rupture of the marginal sinus. Fifty per cent of the surface of the uterus had the discoloration typical of Couvelaire uterus.

From the data I have, let me construct a picture of the hypothetical, typical patient who has rupture of the marginal sinus. She is a multipara and not yet at term. She may be of any race or age. Painless bleeding began close to the time she thought she went into labor. The amount of bleeding was not life-threatening When I did a vaginal examination I learned that she was in the first stage of labor, the membranes were intact, and the placenta could not be palpated. It did not seem to be a case of abruptio but to play it safely I ruptured the membranes to hasten labor. Labor proceeded at a normal pace and there was enough bleeding to be a little worrisome. The infant to my relief did not appear to be affected by the hemorrhage. I delivered the placenta carefully in order not to dislodge the clots. I examined the placenta immediately and on the placental margin, at the side nearest the rent in the membranes, I found an elongated clot. This clot was attached to clotted blood in the marginal sinus.

Bleeding of Undetermined Origin

In the table listing the causes of bleeding in a six-month period you may have been surprised to see there were 30 cases in which the cause of bleeding was unknown In the 1951-1952 series there were 30 such cases documented

and, I am sure, many more undocumented. A digression may be in order for a moment on this subject, which is really not remote from our attempt to establish a place for rupture of the marginal sinus. I believe that bleeding of undetermined origin is a comparatively frequent occurrence and that it does not happen only at the Charity Hospital. It is an event that goes unnoted, unremembered, unrecorded in the literature, and unmentioned in the next day's doctors' dressing room conversation because of a failure to provide a dramatic quality.

When I read reports on the incidence and management of bleeding in the last trimester I am surprised that in so many papers all of the cases are neatly packaged into the various diagnoses. They are either able to make a diagnosis in each bleeding case or are omitting cases in which the diagnosis was uncertain. In some, if they have rupture of the marginal sinus, these cases are being diagnosed as something else or are among the cases unmentioned. I suspect many cases of rupture of the marginal sinus are being labeled abruptio, low-lying placenta, or placenta previa.

This classification of bleeding of undetermined origin is slighted in many reports because this diagnosis does not get on the face sheet, the first sheet, of the patient's chart and is therefore uncoded. There is a code for this diagnosis. This bleeding did not finally threaten the mother's life and did not kill the baby so when the time came in the record library to write the diagnosis it was forgotten. In my personal experience as a laborer in record libraries I learned that when a woman had bled at the end of her pregnancy and no placenta had been found over the cervical os by vaginal examination or at cesarean section the case was often called an abruptio, possibly a "mild" abruptio. In some medical communities "low implantation" may be popular. Contributing to this spurious extinction of the diagnosis of bleeding of undetermined origin is the feeling that such a diagnosis is an admission of professional ineptitude.

Comment

Could it be possible that the placenta with the rupture of the marginal sinus is the placenta with one edge not sufficiently low on the uterine wall to qualify for marginal placenta or low implantation yet is low enough to have its marginal sinus torn by the actions of the uterus in labor or in the preparation for labor? Some observations I have made tend to substantiate this. The location of the laceration in the membranes often suggests that the placental margin was not far away from the cervix. Also, if you will carefully examine any placenta and its membranes, taking care not to extend the rent in the membranes, you will see that this rent is usually not in the apex of the sac but is eccentric. This year in 18 cases of rupture of the marginal sinus we noted the relationship between the sinus rupture site and the tear in the membranes. In 2 of the sacs the rent was exactly at the apex but in all of the remaining 16 specimens the sinus rupture and the rent in the sac were on the same side. This observation seems to strengthen the concept of bleeding from the marginal sinus.

During these months of investigation into the marginal sinus 2 normal deliveries have occurred in which the placenta, examined immediately after delivery, had a large clot at its margin and that clot was connected to clotted blood in the marginal sinus. But there had been no bleeding at any time! In

other words it was the exact picture of rupture of the marginal sinus without the external bleeding. At first this was rather disconcerting but have we not always had cases of concealed hemorrhage in abruptio? So why not in rupture of the marginal sinus? A number of reasons could be postulated why the blood did not pry between the membranes and the uterus to the cervical os: e.g., all of the blood promptly clotted, the blood lacked pressure, the membranes were too adhesive, the distance from the placental margin to the cervix was too great, or there was not enough time. To learn if this symptomless variety of rupture of the marginal sinus was frequent 47 placentas, taken completely at random, were examined closely for evidence of this lesion and none was found.

It is natural that we should think of bleeding from the marginal sinus in terms of abruptio, placenta previa, and low implantation of the placenta because they are the conditions from which it will have to be distinguished. Jacquemier in 1839 pointedly warned against thinking that separation of the placenta had taken place when it was only a rupture of the circular sinus. A certain amount of blending of one of these placental complications into the other may be inevitable.

Abruptio at times has been a diagnosis to which cases have been assigned without sufficient justification. Abuse of the diagnosis of either abruptio or rupture of the marginal sinus can be avoided by strict adherence to definitions. As we collect more and more information about rupture of the marginal sinus and it attains the secure place in our teaching and practices that it deserves, what are we going to think about studies of abruptio that originate in institutions where the diagnosis of rupture of the marginal sinus is not made? We are going to think that some of the abruptions were ruptures of the marginal sinus! When groups of cases of abruptio are reported and the cases classified by the gravity of the condition of the mother, a large number, sometimes over 50 per cent, may be listed as "mild." Might not some of these be ruptures of the marginal sinuses? The practical importance of this is that, when we subtract these "mild" cases, abruptio becomes a more serious condition and possibly the indication for radical management is augmented.

We have been thinking of abruptio in terms of reports in the journals and in our own experience; in both of these backgrounds the cases of abruptio were diluted with cases of rupture of the marginal sinus. Because of the grave potentialities of abruptio it is important for us to learn more about rupture of the marginal sinus, separate it from abruptio, and reappraise abruptio in the light of our new information.

