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A CLASSIFICATION OF THE TOXEMIAS OF THE LATTER HALF OF PREGNANCY

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THE present method of classification of the toxemias of pregnancy is admittedly inadequate, and it occurred to us that by correlating the findings in a large series of patients it might be possible to gain information which would throw light on the problem. It will be apparent even to the casual observer that studies upon repeated pregnancies occurring in the same individual should be of especial value in an endeavor to find a basis for such classification. With this in mind we studied the histories of the patients with toxemia of pregnancy who were admitted to the clinic during the past five years, and we have paid particular attention to those with more than one admission. Viewing the data obtained in a perspective manner, rather than by studying an isolated case, has led us to somewhat surprising conclusions.

In the tables we have given only such information as was considered to bear upon the question under discussion. Age, parity and the duration of pregnancy are undoubtedly essential. The common complaint of headache, swelling of the feet, ankles, and other parts of the body, and disturbances of vision, as well as the objective findings upon ophthalmologic examination, have been recorded. The systolic and diastolic blood pressure and the laboratory findings on the urine and blood furnish perhaps the most important information. In addition, we have given the number of convulsions, if any, the weight, the fluid intake and output, the results of the phenolsulphonephthalein kidney test, the treatment in brief outline, together with some remarks regarding the patient's dispensary history, and the type of delivery, with especial reference to the outcome both to the patient and to her child.

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The laboratory findings constitute two groups: those on the urine and those on the blood. In the first group we have given the albumin, as determined by the Esbach method, in grams per liter of urine. Both the urea and the ammonia nitrogen are expressed as percentages of the total nitrogen in the urine, and are shown in the columns labelled "Urea-N% of T. N." and " $\text{NH}_3\text{-N}\%$ of T. N.," respectively. In the microscopic examination we have recorded only the presence or absence of casts and their types. The blood analyses consist of the determination of the nonprotein nitrogen (N. P. N.), the uric acid, the urea nitrogen expressed as a percentage of the nonprotein nitrogen (Urea-N% of N. P. N.), as well as that of the sugar, the carbon dioxide combining power, and the chlorides. All of these, with the exception of the urea nitrogen and CO_2 , are expressed in milligrams per 100 c.c. of blood. The CO_2 is written in volumes per cent. The methods employed in these analyses are those referred to in previous publications from this department.

In the column designated "Diagnosis" we have given the diagnosis made at the time of discharge, while in another column, appearing on the extreme right side in some of the tables, we have added a "Corrected Diagnosis," containing our own opinion with reasons.

By a study and evaluation of all the findings under the different headings, we have been able to arrange the toxemias into different groups. We shall first discuss the more definite types and then give our views concerning a new group.

GROUP I. ECLAMPSIA

Table I gives the findings for all the cases of typical eclampsia, for the period Jan. 1, 1923, to Feb. 1, 1926. There were 41 admissions, and two of them concern the same patient. There were actually more cases of eclampsia during this period, as will be shown in the discussion under Group II.

The predominating features of the eclamptic group are as follows:

1. Usually a very high blood pressure, a large amount of albumin in the urine and a definite increase in the uric acid in the blood during the time of the convulsions.
2. A complete disappearance of these abnormal findings within two to three weeks following the attack of eclampsia.
3. In certain cases an exceedingly low carbon dioxide combining power and an elevated blood sugar, as has already been outlined by one of us. Such patients usually have a high ammonia coefficient.
4. In over 60 per cent of the cases eclampsia appears in the primiparous woman.
5. Nearly all the patients in this group present marked edema.
6. A fatal outcome for the mother is not always associated with a large number of convulsions, although this is usually the case.

The eclamptic group constitutes a definite entity and thus further discussion here hardly seems warranted.

GROUP II. PRE-ECLAMPSIA

There are a few patients who do not fall into the eclamptic class, although they present a picture almost identical with it, except that there are no convulsions or coma. It is this type of toxemia which we

believe may be called "pre-eclampsia." The last two patients in Table II are the only ones among all of our toxemia studies whom we believe can be designated as "pre-eclamptic." These show a great amount of albumin in the urine and a high blood pressure level prior to delivery. After birth of the child, there is a prompt return to a normal blood pressure level and an albumin-free urine. We have grouped these two patients with four eclamptic women on whom we have made repeated studies, and we shall discuss their subsequent pregnancies after the other groups have been considered.

From the figures in Table II it appears that "pre-eclampsia" is the stage just preceding the outbreak of convulsions, or what we designate as typical eclampsia. It is indeed quite probable that pre-eclampsia is a manifestation of the same disease entity as eclampsia and differs from it only in so far as coma and convulsions do not occur. For this reason the pre-eclamptic patient should be considered as a potential eclamptic, and as soon as the existence of the condition is recognized it should be regarded as an urgent indication for termination of the pregnancy in order to prevent the outbreak of actual eclampsia.

It is interesting to note how small a proportion of the total number of our toxemic patients fall into this group; so that if our views are accepted they will effect a marked diminution in the number of cases designated as pre-eclamptic toxemia.

GROUP III. CHRONIC NEPHRITIS COMPLICATING PREGNANCY

A study of the cases in Table III will show that they all reveal signs of permanent kidney damage. The outstanding characteristics of this class are as follows:

1. The last pregnancy shows more renal involvement than the one preceding it. Usually this is shown by the fact that a rising blood pressure and the presence of albumin in the urine are noted far earlier in pregnancy than was the case in the previous pregnancy. This is true for all of our patients except one, and even in that case there was a higher blood pressure and more albumin in the urine at the end of the puerperium following the second pregnancy than after the first pregnancy.
2. The nitrogen partition in the urine is often disturbed, the ammonia nitrogen increasing and the urea nitrogen being relatively less in amount.
3. In some cases nitrogenous retention in the blood becomes quite appreciable, as is shown by a rise in the nonprotein nitrogen, as well as in the urea nitrogen.
4. Edema is quite marked in a large percentage of cases and sometimes persists throughout the puerperium.
5. At the end of the puerperium following the last pregnancy the blood pressure, especially the diastolic, has not returned to the normal level; and there is usually some albumin in the urine.

