

TABLE II.
Routine Assay of Tryptase in Dog Prostatic Fluid.
A. Untreated; B. CHCl₃-treated.

Enzyme conc.	Incubation period						
	5'	15'	20'	30'	60'	75'	90'
Sample A	+	+	+	+	+	±	∞
Sample B	+	+	+	+	+	±	∞
10 units	+	∞					
5 "	+	+	+	+	+	±	∞
2.5 "	+	+	+	+	+	+	+

with untreated and CHCl₃-treated fluid.

Discussion. Numerous applications of the method to the assay of tryptic enzymes in plasma, serum, cell- and other materials are envisaged. The effects of inhibitors and other conditions modifying the action of known tryptases also lend themselves to quantitative investigation by simple modification of the cited technic. The new method (which may be styled Method B) offers the following advantages over the original¹ assay (Method A): 1. tenfold increase in sensitivity; 2. independence of enzyme-inhibitors in thrombin; 3. much less time-consuming—a matter of minutes or hours (actual test), instead of days, even with very weak enzymes; 4. sharper

“end-point,” since the enzyme acts in water-clear homogeneous colloidal solution, instead of on the grossly biphasic fibrin gel; 5. no special apparatus (*e.g.*, turbidimeter) required. Within their respective ranges and limitations, both methods are useful practical means of estimating natural trypsin-like proteolytic enzymes. Such enzymes play an important role in blood-coagulation¹¹ and other functions, to the elucidation of which it is believed that these technics may offer a material contribution. The methods are sufficiently simple to open up new fields as a clinical laboratory test.

¹¹ Ferguson, J. H., *Science*, 1943, in press.

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Toxemias of Pregnancy and the Inulin-Diodrast Clearance Tests.

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The role of the kidneys in the production of toxemia of pregnancy has been studied for many years, and as yet we have only a paucity of information. As one new kidney function test after another has been announced, investigators have applied them to the toxemias of pregnancy and have found them inadequate to detect alterations in the status of the kidneys.

It would seem so even with the newest of function studies, the inulin and diodrast clear-

ance tests. Chesley *et al.*¹ conclude that the renal blood flow is essentially normal in eclampsia, pre-eclampsia, and recurrent toxemia of pregnancy, as measured by the diodrast clearance. Corcoran and Page² feel that if the filtration fraction is

¹ Chesley, L. C., Connell, E. J., Chesley, E. R., Katz, J. D., and Glissen, C. S., *J. Clin. Invest.*, 1940, **19**, 219.

² Corcoran, A. C., and Page, I. H., *Am. J. Med. Sc.*, 1941, **201** n. s., 385.

TABLE I.

Averages of Tests Done Ante-partum and up to 12 Days Post-partum.					
No. of tests	Type of case	Plasma clearance of		Filtration fraction, %	Total renal blood flow, cc/min
		Inulin, cc/min	Diodrast, cc/min		
8	Normal	150	754	20.9	1208
7	Mild pre-eclampsia	109	579	19.0	938
7	Severe pre-eclampsia	115	531	21.4	879
3	Eclampsia	83	426	18.9	641
8	Hypertensive disease	145	613	23.6	990
Averages of Tests Done More Than 12 Days Post-partum.					
2	Normal	141	653	21.7	1097
7	Mild pre-eclampsia	121	553	21.9	901
9	Severe pre-eclampsia	138	612	21.9	1064
4	Eclampsia	112	539	20.0	938
6	Hypertensive disease	118	521	24.8	937

increased, the patient is not truly toxemic but rather pre-existingly or latently hypertensive, and that only those cases showing normal clearance can be classified as true toxemias. It is generally agreed^{3,4,5} that hypertensives show a decrease in total renal blood flow, with an elevated filtration fraction. However, hypertension with pregnancy is not a toxemia, it represents merely the co-existence of an abnormal with a normal condition in the same patient.

Welsh *et al.*⁶ studied 21 normal women, some of whom were tested both before and after delivery, by means of inulin, phenol red, and diodrast clearance tests. They conclude that kidney function is not altered in pregnancy nor in the puerperium. It is to be noted however that they record a slight decrease in the plasma clearances of both inulin and diodrast in the post-partum phase as compared to the ante-partum. These same authors⁷ using the same methods as above, and studying toxemic patients, believe that the inulin clearance is decreased during toxemia, but not sufficiently for the results to be out of the range of normal. The diodrast

clearance is normal or above normal in the ante-partum tests with a slight fall post-partum. The filtration fraction consequently is reduced ante-partum, and rises to and above normal post-partum. They believe that if clearance studies are done ante-partum and post-partum some aid as to the ultimate prognosis of the disease may be obtained.

We wish to report our findings on pregnant and post-partum women who have had one of the toxemias of pregnancy, and whom we studied with the inulin and diodrast clearance tests.

