PREMATURE SEPARATION OF THE NORMALLY IMPLANTED PLACENTA WITH SPECIAL REFERENCE TO THE KIDNEY IN THESE CASES

By Foster S. Kellogg, M.D., Boston, Mass.
(Instructor in Obstetrics, Harvard Medical School)

In Collaboration with Joseph V. Taylor, M.D., Marion F. Eades, M.D. and Theodore W. Weller, M.D.
(Late Residents Boston Lying-In Hospital)

Purpose.—It is not the purpose of this paper to reconsider the question of premature separation of the normally implanted placenta from the standpoints of multiple etiology, pathology, symptomatology, classification for obstetric treatment, obstetric treatment itself and results or bibliography. Williams,[21, 22] Holmes,[12, 13] Polak,[17] Willson,[23] Portes,[18] Phaneuf,[19] and others have well covered these aspects of the condition. Goethals, of the Boston Lying-In staff, working independently has just now done the same with the series from which the bulk of our material is taken.

Our purpose at the start of this study was to link up the group of these cases in which the kidney is involved with our previous work on the "toxemic-chronic nephritic" group. We sought to clear up in our own minds certain questions regarding the kidney which presented themselves to us as we debated treatment in a given case. We felt that though much had been accomplished along lines of obstetric treatment by our predecessors, much room was left for a better understanding of the treatment in relation to the kidney. We felt that if we could obtain this understanding by study, we could lower our mortality rate. We were particularly impressed by the group of patients with separated placentas—clinically distinct from anuric eclamptic, patients who showed marked anuria. We were totally at a loss to explain the urine and blood chemistry findings observed over a period of days in some of these cases by the pathology implied by the terms chronic nephritis and acute nephritis. We hoped that a study of our material would throw some light on these and other puzzling questions.

Literature.—From the voluminous literature on "separated placenta" we wish to consider only those contributions which bear on the subject under discussion.

The association between nephritis and premature separation of the placenta, according to Essen-Möller[7, 8] was first pointed out by Chantrenil in 1881. Winter,[25] in 1885, presented three cases and noted the occasional presence of nephritis with the condition. Secondarily, he advocated endometritis as an etiologic factor. His observations were corroborated by Hennig,[10] Weiss,[24] Lehman,[14] and Hofmeier.[11] Holmes,[12] in 1901, was not impressed by the presence of albuminuria in these

Cesarean section was performed. This patient had a partial suppression, certainly during the first two days postoperative, and died on the third day. His second case, a primipara, eclamptic, with premature separation of the placenta delivered normally, and had thirty-four hours with absolute anuria for two days postpartum. A bilateral decapsulation of the kidneys was performed, but the patient died thirty-four hours after delivery. On autopsy, edema of the perirenal tissue was found. The kidneys showed only congestive changes consistent with capillary dilatation. The convoluted tubules were occupied with cellular detritis and fine granular cylinders.

Oldfield and Hann[16] report a more typical case. Their patient was a primipara, thirty-eight years old. with signs and symptoms of premature separation of the placenta. At the time of operation only 1.5 ounces of blood-stained urine was obtained, "loaded with albumin." Complete urinary suppression followed for thirty-six hours and partial suppression for three or four days, after which the urinary output increased, and the patient made an uneventful convalescence and was albumin-free on the seventeenth day. These authors are the first and only ones, as far as we have found, to note that urea excretion was diminished and to describe the urinary sediment.

Material.—The original material on which this study is based consists of approximately 165 cases indexed as "separated placenta." All but 13 of these occurred in the last ten years of the Boston Lying-In Service. The others were seen by me (F. S. K.) in my private practice and are included because most of the patients have been under observation three years or more, a point of great importance. These 165 cases briefed and studied were immediately reduced in number to 60. The other patients had definitely separated, low-attached placentas, or were definitely traumatic, or gave insufficient recorded data to make them of any value to us. The remaining 60 cases were all associated with what we have called the "toxemic-chronic nephritic group." Intensive study of these 60 cases led us to omit 31 more. The reason for this reduction was that though they belonged in the group, we saw that the data were insufficient to advance our ideas. Of the remaining 29 cases, each, for one reason or another, seemed to us to possess more merit for study than the usual reported case.