The cases in this class can probably be divided into two subgroups, namely, those who had developed a chronic nephritis prior to their first pregnancy, or between pregnancies, from such causes as scarlet

TABLE I—ECLAMPSIA
(Total 41 cases; 13 shown in this table)

NUMBER	AGE	PARA	PREG- NANCY	DATE	HEAD- ACHE	EDEMA	EYES	CON- VUL.	B. P. SYS.	B. P. DIAS.	URINE				BLOOD				REMARKS	
											Alb. Gm.	Urea % T. N.	NH ₂ N % T. N.	Micro- scopic	N. P. N.	Uric Acid	Urea N % N. P. N.	Sugar		CO ₂
13,923	16	1	7 mo.	8/31/24	++	++		15	180	110	9.5	66.1	21.1	Many casts	40.8	7.3	69		24.5	Child premature Stillborn. Macerated
14,051	44	15	9 mo.	9/14/24	++++	++		22	128	88	0.1	86.8	4.8	No casts	60.0	8.8	22		12.4	Delivery spontaneous Premature Child died 1st day
				184					110	32.5	41.4	3.2	Many casts							
14,096	22	1	Term	10/20/24	No	No		25	130	100	0.1	78.2	8.4	No casts	40.0	4.0	50	189	48.1	Delivery (forceps) on 10/12/24 Child normal
				160	110	1.0			68.1	13.7	Few casts	40.0	7.3	30	15.5					
14,106	18	1	Term	10/11/24	++	++		8	105	70	0.1	72.1	10.1	No casts	37.5	5.3	30	109	55.7	Delivery spontaneous (Bougie on 10/21/24) Child normal
				150	112	0.7			81.1	8.5	No casts	60.0	5.3	21	400	16.8				
14,124	17	1	Term	10/15/24	+++	+++		11	120	90	0.0	86.0	4.2	No casts	28.2	4.7	33	133	33.8	Delivery (forceps) on 10/23/24 Child normal
				192	124	2.2			74.3	11.9	Few cast									
14,127	18	1	9 mo.	10/22/24	No	++	Few retinal hemorrhages	7	108	70	0.2	80.2	4.1	No casts	35.3	3.6	33	127	52.6	Delivery (forceps) on 10/22/24 Child normal
				194	119	5.0			66.1	5.4	No casts	35.3	5.3	20	167	49.8				
14,344	33	4	Term	10/20/24	No	No	Retinal edema	1	114	72	0.1	70.1	6.0	No casts	41.0	4.0	118	52.8	Delivery spontaneous on 12/30/24 Child normal	
				126	82	0.75			55.0	9.0	No casts									
14,529	29	1	Term	11/10/24	+	++++	Some retinal edema	7	200	104	6.0	62.7	7.6	No casts	35.3	3.1	32	122	46.2	Delivery (Breech) twins Children normal
				116	74	0.1			72.4	7.0	No casts	37.5	3.6	35	143	31.9				
14,532	23	1	Term	2/ 7/25	+	+++	Slight retinal edema	1	203	124	8.0	70.5	7.8	Many casts	31.6	3.6	21	130	38.7	Delivery spontaneous Child normal
				134	84	0.1			76.1	7.8	No casts									
14,613	25	1	Term	3/ 2/25	No	++	Exam. neg.	2	170	105	15.0	76.5	10.9	No casts	35.5	4.7	41	190	29.8	Delivery (forceps) Child normal
				96	68	0.3			60.9	10.9	No casts									
14,633	36	4	9 mo.	3/20/25	No	No	Exam. neg.	11	220	120	28.0	64.5	11.1	No casts	31.6	4.0	50	125	43.1	Delivery (Bag) on 3/3/25 Child stillborn
				116	82	0.1			73.5	6.6	No casts									
14,941	15	1	9 mo.	5/21/25	+++	+++	Exam. neg.	3	165	90	0.0	79.2	3.2	No casts	33.3	4.0	105	27.1	Delivery (forceps) on 5/22/25 Child normal.	
				120	38	0.1			85.4	7.4	No casts									
15,002	37	4	7 mo.	5/28/25	+++	+++	Exam. neg.	4	165	110	25.0	60.0	22.1	No casts	182	28.1	182	28.1	Delivery spontaneous (Bougie) on 6/7/25 Child premature. Stillborn	
				140	100	0.1			80.9	9.6	No casts									

fever, tonsillitis, infectious diseases, myocarditis, or any of the conditions which may lead to chronic nephritis; and those in whom repeated pregnancies might have played a rôle in the development of the nephritis. The past history of the patient will prove of value in determining such relations.

It is highly important that the obstetrician determine whether or not the toxemia falls into this group, for his advice to the patient and the treatment of the pregnancy will be governed accordingly. When there are definite signs of chronic nephritis it is unwise to allow the occurrence of further pregnancies, for each subsequent pregnancy leads to an earlier "break" in the kidneys and to more permanent damage to the renal tissue. In exceptional instances the mother is overanxious to have a living child and is willing to make any sacrifice for that purpose, but such are very rare.

GROUP IV. ECLAMPSIA SUPERIMPOSED UPON NEPHRITIS

In Table IV appear the data afforded by a number of patients who were discharged with the diagnosis of "nephritic toxemia with convulsions." In this table, as well as in Table I, we have given only the findings for the day before delivery, or during the convulsion period, and for the day of discharge.

Of the five patients in this table, three undoubtedly have a definite chronic nephritis, while the other two present signs of a mild nephritis; at the same time, it seems quite doubtful to us that the convulsions in these five patients were due to a uremia rather than to true eclampsia. Out of a total of 50 patients in our series with convulsions (40 in Table I, 4 in Table II, 5 in Table IV and 1 in Table III), we feel that we can classify 45 as typical eclampsia, i.e., 90 per cent, and we are of the opinion that the remaining 10 per cent are probably also of the same nature; if this is the case we have to deal with an eclampsia superimposed upon a chronic nephritis. This belief seems justified when one studies carefully the doubtful cases in Table IV, and when one bears in mind that in all the toxemia patients without convulsions, studied during the period under consideration, there are distinctly more than 10 per cent with permanently damaged kidneys. Moreover, while there may be signs of a moderate retention of nitrogenous material in the blood, the figures never approach the height of those observed in actual uremia.