Is it possible that some cases of abruptio begin with rupture of the marginal sinus? The easiest way out for the blood would seem to be toward the cervical os, drawn there by gravity, a point of lower resistance, and the myometrial activity. Is it possible that when rupture of the marginal sinus occurs in some selected women, for example toxemic women, the blood might dissect under the placenta instead of between the membranes and the uterus? Could a placenta that is altered, for example the placentas of toxemic women, be one in which it would be easier for the blood to go under the placenta than else-

where? Infarcted placentas may not be as firmly attached as others and thus may permit blood to get under them. Only 6 placentas of abruptio have been closely examined for details of the marginal sinus and rents in the membranes. For 3 of them it was simply recorded that there were clots in some portion of the marginal sinus. In 3 more recent cases the clots in the marginal sinus were on the same side as the rent in the membranes. These few observations serve as nothing more than a stimulus to search further for a possible connection between abruptio and rupture of the marginal sinus.

The abnormally implanted placenta has a sinus that could be very easily torn by the changing shape of the cervix. There is really nothing new about this idea. It was all told in the last century. Jacquemier recognized the possibility. Seventy-five years ago Duncan described bleeding from the marginal sinus in a marginal placenta previa without detachment of the placenta. As the marginal sinus is only a part of the uteroplacental sinus network that bleeds in placenta previa this should not be difficult for us to accept. I have seen placentas from cases of marginal placenta previa that were indistinguishable from the placentas of rupture of the marginal sinus.

Summary

Rupture of the marginal sinus is found to be the most common cause of antepartum bleeding during a six-month period that included 2,251 deliveries. The next largest number of cases of hemorrhage was in a group in which the cause could not be determined. Abruptio and placenta previa were less frequent causes of hemorrhage. The anatomy of the marginal sinus and some characteristics of its rupture are described. Many cases of rupture of the marginal sinus have been misdiagnosed as abruptio, there is a need to differentiate these two conditions.

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Discussion

DR. W C. KEETTEL, Iowa City, Iowa.—There have been many excellent papers written concerning placenta previa and premature separation of the placenta; unexplained antepartum bleeding, however, although very common, has received little attention until recently. This increased interest in placental pathology directed toward ascertaining the cause of such bleeding is gratifying.

In the past the existence of the marginal sinus had been questioned, though now the majority recognize the sinus as an anatomical entity. Most agree that this sinus occasionally ruptures during pregnancy, producing varying amounts of vaginal bleeding

The confusing issue then is whether marginal sinus rupture is to be considered as a new and distinct clinical entity, or should it be included as an occasional causative factor in the bleeding of the placenta previa and premature separation of the placenta. The essayist, along with Fish, feels that one can clearly distinguish between rupture of the marginal sinus and premature separation of the placenta. The criteria being: (1) the presence of a clot at the margin of the placenta that is continuous with clotted blood in the sinus, and (2) painless bleeding at term. They mention that at times the bleeding of placenta previa and premature separation may be caused by marginal sinus rupture.

It is hard for me to see how bleeding at the margin of the placenta, particularly where there is an adherent clot that may depress some of the marginal placental tissue, is materially different except in location from premature separation of the placenta. Where the membranes are dissected away from the decidua by blood because this is the path of least resistance, is this not really premature separation of the membranes and a form of placental separation?

Two years ago before this Society, Dr. Paalman discussed circumvallate placenta and pointed out how frequently antepartum bleeding was encountered. He and others have maintained that the bleeding with this type of placenta is due to the fragility of the decidual covering of the marginal sinus. I wonder what Dr. Ferguson's experience has been concerning this point?

In our clinic and in others the diagnosis of premature separation of the placenta includes both the toxic and nontoxic type of separation. The diagnosis of the mild type of separation must not be construed as a "waste basket" diagnosis as the author mentioned. Naturally, with this broader concept, minor degrees of separation are recognized, and on occasion even though the bleeding is painless and the uterus is nontender, if the placenta shows significant signs of separation, they are included. Is it less exact to state that the bleeding is from placental separation which at times is due to sinus rupture than to state that marginal sinus rupture is a distint clinical entity?

Sexton, Hertig, Reid, and Harris have written concerning this problem and have felt that the rupture of the marginal sinus should be included as one of the causes of nontoxic placental separation. To me this seems more logical and will lead to far less confusion. The treatment by necessity must be the same as that employed in the management of mild nontoxic separation, since the diagnosis cannot be made until after the delivery of the placenta.

This presentation has been well organized and presented and I have enjoyed reading it The paper emphasizes the following points. (1) There are many causes of antepartum bleeding (2) The treatment of antepartum bleeding must be individualized according to the cause. (3) Abdominal delivery should never be resorted to for the treatment of undiagnosed antepartum bleeding (4) Significant bleeding from the marginal sinus does occur.

TOXEMIA OF PREGNANCY AT THE CHARITY HOSPITAL IN NEW ORLEANS

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MANY NEW ORLEANIANS have been asked, "What is toxemia of pregnancy like at the Charity Hospital? You have more deliveries than any other hospital in the United States and you are reputed to have so much toxemia. How much do you really have? Is toxemia frequent because you have such a large Negro population? Do many of these women have chronic hypertensive disease? Is the fetal loss from toxemia high? How many of these patients do you section?"

The present article attempts to define the problem of toxemia of pregnancy at the Charity Hospital and to answer the above questions. To accomplish this the authors personally reviewed the hospital records of all of the women who were delivered on the Tulane Service of the Charity Hospital in 1 calendar year, 1950. With the use of rigid definitions, we selected the patients who had toxemia and grouped them according to their type of toxemia. The hospital records of the babies born to these mothers were also examined. A number of important data on the course of pregnancy and fetal outcome were collected and analyzed. This afforded an opportunity to compare our experience with that of other hospitals, to evaluate our treatment and to provide base lines for current and contemplated research.