The Groups.—It is impossible in a paper of this length to enter into the detail of these 29 cases. If we indicate why we venture to state that they possessed more than average merit for study; if we detail the single case which first brought to a head our interest in this subject; if we then offer our opinions based on this work, and draw such conclusions as we may, we shall have accomplished all that our time permits. Nor are we disposed at present to publish the cases as they stand in protocol, for the reason that in the next few years opportunity for interval study in most of the surviving cases will have occurred. We therefore offer our effort to you in a tentative and preliminary form.

Our best method of indicating briefly why we think these cases are more valuable than average seems to be to group them under certain

headings. We studied them in this way because each group contains the suggestion of a possible answer to one or more of our questions. Please bear in mind that we are not yet concerned with statistics and figures, that some of the cases fell into more than one group, and that, therefore, the addition of the group figures which we present will not and should not equal the 29 patients from whom the material came.

Group 1.—Five cases not accompanied by eclampsia in which complete anuria was present in 2, and marked incomplete anuria in the other 3. Of these patients 3 died and 2 recovered.

Group 2.—Five cases associated with eclampsia. We would emphasize one feature common to these 5; namely, that each had had her convulsion prior to placental separation.

Group 3.—Eleven cases in which satisfactory and reasonably complete blood chemistry, blood pressure, and urinary data were recorded.

Group 4.—Eight cases. Each patient had been in hospital for treatment of toxemia of pregnancy with elevated blood pressure, albumin in urine, and other symptoms, and had cleared so completely that she was either just home, or on the eve of discharge, when separation occurred.

Group 5.—Twelve cases in which we have partial adequate interval study, or a definite history of marked toxemia in more than one pregnancy.

Besides studying these groups, we think we have made three other observations in this condition. We know or suspect these have been previously made, and we insert them here simply as confirming the observations of others. (1) These patients have high white counts (in so far as our limited data go) and, since high white counts may result from throwing foreign protein into the blood stream, we have a certain amount of added theoretical evidence that this group of separated placentas is caused by a protein toxic agent. (2) Certain of these patients show increased bleeding and coagulation time. (3) As these patients entered the hospital, inspection, as a rule, classified them into one of two types. The first of these is the nephritic type; generally characterized, we think, by relatively moderate parity when seen. The second type, older in years, stringy, worn, many para, looking like the more usual hospital patient with placenta previa. We think that it is in this type that endometritis may be the main etiologic factor; whereas, in the other group we feel convinced that the same etiologic factor as in toxemia plays the major rôle in the premature separation.

Having as briefly as possible outlined the cases in groups, we shall cite in detail the history of a patient who increased our interest in the pathology and treatment of toxic premature separation. She led us to an intensive study of the literature and to a feeling that we could not be content with it. Especially were we impressed by the slight amount of available information, to say nothing of the marked disagreement of authorities, concerning kidney pathology in these

ses. We sought further information from the genitourinary surgeon, from the internist, and lastly by good chance from a well-known student of the physiology of the kidney, and we found only a little suggestion of help from them. It must be said that what actually took place in the kidneys of the patient about to be described is not yet known. Autopsies as we have seen them, and those cited by Willson, do not help. They are few in number and by no means meet the requirements of the clinical picture. We suspect, as with our own, that the ones he reports were done on patients dying relatively soon after delivery. The single autopsy finding, Couvelaire's second case in which at autopsy, "edema of the perirenal tissue was found, the kidneys showed only congestive changes consistent with capillary dilatation; the convoluted tubules were occupied with cellular detritis and fine granular cylinders," corresponds to the clinical picture in those anuric patients who recover.