It is not the purpose of this paper to attempt to discuss the cause of eclampsia, but it seems pertinent to know how far the kidneys may be involved in this disease. The large amount of albumin in the urine appearing rather suddenly may be due to the action of a toxin on the glomerular capillary wall, or to any factor that may change the capillary permeability, or possibly to an arterial spastic contraction, as is assumed by some authors. The high filtration pressure, as evidenced

TABLE II—ECLAMPSIA AND PRE-ECLAMPSIA, FOLLOWED BY SUBSEQUENT PREGNANCY

(Total 7 cases; 3 shown in this table.)

NUMBER	AGE	PARA	PREGNANCY	DATE	HEAD-ACHE	EDEMA	EYES	CONVUL.	B. P. SYS.	B. P. DIAS.	URINE		BLOOD				DIAGNOSIS	REMARKS	CORRECTED DIAGNOSIS
											Alb. Gm.	Microscopic	N. P. N.	Uric Acid	Urea N % N. P. N.	CO ₂			
11,404	35	6	Term	9/30/21	No	++		I	190	100	9.0	No casts						B. P. 150/105, and albumin 3 gm. 1 week before admission	Eclampsia followed by low reserve kidney
				10/ 1/21					185	100	14.0								
				10/ 2/21					220	124	18.0								
				10/ 3/21					160	100	0.75	Hyaline and granular casts					<i>Delivery-manual dilatation of cervix</i>		
				10/ 9/21				152	100	0.7									
				10/12/21					124	80	1.0						Eclampsia	Discharged	
				10/19/21					136	85	0.1								
"	36	7	Term	11/22/22	No	+++	No visual disturbances		180	110	2.8		28.3			50	B. P. 155/105 and albumin +++ past two weeks		
				11/27/22		++	Narrowing of arteries		162	100	0.5								
				12/ 3/22		+			160	94	0.2							<i>Delivery Version, Extraction-Bougie</i> Child normal	
				12/ 5/22					170	110									
				12/ 6/22			Slight retinal edema		125	70	0.6	Few granular casts	59.7	8.2		38.1			
				12/ 9/22					105	65	0.1	Granular casts							
	12/15/22				125	60	0.1	Granular casts					Nephritic Toxemia	Discharged					
"	38	8	Term	10/31/24	No	No			154	100	1.0		39.5	4.4	30	50.4	<i>Delivery Version Extraction.</i> Admitted in labor, child stillborn		
				11/ 1/24					156	98	0.2								
				11/ 5/24					140	85	0.0								
				11/ 6/24					132	80	0.0								
				11/11/24					125	76	0.0	No casts							
																Discharged			

TABLE II—CONT'D

NUMBER	AGE	PARA	PREG-NANCY	DATE	HEAD-ACHE	EDEMA	EYES	CON-VUL.	B. P. SYS.	B. P. DIAS.	URINE		BLOOD				DIAGNOSIS	REMARKS	CORRECTED DIAGNOSIS			
											Alb. Gm.	Microscopic	N. P. N.	Uric Acid	Urea N % N. P. N.	CO ₂						
12,692	18	1	8 mo.	7/10/23	+	+++	Examination Normal	2	166	100	12.0		45.4			45.7						
				7/12/23					170	110	18.0		46.0			38.1						
				7/14/23 7/23/23	No	No			145 120	100 75	5.0 Very faint trace		45.4 39.5			4.7				45.7 47.5		
			8/ 1/23	No	No			110	75	Very faint trace		58.8		55.1	Nephritic Toxemia and Convulsion	Cesarean Section Child premature Died 2nd Day	Eclampsia followed by Nephritis					
"	20	2	9 mos.	3/24/25	No	++	Slight retinal edema and few hemorrhages		200	134	2.6		5.1	29	47.9							
				4/ 3/25	No	+			172	130	0.5		Nephritic Toxemia									
				4/ 8/25	No				166	132	1.8											
				4/17/25	No				118	40	0.4											
				4/23/25	No				120	88	0.2											
13,124	25	8	9 mos.	12/14/23	+	++			202	114	4.5	No casts	29.4	4.0	50	43.3						
				12/16/23	No	+			180	108	2.0		30.0							6.1	37.5	42.4
				12/28/23	No				146	98			39.5							4.7	49	33.8
				1/ 2/24					154	110	0.2		37.2							4.1	40	54.8
				1/10/24					145	95	0.1		Few hyaline and granular casts									
				1/22/24					122	80												
"	26	9	Term	5/15/25	No	+			150	90	0.0											
				5/25/25	No						0.0									Normal	Spontaneous Delivery Admitted in labor Child Normal Discharged	Pre-eclampsia Toxemia followed by probable low reserve kidney

TABLE III—CHRONIC NEPHRITIS COMPLICATING PREGNANCY

(Total 7 cases, 3 shown in the table)