The investigation was started in early 1952, and the year 1950 was selected for no other reason than that it was the most recently completed calendar year which allowed sufficient time to assume that hypertension would persist indefinitely. There is no reason to doubt that 1950 is a representative year.

The patients studied in this report constitute a fair sample of the hospital's patients. The Tulane Service gives maternity care to approximately 40 per cent of the patients delivered in the hospital, and there is no bias in the selection of patients for the 3 services of the hospital.

In 1950 the number of mothers who were delivered on the Tulane Service was 3,899. The hospital records of 4 mothers and of 4 babies of toxemic mothers, all unrelated, could not be found. We verified that these 4

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Huldah Bancroft, Ph.D., Professor of Biostatics, Tulane University, aided in designing and interpreting this survey.

mothers were discharged alive from the hospital.

A 1 year record may introduce some sampling error and where this is possible, restraint will have to be used in drawing conclusions. For example, the incidence and outcome of comparatively unusual cases, like abruptio placenta, may be awry in a period of 1 year. However, a 1 year sample would be sufficient to make valid conclusions on the frequency of the various types of toxemia, perinatal mortality, antepartum care, age, parity, residence, and birth weights.

BACKGROUND OF THE PATIENTS

The patients cared for at the Charity Hospital in New Orleans are drawn from the poorer people of the State of Louisiana. Financial eligibility for admission is determined on an individual basis. Couples with an expected child or 1 child must not have an income in excess of 175 dollars a month.

In 1950, 82 per cent of all the women delivered on the Tulane Service were Negroes. Approximately 65 per cent of the births at the hospital were to mothers from New Orleans, the remainder coming from other parts of the state. The percentages of white and Negro toxemic women with residence outside of New Orleans were 53 per cent and 45 per cent, respectively. These figures may indicate that there is no decided tendency for women of a particular race to come to the Charity Hospital from outside of New Orleans because of this complication.

The diets of the women attending our antepartum clinics have been found by Ferguson and Hinson to be about the poorest recorded in the United States (13, 16). Only 4 per cent of 209 women were eating the recommended daily allowance of 85 grams of protein. In a random sampling of 24 hour food consumption, 45 per cent of the women had had no milk, 31 per cent no meat, 66 per cent no egg, and 28 per cent no vegetable or fruit.

Attendance at clinic is not good. Nineteen per cent of the toxemic women described in this article had no antepartum care and 20 per cent made only 1 to 4 antepartum visits. Thirty-three per cent of the toxemic mothers did not return for a postpartum visit.

CLASSIFICATION OF TOXEMIA

In this report the terms "toxemia of pregnancy," "toxemia," and "toxemic" will have their broadest connotation, embracing all of the hypertensive and albuminuric disorders of pregnancy. "Pre-eclampsia" and "pre-eclamptic" will be used only in the sense defined later. Each case of toxemia is assigned to one of the following subgroups: (1) pre-eclampsia; (2) eclampsia; (3) chronic hypertensive disease; (4) chronic hypertensive disease with superimposed pre-eclampsia; (5) unclassified.

The reported incidence of toxemia in a hospital depends on who writes the diagnosis on the face sheet of the hospital chart and what he uses as criteria of diagnosis. For this study the following definitions were uniformly used by the authors for the evaluation of each patient's chart and for the determination of the diagnosis. The definitions were patterned after those in the Williams-Eastman textbook because it was used by the Tulane medical students. The classification adopted in 1952 by the subcommittee of the American Committee on Maternal Welfare was not available when we started this study.

DEFINITIONS

Hypertension. Hypertension is the observation of a systolic blood pressure of 140 millimeters of mercury or above, or a diastolic blood pressure of 90 millimeters of mercury or above. The elevation must be found on at least 2 occasions 24 or more hours apart.

Albuminuria. A patient has albuminuria when there is a definite positive test for protein with a catheter specimen of urine that is devoid of pus and blood.

Pre-eclampsia. Pre-eclampsia is defined as hypertension or albuminuria that develops after the twenty-fourth week of pregnancy and disappears after delivery.

TABLE 1.—TOXEMIA OF PREGNANCY AT CHARITY HOSPITAL OF LOUISIANA IN NEW ORLEANS, TULANE SERVICE, 1950

Diagnosis	No. of cases	Incidence on service Per cent	Per cent of toxemic patients	Live births	Stillbirths No.	Stillbirths Per cent	Neonatal deaths	Prematures (live)
Toxemia (all cases)	736	19	—	709	49	6.5	21	109
Pre-eclampsia	349	9	47.4	349	13	3.6	4	34
Eclampsia	10	0.3	1.4	13	1	—	5	8
Chronic hypertensive disease	180	4.6	24.2	167	19	10.6	5	30
Chronic hypertensive disease with superimposed pre-eclampsia	167	4.3	22.7	158	14	6.4	3	29
Unclassified	30	0.8	4.1	28	2	—	1	8

Chronic hypertensive disease. Patients with chronic hypertensive disease are those in whom hypertension appears before the twenty-fourth week of gestation and persists indefinitely after delivery.

Chronic hypertensive disease with superimposed pre-eclampsia. Patients with chronic hypertensive disease who have superimposed pre-eclampsia are those who develop further elevation of systolic blood pressure of 30 or more millimeters of mercury, further elevation of the diastolic pressure of 15 or more millimeters of mercury, or albuminuria.