THE CASE

M. B., para i, forty years old, had scarlet fever when four years old; also tonsillitis when a child. She first came to the prenatal clinic Jan. 21, 1927. Last period was Sept. 1, 1926. Expected date of confinement June 8, 1927. On Oct. 1, 1926 there was slight antepartum bleeding.

On this first prenatal visit, the patient had a systolic pressure of 160. No albumin. According to our system she was referred to the hospital for study.

TABLE I

HOURS	OUTPUT	INTAKE		B. P.
1st 24	4 drops	Subpect. Sal.	1500 c.c.	Low
		25% glu. intra.	300 c.c.	100/70
		Subpect. Sal.	1600 c.c.	High
		Transfusion	500 c.c.	120/80
			3900 c.c.	
		By mouth and rectum up to	6360 c.c.	
2nd 24	45 c.c.	Subpect. Sal.	1500 c.c.	Low
		25% glu. intra.	250 c.c.	125/65
			1750 c.c.	High
		By mouth and rectum up to	6270 c.c.	170/80
		Sal.	3000 c.c.	
		Glu. intra.	250 c.c.	
3rd 24	135 c.c.	By mouth and rectum up to	3860 c.c.	Low 150/85 High 200/120
4th 24	267 c.c.	All by mouth	2610 c.c.	Low 155/85 High 200/120
5th 24	217 c.c.	Subpect sal.	1500 c.c.	Low 160/85
		By mouth and rectum up to	3460 c.c.	High 180/95
	Total 634 c.c.	Total	22560 c.c.	

Hemoglobin, 30 per cent; red count, 3,516,000. Blood chemistry was within normal limits (see Table II). Eyegrounds negative. Pthalin 35 per cent. One hour renal test was normal.

During eight days in the hospital her blood pressure dropped to 120/80. She was discharged to the toxemic clinic. She reported there four days later, and from February 11 to March 8 her blood pressure ran from 154 high to 136 low, and no albumin.

At 3:00 P.M. on March 27, 1927, she vomited and lost one ounce of fluid blood from the vagina. She felt giddy and faint, had blurred vision, but no loss of consciousness, headache, or abdominal pain; fetal movement ceased. On entrance to hospital blood pressure was 160/100, pulse 120, temperature 98.2°; uterus was board-like and tender; fetal parts could not be mapped out, and fetal heart could not be heard; there was slight red vaginal staining. No rectal or vaginal examinations were made. Reflexes were active; she had moderate edema of extremities, and slight edema of face and retina. Urine at this time was 4 c.c. in amount, cloudy red, with trace of albumin, occasional red blood cells, hyaline, and granular casts.

To recapitulate: February 7, 1927, a patient is discharged from hospital with normal blood pressure and urine, negative blood chemistry, and negative kidney tests. She is followed as carefully as possible in the special toxemia clinic. Fifty days later she appears, an undoubted case of toxic separation, in excellent condition for section, and with a good prognosis in comparison to that of a similar patient bled out. Cesarean section, confirmation of the diagnosis by the appearance of the uterus, separated placenta, dead baby, and free blood and clots. Uterus acted well and is left in, little postpartum bleeding; pulse, and pulse pressure satisfactory.

By this time we have learned that hemorrhage is not the only thing that may kill a patient with separated placenta, even in the nonecclamptic group, and that speedy surgery applied early and ample transfusion do not always save such patients. Accordingly, the patient is catheterized every eight hours, has four-hour blood pressure readings, and these observations are checked up against our treatment. Table I shows results by twenty-four hour periods.

From the fifth day on, the output steadily rose to a maximum of 112 ounces on the ninth day when that side of the matter was considered closed. During these nine days the albumin dropped to the slightest possible trace, then cleared up except occasional S. P. T., apparently from pus in the urine. The urine became pale, and casts and cells disappeared in five days. The blood pressure dropped to 160, and ultimately to 120.