NUMBER	AGE	PARA	PREG-NANCY	DATE	HEAD-ACHE	EDEMA	EYES	CON-VUL.	B. P. SYS.	B. P. DIAS.	URINE		BLOOD					PTHAL-EIN	DIAGNOSIS	REMARKS	CORRECTED DIAGNOSIS		
											Alb. Gm.	Microscopic	N. P. N.	Uric Acid	Urea N % N. P. N.	CO ₂	Cl.						
12,588	25	4	4 mo.	11/ 4/21	No	No	Slight disturb- ance		175	110	1.0	No casts									First three pregnancies showed no signs of toxemia although last two resulted in miscarriages	Signs of kidney involvement early in 4th and 5th pregnancies Nephritis	
				11/ 5/21	No	No	Examination Arteries con- tracted		110	70	0.1												
				11/ 6/21	No	No			135	95	0.1												
				11/13/21	No	No	Examination negative		105	70	Faint trace							87	Pre-eclamp- tic tox- emia	Discharged			
				11/14/21	No	No			100	70													
26	5	5	6 mo.	1/25/22	+++	++	Examination negative		190	120	3.0	No casts											
				1/28/22	++	+			170	115	1.0												
				2/ 2/22	+				160	95	0.5		23					591	58				
				2/ 8/22					155	95	0.5												
				2/12/22					150	100	0.3												
				2/16/22					150	100	0.3												
27	6	5 1/4 mo.	5 1/4 mo.	6/16/23					195	130	1.0	No casts											
				6/18/23					200	130	0.5												
				6/20/23	+	No			205	140	0.5		48.9						39.1				
				6/22/23					155	110	0.6												
				6/24/23					155	115	0.5												
				6/26/23			Examination negative		150	100			65.6							43			
				11/21/23	++	+			180	135	1.0												
				11/25/23					155	115	.5		29.7	4.2							35		
				12/ 5/23					156	102	1.0												
				12/30/23	+	++++			140	108	1.0		44.4	5.7									
				1/ 6/24		+++			170	125	0		26.9	4.7									
1/12/24		+++			175	120	0																
1/15/24		++			170	115	0.5																
				1/28/24		+			160	110													

TABLE III--CONT'D

NUMBER	AGE	PARA	PREGNANCY	DATE	HEAD-ACHE	EDEMA	EYES	CON- VUL.	B. P. SYS.	B. P. DIAS.	URINE		BLOOD					PHTHAL- EIN	DIAGNOSIS	REMARKS	CORRECTED DIAGNOSIS											
											Alb. Gm.	Micro- scopic	N. P. N.	Uric Acid	Urea N % N. P. N.	CO ₂	Cl.															
13,513	20	1	Term	8/13/23	No	+	Normal		130	85	2.0	No casts																				
				8/21/23	No				115	70	0.0																					
				8/25/23	No						0.0																					
	21	2	4 mo.	3/15/24		++	++++			135	90	34.0	Few casts	19.9	2.6			67														
					3/20/24		++++			155	100	36.0		24.3	1.7																	
					4/ 7/24		+++			140	90	24.0		21.8	2.4																	
					4/29/24		++			140	85	8.0		20.1	2.7														49.2	488		
					5/15/24		++			135	75	1.0																	45.1	554		
					5/17/24		+			140	80	1.0		34.5	3.4														43	43.5	544	
					5/26/24					135	85	0.3		42.8	4.2														26	47.1	544	
6/13/24							137			94	4.0	27.3		3.4																		
6/22/24																																
11,805	26	9	9 mo.	2/23/16	+	No	Examination normal				1.0	No casts																				
				3/ 1/16	No																							170	100	0.5		
				3/ 6/16	No																							170	95	0.1		
				3/11/16	No																							170	95	0.1		
	29	10	Term	2/23/19	No	No	Normal	Normal				0.0																				
					Normal	Normal delivery at home																										
	31	11	9 mo.	2/ 2/21	No	No	Examination acute exuda- tive retinitis			255	220	0.9							50													
					2/ 3/21																									265	220	1.0
					2/13/21																									185	140	0.4
					2/18/21																									215	140	0.9
					3/ 2/21																									190	140	0.2
	3/11/21		170	120	0.0																											
32	12	3 mo.	5/ 3/22	++	No				230	135	0.1	Gran- ular casts	29.1				63.9	501	48													
				5/ 7/22																									175	115	0.1	
				5/ 9/22																									170	100	0.1	
				5/17/22																									190	110	0.1	
				5/27/22																									165	100	0.1	
				Examination Arterioscler- osis																												

TABLE IV—ECLAMPSIA SUPERIMPOSED UPON NEPHRITIS

NUMBER	AGE	PAR-ITY	DURA-TION OF PREG.	DATE	HEAD-ACHE	EDEMA	EYES	CON-VUL.	B. P. SYS.	B. P. DIAS.	URINE		BLOOD				REMARKS	
											Alb. Gm.	Micro-scopic	N. P. N.	Uric Acid	Urea %	N. P. N.		CO ₂
12,150	40	VII	Term	11/29/22	+++	++++	Dimness of vision	2	260	130	22.0	Many gran. casts	43.8			46		
				12/22/22	No	No				152	95	1.8		30.6	2.3			62.8
13,120	34	IV	8 mos.	1/ 7/24	++	+++	Retinal edema Retina detached	6	220	140	21.0	Many hya-line casts	34.7	4.9	40	45.3	Delivery—Spontaneous (Bougie) Child premature stillborn	
				1/21/24	No					158	114	0.8	Occas. cast	34.9	3.7	47		45.0
10,917	26	III	Term	1/30/21	No	+++		4	208	160	5.0	No casts		20.0	2.0	65	48	1st preg. 7 convul. delv. by C. S.; 2nd, 1 convul. p.p. Delivery—Spontaneous (Bougie) Stillborn Transferred to medicine Discharged, diagnosis chronic nephritis
				2/ 8/21	No	++	212		152	0.8								
				2/25/21	No		140		100	0.5								
				3/18/21	No	No	134		100	0.1								
11,375	34	II	6 mos.	9/22/21	+	+++	Albuminuric retinitis	3	205	120	12.0	Many casts					Delivery—Spontaneous (Bougie and Bag) on 9-26-21. Child premature—macerated. Died p. m.: Peritonitis, subacute nephritis, beginning arteriosclerosis.	
				10/ 4/21	No	No				150	84	1.5	Many casts					
11,441	25	I	7 mos.	10/24/21	+++	++++		3	190	120	40.0	Many casts					Delivery—Version. Extraction (Bougie, Bag and Manual Dilatation). Child stillborn. On 1-2-21 in dispensary. B. P. 165/100; albumin ++	
				11/12/21	No	No	Slight retinal edema				95	60	1.2	No casts				

by the greatly elevated blood pressure, seems to be definitely associated with this passage of protein through the capillary wall of the glomerulus. On the other hand, the sudden return to an albumin-free urine must mean that the causative factor had functioned only temporarily, and that no permanent damage had been done to the capillary wall. This is highly suggestive of a temporary change in capillary permeability. Furthermore, the postmortem histologic findings in the eclamptic kidney suggest that there is usually no damage to the capillary walls or to the glomerulus itself. The most frequent changes are seen in the tubules and these are most probably the result and not the cause of the clinical picture. We are, therefore, led to the conclusion that eclampsia does not usually damage the kidney, but that in a small percentage of cases the eclampsia has been superimposed on a chronic nephritis.