Methods. The patients used in this study were women who were under treatment for some form of toxemia of pregnancy, or who were admitted to the hospital specifically for this study. The procedures of the test are described by others.^{8,9} The clearance figures in all the tables are corrected to a surface area of 1.73 sq m using the DuBois Body Surface Chart.

Patients were classified as to their toxemia according to the prerequisites laid down in 1939 by the American Committee on Maternal Health.¹⁰

Results and Discussion. Our findings are summarized in the tables. A total of 52 patients were studied. Table I presents the average results found in all the studies, and

³ Foa, P. P., Woods, W. W., Peet, M. M., and Foa, N. L., *Arch. Int. Med.*, 1942, **69**, 822.

⁴ Chesley, L. C., and Chesley, E. R., *J. Clin. Invest.*, 1940, **19**, 475.

⁵ Friedman, M., Selzer, A., and Rosenblum, H., *J. A. M. A.*, 1941, **117**, 92.

⁶ Welsh, C. A., Wellen, I., and Taylor, H. C., Jr., *J. Clin. Invest.*, 1942, **21**, 57.

⁷ Wellen, I., Welsh, C. A., and Taylor, H. C., Jr., *J. Clin. Invest.*, 1942, **21**, 63.

⁸ Smith, H. W., Goldring, W., and Chasis, H., *J. Clin. Invest.*, 1938, **17**, 263.

⁹ White, H. L., and Rolfe, D., *Proc. Soc. Exp. Biol. and Med.*, 1940, **43**, 1.

¹⁰ Stander, H. F., *Am. J. Surg.*, 1940, **48**, 112.

TABLE II.
Eclampsia.

Case No.	Test ante-partum mo.	Test post-partum days mo.	Max. B.P.	Max. urinary alb., g 24 hr	Duration of alb., days	Casts	Hematocrit, %	Plasma clearance of		Filtr. fract., %	Total renal bl. flow, cc/min
								Inulin, cc/min	Diodrast, cc/min		
1 E		10	188/144	7	?	4-5	31	121	554	21.8	748
2 E		14	154/110	8	?	5	38	86	445	19.2	719
3 E		18	?	?	?	?	41.5	181	903	20	1544
4 E	1½		170/116	12	14	0	39.0	44	279	15.7	457
		4	120/88	tr	120	0	38.0	35	220	16.1	355
5 E		17	178/?	?	?	0	43.0	116	597	19.5	1048
6 E		23	204/130	9	?	Occas.	41.5	96	472	20.3	808

further compares the average values obtained on patients tested during pregnancy and up to 12 days post-partum with those obtained after the puerperal period. In the normal patients there is a slight decrease in both inulin and diodrast clearance in those patients studied post-partum as compared to the results in the patients studied ante-partum. This finding is essentially the same as that recorded by Welsh *et al.*⁶ We note a slight decrease in the glomerular filtration rate and total renal blood flow in both the mild and severe pre-eclamptics, but the values still are within normal limits. It is only in the eclamptic patients studied during or immediately after their eclampsia that any appreciable change is seen in the kidney function. In all these cases the filtration fraction is within normal limits. In the hypertensive of course we obtain the usual fall in glomerular filtration rate and total renal blood flow with a rise in filtration fraction.

Although the series of cases of eclampsia is small, the results recorded in Table II are of interest. The interval elapsed between the time of the eclampsia and the time of the test seems to be of some importance. In cases No. 1E, 2E, 4E and 6E where the interval is short the clearance values are definitely subnormal, whereas in cases No. 3E and 5E, where the interval is longer, normal results are obtained. This would lead one to speculate that there is some malfunction of the kidneys during and for a short time after the toxemia, but

that the malfunction is not the result of permanent kidney damage, since the function later returns to normal. Just what the nature of the functional abnormality of the kidneys is, is difficult to postulate since the filtration fraction remains normal throughout.

Case No. 4E is of particular interest, and is possibly an example of pregnancy complicated by nephritis with convulsions, rather than one of pure eclampsia. There is no clinical history of previous renal disease, and the pregnancy was uncomplicated until about 2 months from term at which time the blood pressure began to rise and albumin was first detected in the urine. Function studies done shortly after the onset of clinical symptoms showed a definite decrease in renal function, which is of course highly suggestive of previous renal damage. Very similar results were recorded some 4 months after delivery. Some 12 months after delivery the patient still had a blood pressure of 136/90 and a trace of albumin in the urine. It is to be noted in this case that the filtration fraction is quite low. This may also be indicative of previous kidney disease.

Summary. Results of inulin and diodrast clearance tests performed on 52 pregnant or post-partum females are presented. Eclampsia is the only toxemia which sometimes shows a decreased kidney function as evidenced by a diminution in the clearance of inulin and diodrast. The filtration fraction is normal in all toxemias of pregnancy.