The use of the 25 per cent glucose intravenously three times in the effort to open the kidney was checked up by blood-sugar tests, done as part of the routine blood examinations. These findings are accordingly shown. (Table II.)

The patient, after a stormy convalescence with low grade sepsis in wound and uterus, was ultimately discharged obstetrically well to the Boston State Hospital for the Insane, where she had previous admissions.

TABLE II

DATE	N. P. N.	BLOOD UREA NITROGEN	BLOOD URIC ACID	BLOOD SUGAR	BLOOD CHLORIDE (CHECKED HIGH, LOW)
2/ 2/27	26	8.5	31	74	
Day of 1st ad.					
3/28/27	59	31.9	6.7	143	554
Day after del.					543
3/29/27	64	38	7.3	111	566
					566
3/30/27	86	50	8.8	143	554
					554
3/31/27	67	32.7	10.7	117	531
					531
4/ 1/27	100	66.1	11.4	*166*	508
					496
4/ 2/27	110	66	10	122	507
					496
4/ 3/27	*120*	70	10	126	508
					531
4/ 8/27	60	41	8	100	554
					543
4/15/27	33	16.9	4	52	519
					508
6/ 1/27	18	7.2	2.7	81	514
					508
6/11/27	27	9.3	2.9	100	496
					496
					Mg. per 100 c.c. Whole Blood

These tables taken from the case detailed above, and more or less like the other anuric cases we have studied. illustrate several points. These are (1) the progressive slow recovery of the kidney when it begins to secrete; (2) the tremendous intake of fluids we use in the effort to force the kidney to secrete; (3) at first the progressively increasing blood pressure and later its high stabilization between high point and low point, accompanied by the progressive urinary output; (4) the use of concentrated glucose intravenously to produce hyperglycemia, in an effort to obtain diuresis. This is checked by the daily blood-sugar findings as illustrated in Table II by the figure 166, which represents the culmination of three days of intravenous glucose therapeutically. At this figure or somewhat below, sugar appears in the urine. (5) It illustrates that the kidney must recover its ability to secrete nonnitrogenous material including water, first because it shows the maximum of nitrogen-retention on the seventh day of the puerperium while at this time large amounts of urine of high specific gravity are already being excreted. This is as one would expect from the long time necessary to produce uremic death and uremic blood findings experimentally. One patient in our anuric series died on the sixth day with uremic blood findings and in typical uremic coma with uremic twitchings, though she was not an eclamptic on entrance.

Furthermore, Table II illustrates a patient who comes to us with a history, of an age, with appearance, with blood pressure—all sugges-

tive of chronic nephritis, but whose blood chemistry, eyegrounds, reaction to treatment demonstrate that she is not a chronic nephritic in the accepted sense of the term. She then passes through an almost complete kidney shut-down and during this time shows urinary findings and blood-chemistry findings approaching those of a woman about to die of uremia. Yet two months later she emerges with the same normal blood chemistry, urine, and blood pressure that she had in the beginning. If we attempt to place the rôle of chronic nephritis in these cases, we are in no position to do so accurately with our present knowledge. The appearance of albumin in the urine, elevated blood pressure, etc., in more than one pregnancy does not permit of this diagnosis on the one hand, and on the other, retained nitrogen products in the blood does not mean simply chronic nephritis, but means a decompensated nephritis, since upwards of two-thirds of the kidney tissue must be out of commission before sufficient nitrogenous products are piled up to be demonstrable in the blood. We have in this series data of four cases which lead us to believe that they are at present, and presumably were chronic nephritic patients at the time of separation, but we are not yet sure. We have a feeling that not a few will turn out to be chronic nephritic patients, but this feeling is based more on the inspection of the patient than on anything we are yet able to demonstrate. When we make this statement, we are sensible of the observations made in other toxemic clinics, particularly in Baltimore and in New York, as well as in our own, on the development or at least on the discovery of chronic nephritis subsequent to various forms of toxemia of pregnancy. As yet, these are not convincing to us in anything like the proportion of cases so described. We feel that only by many years of observations of many of these patients, or better by the development of some more delicate test of kidney insufficiency than has yet been offered, can the true rôle of chronic nephritis be known in separated placentas.