GROUP V. LOW RESERVE KIDNEY

Table V includes a series of cases which present what we call, for lack of a better name, "low reserve kidney." From a study of these patients one is immediately struck by the following features:

1. An elevated blood pressure which at the end of the puerperium has dropped to a normal level. In most instances this elevation is not very marked, being approximately 150 systolic and 90 diastolic.
2. The amount of albumin in the urine is never very great, varying before delivery between a fraction of a gram and two grams per liter, although the lower figures are most usually observed. The albumin disappears during the puerperium, and the patient leaves the service either with no albumin at all, or with at the most 0.1 gram per liter.
3. The outstanding characteristic is the fact that in subsequent pregnancies, the patient's condition does not become aggravated, and she is as well as, or better than, in the preceding pregnancy. Each of our fourteen cases clearly demonstrates this point.
4. The blood chemistry, as well as the urine chemistry, reveals nothing abnormal.

That the number of pregnancies through which the individual may go plays any rôle in the development of this entity is very doubtful, for the reason that we observe it in primipara as well as in all degrees of multiparity. Moreover, this type of kidney does not seem to be permanently injured by pregnancy. As the woman approaches term a certain amount of albumin may pass through the glomerular membrane, the blood pressure become elevated, and some edema exist. With regard to the latter point it is interesting to note that in subsequent pregnancies there is either no edema or at the most a slighter degree than before.

It is well known that in a healthy person, under normal conditions, all of the glomeruli are not functioning at capacity at any one time, and it has been estimated that there is usually a margin of safety which approaches 50 per cent. In other words, there is a decided

TABLE V—LOW RESERVE KIDNEY

NUMBER	AGE	PARA	PREG-NANCY	DATE	HEAD-ACHE	EDEMA	EYES	CON-VUL.	B. P. SYS.	B. P. DIAS.	URINE		BLOOD				ORIGINAL DIAGNOSIS	REMARKS		
											Alb. Gm.	Microscopic	N. P. N.	Uric Acid	Urea N % N. P. N.	CO ₂				
12,992	21	3	8½ mo.	7/15/20	+	+			172	114	1.0	Hyaline and granular casts						B. P. 180/115 and 1 gram albumin in dispensary on 7/1/20		
				7/26/20					140	100	0.8									
				8/ 9/20					128	100	0.3									
				8/25/20	No	No			125	90	0.7	Hyaline casts								
				9/ 3/20																
					9/13/20					114	75	0.3 0.0						Pre-eclamptic toxemia	Delivery spontaneous Child stillborn, macerated. Discharged	
		22	4	Term	7/15/21	No	++ No			120	80	0.8	No casts						Nephritic toxemia	Edema and slight hypertension, since 3rd month Delivery spontaneous Child normal Discharged
	7/21/21								122	80	0.1									
	7/23/21								115	80	0.1	No casts								
	7/25/21								120	80	0.1									
				8/ 5/21					120	80	0.0	No casts								
	24	5	9 mos.	11/23/23	No	No			134	68	0.0 0.0	No casts						Nephritic toxemia	Delivery spontaneous Slight hypertension and trace of albumin since 8th month admitted in labor. Discharged.	
						12/ 3/23														
15,475	27	8	Term	5/20/21	No	+++ No	Dimness of vision		195	125	0.3							Nephritic toxemia	Delivery spontaneous Child normal Discharged	
				5/28/21			Exam.: nerve head blurred few hemorrhages Retinal edema with exudate		165	110	0.1									
				6/ 6/21					135	95	0.0									
		29	9	8½ mo	2/24/23					130	80	0.1							Admitted for bronchitis and pyelitis Discharged—improved before delivery	
	3/ 3/23								125	80	1.5									
					3/ 9/23					120	80	0.1								
		29	9	Term	3/29/23			Slight blurring of optic nerve		145	100	0.1	No casts						Nephritic toxemia	Delivery spontaneous (Watson) Child normal Discharged
	4/ 3/23								135	85	0.1		26.1							
	4/ 6/23								130	78	0.1 less than		*			47.6				
					4/14/23					130	88	0.1								
				4/21/23					130	90	0.0									
	31	10	Term	10/ 1/25					125	80	0.0							Nephritic toxemia	Delivery spontaneous Child normal Discharged	
10/ 5/25								96	70	0.0										
				10/13/25																

TABLE V—CONT'D

NUMBER	AGE	PARA	PREG-NANCY	DATE	HEAD-ACHE	EDEMA	EYES	CON-VUL.	B. P. SYS.	B. P. DIAS.	URINE		BLOOD				ORIGINAL DIAGNOSIS	REMARKS				
											Alb. Gm.	Microscopic	N. P. N.	Uric Acid	Urea N % N. P. N.	CO ₂						
11,383	34	4	9 1/2 mo	9/12/21	No	No	No visual disturbances		122	86	0.2	Few casts Hyaline and granular casts					Pre-eclamptic toxemia	Discharged				
				9/28/21	No	No	Examination negative	140	95	0.5										Spontaneous delivery Admitted in labor		
				10/ 3/21				122	84													
				10/ 8/21					136	90	0.1								Pre-eclamptic toxemia	Child normal Discharged		
	35	5	1 1/2 mo	9/ 5/22	+	No			160	110	0.1	Hyaline and granular casts										
				10/ 5/22			Examination negative	130	100	0.1												
10/14/22				138				92														
10/18/22				118				82														
		10/25/22						0.1	0.1	No casts								Nephritic toxemia	Spontaneous delivery Child normal Discharged			
13,517	23	1	Term	4/10/21	No	++			155	95	0.1	No casts										
				5/ 5/21	+	+	160	100	0.0													
				5/ 8/21			170	120	0.1													
				5/11/21			160	110	0.0													
				5/19/21			130	85	0.1													
				5/22/21			110	70	0.0													
	26	2	Term	3/11/24	No	No			150	80	0.2	No casts										
				3/14/24	No	No	120	70	0.1													
				3/26/24			116	74	0.0													
13,174	40	5	Term	4/ 1/22	No	+			135	65	1.0	Many granular casts										
				4/ 4/22	No	No	130	75	1.0													
				4/11/22			118	76	0.1													
				4/14/22			120	74														
	42	4	Term	1/ 8/24		+			130	80	0.2	No casts										
				1/10/24			135	80	0.1	No casts												
		4	Term	1/15/24	No	+			140	85	2.0	No casts	33.3	2.9	48	39.5						
				1/18/24	No	+	140	82	1.0	No casts	30.0	3.9	50	41.4								
				1/25/24			135	85	0.1													
1/28/24				110			74	0.1														
2/10/24	114	70	0.1	No casts																		