Difficulties of classification. Many unquestionable cases of toxemia were difficult to classify because of an insufficient number of observations on the patients. This was usually due to the patients' laxity in participating in antepartum care and in returning for the postpartum visit. Women referred to the hospital were often not accompanied by a case record. Even when the patients' records furnished what should have been sufficient data, classification was sometimes difficult because the cases did not fit well into the classification used here (nor the classification formulated by the American Committee on Maternal Welfare). Perplexing hypertension ensembles which recurred with some regularity were: (a) hypertension that began after the twenty-fourth week of pregnancy and persisted indefinitely, (b) hypertension in several pregnancies, and blood pressure normal in the 1950 pregnancy until the end of pregnancy, when hypertension reappeared, (c) hypertension that appeared late in two or more pregnancies and late in the 1950 pregnancy but was inconsistently found in the intervals between pregnancies, (d) hypertension at the postpartum visit and only then, (Meyer has described the local experience with this phenomenon and Kaltreider and Gilbert the experience elsewhere), (e) hypertension that began before the twenty-fourth week of pregnancy and was not present at the postpartum visit or in a subsequent pregnancy, (f) hypertension in 2, 3, or more pregnancies and at postpartum visits, but did not appear in the 1950 pregnancy. (a), (b), and (c) are considered in this report to have chronic hypertensive disease. So frequently was it difficult to decide which were chronic hypertensive diseases and which was pre-eclampsia that we were tempted to suggest that they were not two diseases but one.

Albuminuria in labor. There was no attempt made to separate cases in which albuminuria was found only during labor from those in which it was discovered at other times. Ideally this should be done. The observation that labor can cause transient albuminuria without other evidence of toxemia has been made variously. Winnifred Seegars examined catheter specimens of 50 nontoxic women in labor at the Sara Mayo Hospital, New Orleans, and found that 16 gave a positive test for protein. Douglas remarked that at the New York Lying-in Hospital protein was observed in the urine of the majority of normal women at the time of delivery.

INCIDENCE OF TOXEMIA

Seven hundred and thirty-six mothers on the Tulane Obstetric Service had toxemia of pregnancy in 1950. This is an incidence of

19 per cent. A separation of these cases into the various subgroups of toxemia is given in Table I and the subgroups are individually considered later in this paper. There was 1 maternal death.

It is impossible to compare accurately our incidence of toxemia with those of other hospitals because of the differences in definitions and methods of reporting. Comparisons of the frequency of toxemia in the local populations are even less reliable because of dissimilarities in the service that each reporting hospital performs in its community, the differing eligibility of patients for hospital admittance, varying regional dependence as a referral point for seriously ill patients, and other selective factors that would not be recognized by the casual reader. These shortcomings should be kept in mind as we examine the frequency with which some hospitals have recently been seeing toxemia. By any standard the Charity Hospital patients have a good deal of toxemia. The figure of 25.2 per cent for nonconvulsive toxemia at the "University of Tennessee-Gaston, 1946–1949" (given by Dieckmann) is the only higher incidence we can find. Wellen (28) reported an incidence of 5.17 per cent of hypertensive conditions in pregnancy at the Bellevue Hospital in a 15 year period ending in 1950. Lundgren reported that the incidence of toxemia in 1950 at the Margaret Hague Maternity Hospital was 11.9 per cent. From the ward service of the Sloane Hospital for Women, 1931 to 1950, the toxemia rate was 12.2 per cent. In 1947 to 1949, 3.1 per cent of the parturients were toxic at the Royal Victoria Montreal Maternity Hospital.

The high rate of toxemia at the Charity Hospital is probably not because of its large colored census. In 1950, 18 per cent of the women delivered on the Tulane Service were of the white race and 17 per cent of the toxemic mothers were white. The proportion of the women in the pre-eclampsia-eclampsia groups that were white was 21 per cent; 12 per cent of the chronic hypertensive women were white.

This investigation provided a unique opportunity to measure the incidence of toxemia, and each of its components, in a population. In 1950, 89 per cent of all the Negro babies born in New Orleans to mothers with residences in New Orleans were born at the Charity Hospital. This is a relatively high proportion of all the Negro babies born in New Orleans. It has previously been stated that the mothers on the Tulane Service are an unbiased sample of the mothers delivered at the hospital and should be considered adequate for the estimation of the frequency of toxemia in the Negro population. The residence and race of each mother were recorded in this survey and from these data it is estimated that approximately 19 per cent of the New Orleans Negro mothers must have toxemia.

PRE-ECLAMPSIA

The number of mothers who had pre-eclampsia was 349. They represented 9 per cent of the entire service and 47 per cent of the toxemic patients. Forty-seven per cent of these pre-eclamptics were primigravidas and 32 per cent were 19 years old or younger. The incidence of pre-eclampsia among all the Negro women on the service was 8.6 per cent.

This incidence of pre-eclampsia would have been much higher if, instead of the requirement that hypertension be observed on 2 occasions 24 or more hours apart, we had used the American Committee on Maternal Welfare's classification, which utilizes a 6 hour interval. If that committee's criteria of edema and weight gain had been used to diagnose pre-eclampsia, a very much greater number of women would have to be considered pre-eclamptic. Our insistence that albuminuria be claimed only on a catheter specimen devoid of pus and blood reduced the number of patients diagnosed as pre-eclamptic. The diagnosis was based on albuminuria alone in 5 cases.

To make certain that our collection of pre-eclamptics was not heavily weighted with women who had minor hypertension

those women who had minimal blood pressure elevation were sorted. There were 61 women, 17 per cent of all the pre-eclamptics, whose systolic blood pressure was always recorded as below 146 millimeters of mercury and whose diastolic blood pressure was always below 96 millimeters of mercury. These women had no perinatal fetal deaths. Some of our eclampsia appears in women with these false security engendering levels of hypertension; we will have to continue treating with vigor these "mild" cases.

When we compared the monthly incidences of pre-eclampsia in 1950 we saw no seasonal trend except for an unremarkable tendency to be more frequent in January through May. The monthly rate ranged from a low of 4.3 per cent in November (the month in which most eclampsia appeared!) to 12.2 per cent in March.

"Severe" pre-eclampsia is frequently defined as pre-eclampsia marked by a systolic blood pressure of 160 millimeters of mercury or over, or a diastolic blood pressure of 110 millimeters of mercury or over. The same definition will be used in this essay. One hundred and seventy-three women, which was 50 per cent of our pre-eclamptics, qualified for this category. They provided 10 of the 13 stillborn babies that the pre-eclamptic women had.