CONCLUSIONS

1. We believe that the major result of this study has been to show us more tangibly than before how we should approach and follow each case of so-called toxic separated placenta.

2. We believe that anuria in separated placenta is a complication to be feared and to be combated as we have outlined, from the first moment that the patient is seen, with forced fluids by mouth and rectum and under skin, glucose 25 per cent in vein, and usually transfusion, fluids up to from 6000 to 7000 c.c., checked up by daily blood chemistry, by blood pressure and by eight-hour interval catheterizations with urine analysis.

We believe in this connection that the preservation of a relatively high blood pressure is an important part of the treatment and that it represents a protective mechanism against the anuria.

4. We believe that in the eclamptic group of separated placentas, dropping pressure to control convulsions should be exercised with great caution lest the patient be aided to become anuric.

5. We believe that on the chances the etiologic factor in toxemia of pregnancy and toxic separation of the placenta is sometimes, at least, the same. We base this belief on the fact that we have been able to collect 8 cases of definite toxemia without convulsions (nonnephritic as far as we can say at present) that separated just as the signs and symptoms of toxemia had abated.

6. We believe from this group that extreme supervision should be exercised after a toxemic patient has improved to the point of discharge, and that she should be warned to remain quiet and report if she has the slightest bleeding or abdominal pain.

7. We believe that the explanation of what actually takes place in the kidney in these cases, whatever its pathologic background, must be sought in further study of the physiologic exchange in the kidneys, rather than along lines of autopsy pathology.

8. We believe that decapsulation of the kidney has no place in these cases.

9. We believe that every effort should be made by every obstetrician and clinic to link up these cases with the "toxemia-chronic nephritic" group, and study them with careful tests and gather all available data, over the longest possible period. This so that as the scientific laboratory comes forward with more light on the etiology or etiologies of these conditions, the clinical laboratory will not be behind in case groupings to fit.

REFERENCES

(1) *Ahlström, E.:* Arch. f. Chirurg, 1919, li, 423. (2) *Bar, P.:* Arch. mens d'obst. et de gynéc., October, 1912, p. 162. (3) *Bar, P.:* (quoted by Essen-Möller). (3) *Bar and Kervily:* Bull. Soc. d'obst. et de gynéc., de Par., 1906, ix, 118. (4) *Couvelaire, A.:* Ann. de gynéc. et d'obst., 1912, ix, 539. (5) *DeLee, J. B.:* Principles and Practice of Obstetrics, Philadelphia, ed. 4, 1925, W. B. Saunders Company, p. 466. (6) *Dorman, F. A.:* Sloane Hospital Reports, 1913, i, 57. (7) *Essen-Möller, E.:* Arch. mens. d'obst. et de gynéc., 1913, iv, 145. (8) *Essen-Möller, E.:* Tr. xvii Internat. Cong. Med., Section 8, 1914, p. 25. (9) *Gaston, A.:* Ann. de gynéc. et d'obst., 1906, iii, 667. (10) *Hennig, C.:* Arch. f. Gynäk., 1875, viii, 336. (11) *Hofmeier, P.:* Winkel's Handbuch d. Geburtsh., 1904, ii, 1185. (12) *Holmes, R. W.:* Am. Jour. Obst., 1901, xliv, 753. (13) *Holmes, R. W.:* Am. Jour. Obst. and Gynec., 1923, vi, 517. (14) *Lehman, M.:* Thèse de Paris, 1898. Rev. prat. de gynéc., d'obst. et de pédiat., May, 1899, No. 133, p. 145. (15) *Muus,* (quoted by Essen-Möller.) (16) *Oldfield, C., and Hann, R. G.:* Proc. Roy. Soc. Med. (Obst. and Gynec. Section), 1916, x, 17. (17) *Polak, J. O.:* Med. and Surg., 1917, i, 154. (18) *Portes, L.:* Gynéc. et Obst., 1923, vii, 56. (19) *Phaneuf, L.:* Boston Med. and Surg. Jour., 1925, excii, 1037. (20) *Shaw, W. F.:* Proc. Roy. Soc. Med. (Section Obst. and Gynec.),