TABLE V—CONT'D

NUMBER	AGE	PARA	PREG-NANCY	DATE	HEAD-ACHE	EDEMA	EYES	CON-VUL.	B. P. SYS.	B. P. DIAS.	URINE		BLOOD				ORIGINAL DIAGNOSIS	REMARKS	
											Alb. Gm.	Micro-scopic	N. P. N.	Uric Acid	Urea N % N. P. N.	CO ₂			
15,972	24	4	7 mo.	9/20/15	No	No			—	—	0.0						Previous pregnancies quite normal <i>Delivery normal</i>		
			5	Term	12/15/21				—	—						Normal	Delivered by obstetrical outside service of hospital Child normal, discharged		
	34	6	9½ mo.	12/26/24		++++			204	128	0.5	No casts	24.2	4.2	33	48.6	On 10/21/24 an elevation of B. P. was noted in the dispensary <i>Delivery spontaneous (Foorheer bag)</i> Child stillborn		
				12/28/24			220	128	0.5										
1/ 1/25			185	128	0.5														
1/ 3/25			206	130	1.0														
				1/ 6/25				160	95	0.1							Pre-eclamptic toxemia	Discharged	
				1/14/25				138	90	0.1									
	35	7	Term	2/14/26	No	No		140	90	0.1		24.0	4.0	47.		<i>Delivery spontaneous</i> B. P. 140/80 on 11/10/25 in dispensary Admitted in labor Child normal Discharged			
			2/16/26				130	80	0.0										
			2/24/26				118	70	0.0										
11,569	20	3	7 mo.	1/ 1/21	No	No	Examination negative	190	130	1.0	Few granular casts						For past two weeks swelling of ankles and ++ albumin in dispensary First 2 pregnancies were premature at 6th and 8th months Discharged Improved		
				1/19/21				175	125	0.5									Pre-eclamptic
				1/23/21				140	105	0.25									
				1/25/21				115	85	0.0									
				8 mo.	2/ 4/21	+	No		150	100	0.1							<i>Spontaneous—premature</i> Child premature Stillborn macerated Discharged	
					2/ 6/21				130	85	0.1								
				2/14/21				130	95	0.0									
	21	4	8 mo.	1/ 6/22	No	No		160	120	2.0							<i>Spontaneous—premature</i> Admitted in labor Child premature, lived 1 day Discharged		
				1/ 9/22				145	100	1.0									
				1/14/22				110	80	0.5									
				1/15/22				110	80	0.1									
13,856	22	4	Term	6/10/21	No	No		130	85	1.6	No casts						<i>Spontaneous delivery</i> Child normal Discharged		
				6/20/21	No	No		115	65	0.0	No casts								
	24	5	Term	2/17/23				124	90	0.1	Few granular casts						Normal	<i>Spontaneous delivery</i> Child normal Discharged	
				3/ 1/23				120	80	0.1									
	25	6	Term	8/14/24	No	No		102	68	0.0	No casts						Normal	<i>Spontaneous delivery</i> Child normal Discharged	
				8/25/24	No	No				0.0	No casts								

NOTE.—There are 6 more patients (hospital numbers 11,317, 11,954, 13,908, 13,946, 13,985 and 14,134), not shown in this table because of lack of space. They all had a pregnancy with low reserve kidney, practically almost identical with the above, and followed by a subsequent normal pregnancy in which there was no sign of any form of toxemia.

kidney reserve which may be called into play. It seems reasonable to suppose that in certain individuals this kidney reserve may be greatly decreased, due either to congenital causes or to such factors as may have lessened the number of functioning glomeruli without producing a chronic nephritis. As we have seen in another group of cases, the strain of pregnancy always aggravates a chronic nephritis, so that later the kidneys are less well prepared to stand the strain of subsequent pregnancies. In the type of kidney under consideration this is not the case. All we can say is that the kidney reserve seems to be too low to meet the extra demands of pregnancy, as is manifested by the passage of a certain amount of albumin through the glomerular epithelium and by a moderate elevation of blood pressure, and that these manifestations usually disappear completely within two weeks after delivery. Furthermore, the kidney substance does not seem to have been injured by the pregnancy and the kidney reserve is certainly not lower for subsequent pregnancies. Such kidneys appear to be quite capable of functioning adequately while the woman is not pregnant, as well as for her and her fetus up to about the eighth month of pregnancy, when manifestations of the low reserve kidney begin to make their appearance.

In addition to the eight cases reported in Table V, we have been able to find six more patients who, during the period studied, had had a pregnancy with the typical signs and symptoms of a low reserve kidney, which was subsequently followed by a normal pregnancy. Such observations may be regarded as indisputable evidence that the occurrence of a mild toxemia in a given pregnancy is not necessarily followed by trouble in a subsequent one, and would accordingly indicate that the kidneys had not been permanently damaged.

Table II, as stated above, represents the findings in patients who have had eclampsia or pre-eclampsia, and who have been observed in subsequent pregnancies in this hospital. An examination of the results tabulated in this table will convince us that eclampsia or pre-eclampsia can be followed by eclampsia in a succeeding pregnancy, or by a low reserve kidney, as well as by definite nephritis.