It has been said that modern antepartum care has not reduced the frequency of pre-eclampsia but it has curbed severe pre-eclampsia and eclampsia. This has also been our impression. Wellen claimed that at the Bellevue Hospital antepartum care did not influence the incidence of severe pre-eclampsia (27). For each toxemic woman in this Charity Hospital study, the week she began antepartum care and the number of her visits were recorded. Similar data are not available from any large group of normal patients at this hospital for comparison. An attempt was made with this information to show that early institution of antepartum care and a greater number of visits increased the likelihood of the mild form of this complication rather than the severe form. The week in which antepartum care began was plotted against the number of visits and many comparisons made between the patients with mild pre-eclampsia and those with severe pre-eclampsia. As far as these data could demonstrate there were no differences between the mild and the severe pre-eclamptics that were statistically significant. Because of the numerous variables involved we do not believe that these observations disprove that good antepartum care prevents severe pre-eclampsia.

Seventy-six of the women with pre-eclampsia were hospitalized before labor for a total of 410 hospital days, an average of 5.4 days per hospitalized pre-eclamptic patient.

Fifteen of the pre-eclamptic women (4 per cent) were delivered by cesarean section, only 4 of those because of the pre-eclampsia.

These pre-eclamptic mothers had only 13 stillbirths (3.6 per cent) and 4 babies that expired in the neonatal period. This is a perinatal death rate of 4.8 per cent, or 49 per thousand live births.

In 1950 our management of pre-eclampsia and other forms of toxemia was generally conservative. The low section rate speaks for itself. Immediate hospitalization on the appearance of pre-eclampsia was desired but was an ideal frequently unattained. In the hospital bedrest and sedation were the mainstays of therapy; phenobarbital was the drug used most often, while morphine or meperidine were used when greater sedation was indicated. Ammonium chloride and 10 per cent dextrose infusions were close to routine measures. Mercurial diuretics were used infrequently then and on an experimental basis. Hypotensor drugs were untried.

The choice of induction of labor was influenced by response to treatment, severity of the pre-eclampsia, week of gestation, size of the fetus, distance from home to hospital, tractability of the patient and favorableness of the cervix. Seven per cent of the pre-eclamptics had induced labors that could be recognized by reading their charts and the most frequent method was pitocin infusion.

Stimulation of the uterus by "stripping" of the membranes during vaginal examination was widely practiced. Local anesthesia for delivery was frequently used and general anesthesia comparatively little.

ECLAMPSIA

There were 10 cases of eclampsia on the Tulane Service in 1950. These patients formed 0.26 per cent of all the patients delivered on the service and 1.4 per cent of the toxemic patients. Two of these patients had no antepartum care and 1 had been attended by an outside practitioner. Only 1 eclamptic had made more than 1 antepartum visit. Half of the eclamptics lived outside of New Orleans.

Youth predominated in this group. Only 1 was over 30 years of age. All were Negroes. Seven were primigravidas. Our convulsive toxemia showed some tendency to be grouped together by month. Four cases appeared in November, 2 in September, and 2 in March.

One patient was delivered by cesarean section. There was only 1 stillborn and that infant was born at home without an attendant. The patient was transferred to the hospital after delivery and had a postpartum convulsion. She had had no antepartum care. One mother had twins that survived and another had quintuplets that all died in the neonatal period. There were 3 premature babies among the single births and all survived; 1 was of less than 28 weeks' gestation.

The treatment of eclampsia followed closely that of pre-eclampsia. No unusual techniques were used until tracheotomy was introduced in November 1950, for the eclamptic with respiratory embarrassment. It was used in one of these patients and has been increasingly used since.

CHRONIC HYPERTENSIVE DISEASE

There were 347 women with chronic hypertensive disease delivered on the Tulane Service in 1950. This number constituted 47 per cent of the toxemic patients and 9 per cent of all the patients delivered in that year. Thus the Tulane experience was composed of almost exactly the same number of women with chronic hypertensive disease as with pre-eclampsia. Eighty-eight per cent of the women with this persistent hypertension were Negroes and they formed 9.5 per cent of all the Negro women delivered on the service. Of the 347 women with chronic hypertensive disease, 167 (48 per cent) had superimposed pre-eclampsia as described in "Definitions." The women with and those without superimposed pre-eclampsia are discussed jointly in this section and will be considered separately in the two succeeding subsections.

As anticipated, these women were older parturients. Forty-six per cent were 30 years of age or over and 7 per cent were 40 years or over. Nevertheless, chronic hypertensive disease proved to be a disease not exclusively of older nor of multiparous women. Forty-eight women were pregnant for the first time and 29 were less than 20 years of age.

The women with a chronic hypertension background provided a formidable portion of the stillbirths born to toxemic mothers, specifically 33 stillbirths or 70 per cent of all the dead born babies. However, the effect of a chronic hypertensive condition on our prospects of a live baby were not as pessimistic as others have found nor was the stillbirth rate adversely affected by the superimposition of pre-eclampsia.

Due to their small number these cases cannot validly be used to test the thesis that it is better, from the viewpoint of fetal salvage, to induce labor rather than to wait for a spontaneous onset. It is impossible to learn from the patients' records how many had their date of delivery advanced by vigorous loosenings of the membranes during vaginal examinations. Furthermore, as would be expected, the patients with the greatest hypertension, the most intractable albuminuria, and the poorest fetal survival record were in general the ones selected for induction. Thirty-six patients with chronic hypertensive disease (17 of them with superimposed pre-eclampsia) were induced by one

of the more overt methods and they delivered 7 stillborns. The mothers of 6 of these 7 stillborns also had abruptio, so possibly the abruptio was the indication for induction rather than the hypertensive disease.