1916, x, 23. (21) *Williams, J. W.:* Surg., Gynec. and Obst., 1915, xxi, [redacted] (22) *Williams, J. W.:* Obstetrics, New York, ed. 5, 1924, D. Appleton & Company, p. 920. (23) *Willson, P.:* Surg., Gynec. and Obst., 1922, xxxiv, 57. (24) *Weiss, O.:* Arch. f. Gynäk., 1894, xlvi, 256. (25) *Winter:* Ztschr. f. Geburtsh. u. Gynäk., 1884, xi, 356.

DISCUSSION

DR. PAUL TITUS, PITTSBURGH, PA.—One of the most important points brought out by Dr. Kellogg is that increased blood pressure is probably a protective measure. We should be exceedingly cautious about overbleeding the ordinary toxemia patient for fear we might destroy this very protective measure.

There is no question that chronic nephritis has a definite association with these conditions, but is it not likely that chronic nephritis adds merely a general susceptibility rather than that chronic nephritis is always to be found in a toxemia of pregnancy? It is not always associated with it, nor are all of these cases accompanied by even an acute nephritis. That would tend to confirm the idea that the acute nephritis we see so often in toxemia is a secondary matter rather than a primary one.

Dr. Kellogg pointed out in his chart that the blood chemistry of this patient was normal except for a lowered blood sugar. This I would expect and consider an important fact. May I suggest that following intravenous glucose injections, spill of sugar through the urine is not so much dependent upon the height to which this injection sends the blood sugar as it is upon the rapidity with which the glucose injections are given.

Many times accidental separations of the placenta are seen without toxemia and without nephritis. This is a complex problem beyond doubt, and I believe it must be agreed that in one instance we may have a certain set of concomitant clinical symptoms, and in another instance another set. The observation on blood pressure impresses me as one of the most valuable points that Dr. Kellogg has made in this excellent work.

DR. ROBERT D. MUSSEY, ROCHESTER, MINN.—I would like to ask the essayist concerning the presence of edema in the anuric cases. In our waterlogged cases or in those patients with a marked amount of edema and oliguria or anuria, the fluid intake is kept down until the patient begins to excrete more urine. An effort has been made to dislodge the increased retention of sodium chloride in the cell by using either ammonium chloride or ammonium nitrate. Following the intake of ammonium, there is a freeing of sodium chloride which is held in the cell and which is apparently associated with the retention of water. This is usually followed by the free output of urine. Coincident with this, the edema disappears and the patient's condition improves. Then more fluids are given. If edema is not evident, there is no indication for the restriction of fluid intake.

DR. JAMES E. DAVIS, ANN ARBOR, MICH.—Something might be said about congenital syphilis as a cause, and about developmental conditions. Where the placenta shows a cord attached eccentrically, the plexus of vessels is inadequate; that is, the plexus will spread out with the trunks attached marginally with the main attachment of the cord. This is a developmental condition that always carries a liability. I believe every placenta should be examined to determine the conditions in the chorion laevic zone, chorion frondosic zone, the cord and its position of attachment, the chorionic and amniotic membranes, and the cotyledons.

The chorion laevic zone may be unusually and relatively thickened, ridged, and broadened so as to diminish the frondosic zone. Extreme eccentric cord attachment is always a hazard for the placental circulation. The fusing of cotyledons and the irregularities in their sizes together with their vascularity are usually indicative of important pathologic changes. The gross examination of the placenta