The hospital records show that for the period January 1, 1923, to February 1, 1926, there were 10 eclamptic patients who were subsequently admitted to our service and that these pregnancies following typical eclampsia can be grouped as follows: (a) 4 normal pregnancies; (b) 4 complicated by nephritis; (c) 2 typical eclampsia, and (d) 1 with low reserve kidney.

One of the patients is shown in both groups (b) and (c).

Table VI represents a study of averages, and still further accentuates the differences discussed above. The similarity between eclampsia and pre-eclampsia is outstanding, and it offers conclusive evidence as to how markedly these two types differ from chronic nephritis

TABLE VI. AVERAGES

TYPE	TOTAL CASES	TOTAL ADMIS- SIONS		BLOOD PRESSURE		URINE			BLOOD					
				Systolic	Diastolic	Alb. Gm.	Urea N % T. N.	NH ₃ N % T. N.	N. P. N.	Uric Acid	Urea N % N. P. N.	Sugar	CO ₂	Chlo- rides
Eclampsia	40	41	Before delivery	183	109	9.9	67.97	9.36	34.85	6.3	41	155	37.2	523
			At discharge	116	76	0.1	75.58	6.65	33.23	4.4	39	137	52.2	504
Pre-eclampsia	2	4	Before delivery	181	112	8.0	—	—	39.5	4.7	49	—	33.8	508
			At discharge	116	77	0.1	—	—	37.2	4.1	40	—	54.8	491
Chronic nephritis	7	24	Before delivery	176	112	3.2	46.9	5.4	33.97	6.1	38	110	41.2	536
			At discharge	137	95	0.5	61.3	5.4	37.4	3.3	32	96	47.3	488
Eclampsia superimposed on chronic nephritis	5	5	Before delivery	217	132	20.0	67.9	8.0	39.25	4.9	40	—	45.65	463
			At discharge	138	91	1.1	86.4	3.0	28.5	2.66	56	—	51.73	493
Low reserve kidney	14	36	Before delivery	143	92	0.4 less than	68.7	5.5	26.7	3.9	45	102	42.7	510
			At discharge	120	80	0.1	76.5	6.15	30.1	4.0	—	72	53.6	—

and that associated with a low reserve kidney. Hardly less marked differences exist between chronic nephritis and the low reserve kidney. In this connection it may be stated that the phenolsulphonephthalein kidney test is not of very great value in a study of the toxemias of pregnancy, and it by no means constitutes a method of distinguishing between the several types.

CLASSIFICATION

From a study of the 120 admissions of patients presenting one or other type of the toxemias of pregnancy, we suggest the following classification for the late toxemias of pregnancy: (1) Eclampsia, (2) Pre-eclampsia, (3) Chronic nephritis, complicating pregnancy, (4) Eclampsia superimposed upon nephritis, and (5) Low reserve kidney. It should be clearly understood that an intelligent differential diagnosis can often not be made until the end of the third week of the puerperium. Consequently, we advise that in the borderline cases the final diagnosis be deferred until as late as possible. This is the mode of procedure in this clinic, and in the future in doubtful cases the final diagnosis will be deferred until six weeks after delivery, when the patient will be readmitted to the service and be subjected to searching clinical and chemical investigation.

CONCLUSIONS

1. *Eclampsia*.—This is a fairly definite entity. The convulsions and coma, the relatively sudden appearance of a greatly elevated blood pressure and a large amount of albumin in the urine occurring during the last third of pregnancy, but more frequently in the neighborhood of term, and the complete return to normal at the end of the puerperium constitute the usual picture. Often one sees an increase in the amount of uric acid in the blood, an elevated blood sugar, and a low CO₂ combining power associated with a large amount of ammonia in the urine, all of which rapidly disappear during the puerperium. Ophthalmoscopic examination may show a detachment or edema of the retina, but never any sign of albuminuric retinitis, or of the other changes which are so frequently associated with nephritis.

The edema of the extremities, face, and other parts of the body, which is usually present, disappears completely during the puerperium. Eclampsia is seen more frequently in the young primipara than in the multiparous woman.

There is no evidence that eclampsia per se does any permanent damage to the kidneys and, for this reason, should not be considered a counter-indication for further conception.

2. *Pre-eclampsia*.—This seems to be a definite entity and differs from eclampsia only in so far as the patient has no convulsions or coma, and that the attack may be of a milder character. Our studies seem

to indicate that this is probably the rarest variety of toxemia of pregnancy, and that its incidence will not exceed 5 per cent of all toxemic patients. Pre-eclampsia is probably just what the term implies, a stage immediately preceding eclampsia. Should the condition grow slightly worse, the patient will develop convulsions, unless pregnancy is promptly terminated.

Even casual reference to the literature makes it evident that the term "pre-eclamptic toxemia" has been very loosely used in the past. Some writers group under that designation all types of toxemias, and