Conservatism ruled in the management of chronic hypertensive disease. Only 1.7 per cent of all the chronic hypertensive women had cesarean section primarily because of the hypertension. The Negro chronic hypertensives who availed themselves of antepartum care were seen in a special toxemia clinic because of the unwieldiness of the large regular clinics. The conduct of this clinic has been described by one of us (10). No therapeutic abortion could be found in the records. Hospitalization was the rule when pre-eclampsia appeared and the hospital management was as described under "Pre-eclampsia."

Without superimposed pre-eclampsia. There were 180 women who had chronic hypertensive disease and who avoided the superimposition of pre-eclampsia. This was 24 per cent of all the toxemic mothers and 52 per cent of the chronically hypertensive women.

To learn if these 180 patients included many with a minimal blood pressure elevation we separated all women whose systolic blood pressure throughout this pregnancy was below 146 millimeters of mercury and the diastolic pressure below 96 millimeters of mercury. There were 30 such cases. It is worth noting that in this group of 30 women with "mild" hypertension there were 5 perinatal fetal deaths.

Many of the women in this category had had toxemia of pregnancy before: 27 once before, 27 twice, 14 thrice, and 9 had it 4 or more times. With complete records of the patients' past experiences these figures would be higher. Many had been attended previously by midwives and their blood pressures had been observed only recently in life. Needless to say, no meaningful observations could be made on the frequency of the various types of toxemia that they had had in earlier pregnancies.

Eleven of these women were delivered by cesarean section, only 2 of them directly because of the hypertension.

This group provided 19 dead born infants, an incidence of 11 per cent; 11 of these infants weighed 2,500 grams or less. There were 22 liveborn premature infants, 4 of whom had neonatal deaths; 3 of the survivors weighed less than 1,000 grams at birth. One mature baby died in the neonatal period.

With superimposed pre-eclampsia. There were 167 women with chronic hypertensive disease and superimposed pre-eclampsia. Thus 48 per cent of the women with chronic hypertensive disease had this augmentation of their difficulties. Our patients with chronic hypertensive disease had a chance of developing pre-eclampsia which was not quite 5 times greater than that of our normotensive women in 1950. Jones reported from the Providence Lying-in Hospital that patients with essential hypertension had 14 times the usual expectancy of eclampsia. At the Margaret Hague Maternity Hospital Lundgren, McCaw, and Burnett and their associates found that 24 per cent of the chronic hypertensive women had pre-eclampsia in 1950, while one-third and one-fifth of them had it in 1949 and 1948.

Sixty-six of the women in this group had been hospitalized before labor because of their pre-eclampsia for a total of 608 days, an average of 9.2 days per patient.

Using the previously cited qualifications, the condition of only 26 of these women (16 per cent) could escape being called "severe."

As in the other group of women with chronic hypertensive disease, documented previous episodes of toxemia were common despite incomplete past histories. Thirty-one women were known to have had toxemia once before, 20 twice, 15 thrice, and 10 had it 4 or more times.

These patients showed no distinctive monthly trend in the onset of pre-eclampsia.

The blood pressure standard for this diagnosis could be more sharply defined. In its

present form it allows considerable latitude on the part of the man who determines the diagnosis in each case. In this survey any further elevation of the prescribed magnitude (30 systolic or 15 diastolic) that occurred in the latter weeks of pregnancy satisfied the blood pressure qualification. This highest blood pressure was compared to the highest obtained earlier in this pregnancy. The physiologic lowering of the blood pressure in mid-pregnancy served to confuse. Fifty-nine of these 167 women had albuminuria and allowed no equivocation. Because the separation of chronic hypertensive disease and that disease with superimposed pre-eclampsia was difficult in so many instances we were made freshly aware that the borderline between chronic hypertensive disease and pre-eclampsia was indistinct enough to challenge its existence.

The patients with chronic hypertensive disease and those with chronic hypertensive disease plus pre-eclampsia were compared to see if any prophylactic effect of antepartum care could be observed. The contrast was made by means of data on the week of gestation that antepartum care was started and on the number of visits, exactly as was done in the analysis of mild pre-eclampsia and severe pre-eclampsia. These aspects of antepartum care could not be demonstrated to have influenced whether or not a patient with chronic hypertensive disease acquired pre-eclampsia. Again, the variables involved are numerous, and we do not claim that antepartum care is unimportant in the worsening of this hypertensive syndrome.

Two select groups of women with chronic hypertensive disease at the Charity Hospital clinics are available for comparison with the 1950 patients. Twenty-eight women who as controls received a placebo in a clinical experiment began antepartum care by at least the twentieth week of pregnancy and were usually seen weekly in a special clinic. They had a 37 per cent incidence of superimposed pre-eclampsia (9). A similar control group of 139 chronic hypertensive women who received unusually close attention had 27 per cent of its members develop a superimposition of pre-eclampsia (12). The lower incidence of pre-eclampsia in these groups suggests that careful antepartum treatment is an important factor in curbing this complication.

Thirteen women had cesarean section, 4 of them primarily because of toxemia.

There were 14 stillbirths, an 8 per cent incidence in the subgroup, of which 2 were plural births and 3 were premature. In this classification of toxemia our fetal survival record continues to compare favorably with that reported elsewhere. In the Margaret Hague Maternity Hospital the superimposition of this acute illness on chronic hypertensive disease raised the fetal loss from 18.5 per cent to 50 per cent, according to Cosgrove and Chesley. Contrary to the usual experience, our stillbirth and perinatal death rates were slightly less in the chronic hypertensive women who had superimposition of pre-eclampsia. Why this should be so can only be guessed. Possibly the appearance of pre-eclampsia spurred the decision to terminate pregnancy rather than to allow it to go through the perilous later weeks of a hypertensive pregnancy. The slightly higher percentage of cesarean section, induced labors, and premature babies in the superimposed pre-eclampsia group suggests this is what happened.

UNCLASSIFIED

Thirty women are placed in an unclassified group because they undoubtedly had toxemia, and we cannot accurately catalogue them at this time. The inability to classify the cases is usually due to nonappearance except for delivery, desertion, or referral without a case history. No woman included here, or elsewhere in this report, had the symptom complex frequently termed "chronic nephritis." There were no cases of glomerulonephritis. Section was performed in 3 cases, in 1 of them for toxemia. The only noteworthy observation on the babies is that there were 2 stillborns, 10 premature births, and 1 neonatal death.

FETAL OUTCOME

These 736 toxemic mothers had 709 live born babies of which 45 were plural births. Not distinguishing live born and dead born, there were 22 sets of twins and 1 set of quintuplets.

There were 49 stillbirths including plural births and babies of all weights. This is 6.5 per cent of all the babies delivered of toxemic mothers and a stillbirth rate of 69.1 per thousand live births. This is almost treble that of the hospital rate. In all of our figures on fetal outcome embellishing corrections are not made for any factor. All infants born in the delivery unit or en route to it are included. It will be noted simply that these 49 stillbirths included 29 premature, 4 plural births, and 7 infants of less than 28 weeks' gestation. Patients of 20 weeks' gestation or over are admitted to the delivery unit; the remainder of the pregnant women go to a gynecology ward. The stillbirth rates for the service or the hospital in 1950 are not available for comparison. The most pertinent figure that has been computed is the stillbirth rate of 27.7 per thousand live births at the Charity Hospital for the year ending June 30, 1953.

The analysis of fetal survival in each of the subgroups is given in the paragraphs dealing with them and in Table I. Chronic hypertensive disease was more lethal for the fetus than the acute forms of toxemia. The mothers with pre-eclampsia-eclampsia had 23 perinatal fetal deaths, an incidence of 6 per cent. The mothers with chronic hypertensive disease, both with and without superimposed pre-eclampsia, had 44 perinatal fetal deaths, or 13 per cent. The probability of this difference occurring by chance is less than 1 in 1,000. To test further the peril to the fetus from chronic hypertensive disease, the perinatal fetal mortality of pre-eclampsia-eclampsia can be compared to the 15 per cent perinatal mortality rate of chronic hypertensive disease without superimposed pre-eclampsia. Again, the probability of this difference occurring by chance is less than 1 in 1,000.

Our stillbirth rate of 6.5 per cent and perinatal rate of 9.2 per cent compare well with figures published from other hospitals. Keeping in mind the lack of uniform standards, we can note that Cosgrove and Chesley announced an infant death rate of about 50 per cent in superimposed pre-eclampsia (ours, 8.2 per cent). At the Margaret Hague Maternity Hospital in 1950 the stillbirth rate for toxemia was 15 per cent. Wellen (27) reported an infant mortality of 12.4 per cent in specific hypertensive disease and 15.3 per cent in essential hypertension at the Bellevue Hospital. Jones recorded that at the Providence Lying-in Hospital mild hypertensive disease with superimposed pre-eclampsia had a perinatal mortality of 21.9 per cent. From the Liverpool Maternity Hospital, Hamilton and his associates quoted a perinatal mortality rate of 19.7 per cent for pre-eclampsia. Agüero reported from Caracas a death rate of 20 per cent, 4 times that of the hospital. At the Royal Victoria Montreal Maternity Hospital, Hendelman and Philpott had an uncorrected fetal mortality of 43 per cent in severe pre-eclampsia and 5.3 per cent in mild pre-eclampsia. The total fetal loss with nonconvulsive toxemia at the Chicago Lying-in Hospital (1940–1950) was reported by Dieckmann as 7 per cent (7). A more complete record of the fate of the fetus in toxemia can be found in a paper of Taylor and associates; we appear to have better results than are generally being reported.

Prematurity. A premature infant is defined here as one with a birth weight of 2,500 grams or less. These 736 toxemic mothers had 109 live prematures. This is an incidence of prematurity, as usually computed, of 15 per cent. There were also 29 dead born premature babies. The incidence of prematurity among all the mothers on the Tulane Service or in the entire hospital in that year is not available for comparison. The most germane figure at hand is the 14 per cent incidence of prematurity for the hospital in 1952 to 1953. These two 12 month spans should be comparable. Thus it seems that toxemia cannot account for the high incidence of prematurity.

The number of premature babies produced in each classification of toxemia is given in Table I. The chronically hypertensive mothers had 59 premature babies and the almost equal size pre-eclampsia-eclampsia group had 42 premature babies.

Six of these premature infants resulted from cesarean sections done because of toxemia and 18 prematures were born following induced labors. The inability to say exactly how many had induced labors has already been explained. Twenty-one of the babies born alive weighed 1,500 grams or less and 13 weighed 1,000 grams or less. Among the total of 70 stillborns and neonatal deaths there were 44 prematures.

Neonatal deaths. All infants dying within 30 days of birth are here considered neonatal deaths. There were 21 neonatal deaths of infants born to these toxemic mothers. This is a neonatal death rate of 29.6 per thousand live births. The only figure at hand for comparison is the hospital rate of 23.4 per thousand live births in 1952 to 1953. Fifteen of the 1950 deaths occurred in premature infants, 5 of whom were under 1,000 grams at birth. The number of babies born to the mothers with each toxemia diagnosis were: pre-eclampsia, 4; eclampsia, 5 (quintuplets); chronic hypertensive disease, 8; chronic hypertensive disease with superimposed pre-eclampsia, 3; unclassified, 1.

As in other hospitals our follow-up on neonatal survival is not complete. Healthy mothers and babies are usually discharged on the second or third postpartum day. A good number of the babies are brought back to this hospital for subsequent care for the same reasons that brought the mother to the hospital so surveillance during the neonatal time is reasonably good.

Malformations. Among the 740 live and dead born babies there were 13 considered to have major anomalies, an incidence of 1.7 per cent. There was no remarkable distribution of the cases among the various types of toxemia. Although we do not have a figure for the general incidence of anomalies in the hospital, our percentage for babies of toxemic mothers does not seem to support the concern of de Watteville and others over a meaningful concurrence of fetal malformation and toxemia.