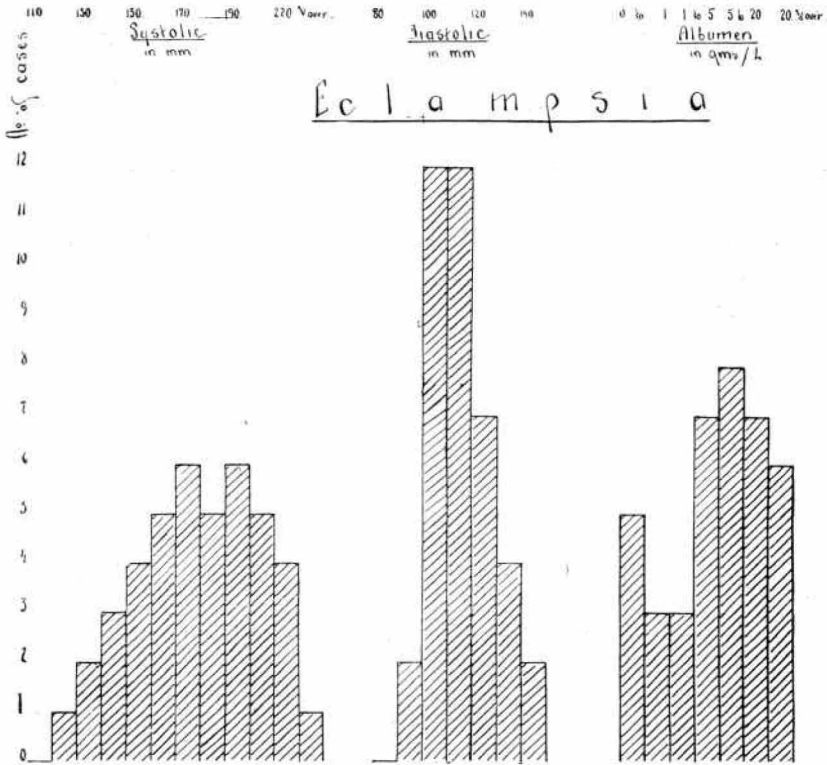


Fig. 1.

for that reason we have preferred to limit the use of the term "pre-eclampsia" or pre-eclamptic toxemia to the cases falling into the second group of our classification. Indeed, it might be well to discontinue altogether the use of the latter term, did it not imply too radical a break from current obstetric terminology.

3. *Chronic Nephritis Complicating Pregnancy.*—In this group the process is progressive. Each subsequent pregnancy is associated with an increasing degree of renal impairment. The existence of chronic nephritis is evidenced by the fact that two or three weeks after delivery the blood pressure still remains above the normal level. In

such cases the diastolic level is of especial value, and in the table of averages, it is noted that the patients with chronic nephritis are usually discharged with a diastolic pressure of well over 90, and in addition with about half a gram of albumin in the urine. The nitrogen partition in the urine may also be upset, together with an increase in the N.P.N. An examination of the eye-grounds may show an albuminuric retinitis and arteriosclerosis, or some other sign of involvement, such as edema or hemorrhage of the retina.

A careful study of all the data obtained during the patient's stay in the hospital, as well as at the time of discharge, will reveal some

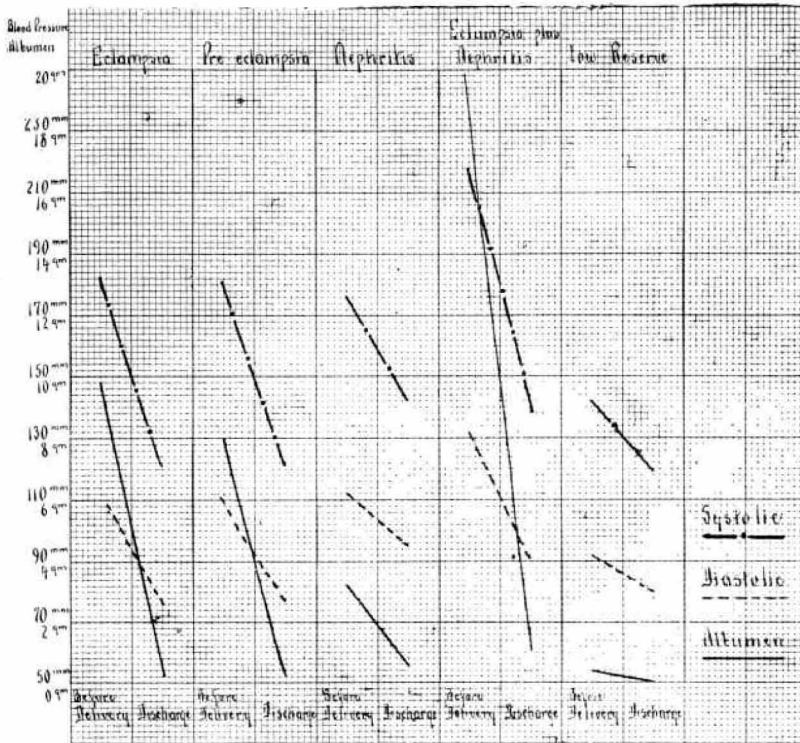


Fig. 2.

manifestation of chronic nephritis. It is of the utmost importance to remember in subsequent pregnancies these manifestations become more marked and usually appear earlier in the course of pregnancy. There is also a greater incidence of abortions and miscarriages.

In the woman with chronic nephritis, pregnancy is indeed a serious matter, as the extra load of each succeeding pregnancy leads to progressive kidney damage.

We believe that the patients who were formerly considered as suffering from "nephritic toxemia in convulsions" in reality had eclampsia superimposed upon a chronic nephritis, and that they rep-

resent only a very small proportion of all eclamptics. This statement should not be understood as implying that pregnant women may not succumb to an acute uremic attack, but no indubitable example of it has been observed in the present series.

4. *Low Reserve Kidney.*—During the last few months of pregnancy, there may appear a moderate rise of blood pressure, usually about 150/90, and relatively small amount of albumin in the urine, ranging from a fraction of a gram to a gram, to very slightly over one gram just before delivery. There may also be some edema and very rarely a complaint of headache. By the end of the puerperium the blood pressure has resumed its normal level, the urine contains no albumin, or only a faint trace, and any edema that may have been present, has disappeared. At no time are there any signs of a disturbed blood chemistry, and the nitrogen partition of the urine is normal. In subsequent pregnancies a similar picture may recur. In other cases it may be less severe, but is certainly not worse, while occasionally the patient is entirely normal.

Pregnancy does not injure this type of kidney, and when we are sure that the toxemia is due to it, we need feel no alarm concerning the course of subsequent pregnancies.

Eclampsia may be followed by a normal subsequent pregnancy, by a pregnancy complicated by a low kidney reserve, by a chronic nephritis, or rarely by a repeated attack of eclampsia.

In conclusion, we would refer to the accompanying graphs (Figs. 1 and 2) in which we have plotted the average systolic and diastolic blood pressures, as well as the albumin in the urine for the various groups. Two values for each variable are recorded, the first referring to the findings before delivery, and the second to those at discharge. We feel that this graphic demonstration illustrates the difference between the several toxemic types even better than our description or than the figures in the various tables.