One baby had congenital syphilis. The diagnosis of retrolental fibroplasia was not made on any baby.

MISCELLANEOUS

Abruptio. There were 24 cases of abruptio, 3 per cent of the toxemia cases. They were distributed as follows: pre-eclampsia, 5; eclampsia, 0; chronic hypertensive disease, 12; chronic hypertensive disease with superimposed pre-eclampsia, 5; unclassified, 2. Six of the cases were terminated by cesarean section with 7 perinatal deaths (twins) and 18 ended in vaginal delivery with 10 perinatal deaths.

Bieber reported that in 1942 to 1952 the incidence of abruptio at the Charity Hospital was 0.44 per cent. On the Louisiana State University Services at the Charity Hospitals in New Orleans and Lafayette, Tatum found an abruptio occurrence of 0.5 per cent. It is important to realize that until 1951 the diagnosis of rupture of the marginal sinus was not recorded at the Charity Hospital; figures on abruptio under these conditions may be open to some adjustment (11).

Anemia. Practically every woman had a hemoglobin or hematocrit determination on admission. In this report hemoglobins of less than 10 grams per 100 milliliters or hematocrits of less than 30 per cent are considered evidence of anemia. When there was disagreement in the two tests a mean corpuscular hemoglobin concentration of less than 30 is used for the criterion of anemia. There were 43 women (6 per cent) with anemia. The distribution of anemia was pre-eclampsia, 20 cases; eclampsia, 2; chronic hypertensive disease, 8; chronic hypertensive disease with superimposed pre-eclampsia, 12; unclassified, 1.

Diabetes. Five mothers were diabetic. Each had a live baby that survived. One had a cesarean section because of the diabetes and the remainder had spontaneous labors and

deliveries. In 1950 early delivery of diabetics was not practiced as frequently as now.

Pyelonephritis. Twenty women (3 per cent) were treated in the hospital for pyelonephritis. Undoubtedly there were others treated on an outpatient basis.

Heart disease. Ten women were recognized as having heart disease that antedated the 1950 pregnancy. Five were clearly due to rheumatic fever. This group does not include women with long standing hypertensive cardiovascular disease and minor depletions of cardiac reserve.

Cesarean section. Forty-one patients (6 per cent) had cesarean sections. The primary indications were listed as: toxemia 12, disproportion 10, previous section 9, abruptio 5, faulty presentation 3, placenta previa 1, and diabetes 1.

Eye grounds. One hundred and thirty-five women had ophthalmoscopic examinations and 80 (59 per cent) were considered abnormal. The group with chronic hypertensive disease and superimposed pre-eclampsia had the greatest number examined and greatest percentage with abnormal fundi.

Electrocardiograms. Significant electrocardiographic changes were found in 36 (18 per cent) of the 205 women tested.

Chest roentgenograms. One hundred and forty-nine patients had x-ray films of the chest during hospitalization and 36 were abnormal. The most common abnormality was some degree of cardiac enlargement.

Other studies. Two hundred and fifteen patients had blood chemistry tests done at least once and 145 patients had at least 1 renal function test but the interpretation of these tests is beyond the scope of this paper.

Urinary suppression. No toxemic woman in 1950 had lower nephron nephrosis. One patient (with chronic hypertensive disease) is considered as having anuria, if we define anuria as no excretion of urine in a 12 hour period; this patient subsequently improved. Oliguria we define as the excretion of less than 600 milliliters of urine in any 24 hours. There were 12 patients with oliguria, 5 of whom had eclampsia.

Maternal death. There was 1 death among the toxemic women on the service in 1950. This patient had chronic hypertensive disease and died of pulmonary embolism after a cesarean hysterectomy.

The patient was a 38 year old colored para 9, gravida 11. She was known to have had hypertension for 17 years. Near term a cesarean section was performed because of 2 previous sections. The first section was done because of a large baby (15½ pounds). The operation was started under local anesthesia and finished under ethylene and ether. After delivery of twins a subtotal hysterectomy and bilateral salpingo-oophorectomy was done. One ovary contained a 7 centimeter dermoid cyst. The lower extremities were examined daily and there was no muscle tenderness or Homans' sign. The postoperative course was febrile due to pneumonitis but she was discharged well on the twelfth postoperative day. The day after discharge she collapsed at home and died suddenly. The coroner's diagnosis was pulmonary embolism.

Induction of labor. Labor was induced in 65 women. Pitocin infusion was the most popular form of induction and was used in 38 instances. We have no hesitancy in the employment of this method of induction in toxemia. Our use of pitocin infusion has increased since 1950. No considerable deleterious effect on toxemia has been observed (23).

SUMMARY

The problem of toxemia of pregnancy at the Charity Hospital in New Orleans was audited by means of a careful study of the hospital records of all of the patients delivered on the Tulane Service in 1950. The patients were from the low income group of the state and 82 per cent were Negroes. The patients with toxemia were designated by scrupulous adherence to definitions and were divided into groups with pre-eclampsia, eclampsia, chronic hypertensive disease without superimposed pre-eclampsia, and chronic hypertensive disease with superimposed pre-

eclampsia; there was a small unclassified group. Three thousand eight hundred and ninety-nine patients were delivered on the service in 1950 and 736, or 19 per cent, had toxemia. Forty-seven per cent of the patients had pre-eclampsia, and 47 per cent had chronic hypertensive disease. Forty-eight per cent of the patients with chronic hypertensive disease had pre-eclampsia superimposed on that illness. There were 10 eclamptics. The large Negro census did not seem to be the cause of the high rate of toxemia. There was 1 maternal death. The stillbirth rate of 6.5 per cent compared very favorably with the rates reported elsewhere. The cesarean section rate was 6 per cent and the primary indication for the operation in the majority of these women was not the toxemia.

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