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RENAL LESIONS IN THE TOXEMIAS OF PREGNANCY*

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This paper is based upon a study of the kidneys from 20 cases of toxemia of pregnancy. Particular attention is given to the structural changes in the glomeruli. The effect of pregnancy upon preëxistent nephritis is also discussed.

The clinical manifestations of the toxemias of pregnancy are so varied that it is difficult to arrange them in a logical classification. For the purposes of discussion, however, they may be divided into five groups: (1) typical eclampsia with convulsions; (2) eclampsia without convulsions; (3) preëclampsia; (4) hyperemesis gravidarum, and (5) pregnancy in association with preëxisting renal disease.

1. TYPICAL ECLAMPSIA WITH CONVULSIONS

The characteristic symptoms and signs in this disease are convulsions, hypertension, albuminuria, edema, headache, visual disturbances, nausea and vomiting, vertigo, restlessness, and, especially in fatal cases, coma. These symptoms are by no means all present in every instance, and apparently no single symptom is necessary to establish the diagnosis of eclampsia, but, by definition, typical eclampsia includes only those cases where convulsions are present.

The pathologist is justified in making a diagnosis of eclampsia if he finds hemorrhagic necroses in the liver in a case of pregnancy, but he cannot exclude eclampsia when no necrosis of the liver is found, since this lesion is occasionally absent.

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In order to form a basis for the interpretation of the renal lesions which are described in this paper, the various features of eclampsia will be discussed in some detail.

Hauch estimates the *frequency* of eclampsia in Denmark as 1 instance in every 569 births. Seitz gives a rate of about 1 to 500 in Germany. The rate in Baden over a period of fourteen years, according to Gessner, was 1 to 620. Hospital statistics naturally show a greater frequency of eclampsia. Schmechel, at the Dresden Frauenklinik, found 238 instances of eclampsia in 27,340 births (1 to 110); Meyer-Wirz at Zürich, 112 eclampsias in 13,139 births (1 to 117); and Strober at the Münich Frauenklinik, 336 eclampsias in 46,711 births (1 to 139). Theobald states that eclampsia is very rare in Siam but he gives no statistics.

Eclampsia is more frequent in *primiparae* than in multiparae. The usual hospital statistics show 70 to 80 per cent in primiparae. Strober, in 336 instances of eclampsia, found 71.1 per cent in primiparae, and 28.8 per cent in multiparae. Büttner found reports of 179 cases of eclampsia from all sources during a ten-year period in Mecklenburg-Schwerin. Of these 60.2 per cent were primiparae and 39.8 per cent multiparae. He suggests that the higher percentage of multiparae in his statistics is due to the fact that this group is less inclined to go to the clinics than the primiparae. On the basis of the relative frequency of primiparous and multiparous births Büttner calculates that 1 instance of eclampsia occurs to every 220 to 270 primiparous, and to every 1100 to 1300 multiparous births. The greater tendency to eclampsia in primiparae is well established but entirely unexplained.

Period of Gestation: Eclampsia rarely develops before the fifth month of gestation. Fehling, in a survey of 516 cases, found only 5 before the fifth month. A good survey of the literature of early eclampsia is given by Ebeler, who found reports of 55 cases before the fifth month. A few instances occurring in the second and third months are published.

Füth reviewed 56 published reports of early eclampsia. He states that there are only 11 postmortem reports, and that the details of even these are rather meager. Goedecke gives the following distribution of 306 cases of eclampsia, based on the weight of the fetus: 2–3rd month, 1; 5–6th month, 13; 6–7th month, 39; 7–8th month, 53; 8–9th month, 85; 9–10th month, 38; full term, 77 cases. In

an analysis of 384 cases Goedecke found that the first convulsion occurred postpartum in 70 (18.2 per cent). Peckham, in a report of 77 cases, found that 38 began antepartum, 24 intrapartum, and 15 postpartum. Schmechel grouped 238 cases as follows: antepartum 26, intra- and postpartum 184, and postpartum 28. Meyer-Wirz reported 62 antepartum, 32 intrapartum, and 23 postpartum. Strober, in a study of 336 cases of eclampsia, found that 80 began antepartum, 189 intrapartum, and 67 postpartum. It is not clear in any of these statistics how often preëclamptic symptoms were present before labor in the group in which the first convulsion occurred postpartum.

It is to be noted that eclampsia develops in the vast majority of instances after the fetus and placenta have attained considerable size. It is estimated that the symptoms are relieved by emptying the uterus in over 50 per cent of the cases. The fact that, in at least 10 per cent, the symptoms first appear postpartum might be explained as a delayed action of the hypothetical toxin, since eclampsia rarely sets in later than twenty-four hours after labor.

Eclampsia may develop as a complication of extrauterine pregnancy (Ebeler), or of ovarian pregnancy (Luniewski).

Wigger reported a case with eclampsia resulting from a hydatiform mole, and gives references to 8 other similar cases. The occurrence of eclampsia in association with moles indicates that if a toxic substance causes eclampsia it is to be sought for in the placenta rather than in the fetus.

Onset: Seitz states that in about 80 per cent of cases of eclampsia preëclamptic symptoms are present before the onset of convulsions. Wolff and Zade also find a gradual onset of symptoms in the usual case. But there is a less frequent type with sudden violent onset in which few or no warning symptoms are noted.

Recurrence: Hinselmann, 1924, from a survey of 10,000 cases of eclampsia collected from the literature, concluded that it recurs in about 1.92 per cent of subsequent pregnancies. On this basis, if we accept the incidence of eclampsia as 1 to 500 pregnancies, eclampsia is about ten times as frequent in those who have had a previous attack.

Some recent writers find a rather high incidence of recurrent eclampsia and toxemia. Schmechel, 1929, traced 83 women who had had pregnancies subsequent to eclampsia. Of these, 35 (42 per

cent) had normal pregnancies; 33 (40 per cent) had preëclamptic symptoms; and 15 (18 per cent) had eclampsia. 58 per cent of the women had eclampsia or preëclampsia in a subsequent pregnancy.

Young, 1929, traced 42 women who became pregnant again following an attack of eclampsia. In the 60 gestations which occurred, there were 3 instances of eclampsia, 15 of albuminuria and 6 of abortion, hemorrhage or premature labor. Complications occurred in about 40 per cent, but the recurrence of typical eclampsia was low.

Apparently a woman who has had an attack of eclampsia runs a great risk of developing some form of toxemia in a subsequent pregnancy, although typical eclampsia does not often recur. Some writers attribute the predisposition to toxemia, following an attack of eclampsia, to renal injury, but this view has not been established.

Convulsions: Convulsions are the characteristic feature of typical eclampsia, but the number of convulsions is very variable. Seitz, in a group of 147 cases, found 2 in which only one convulsion occurred. Some patients have tremors but not true convulsions. The convulsive attacks commonly follow the preëclamptic symptoms, but occasionally they precede the other symptoms. The convulsions are commonly attributed to injuries of the central nervous system, and this view is supported by the frequent finding of small hemorrhages, areas of softening and thromboses in the brain.

Convulsions are not a necessary part of the eclamptic picture. This topic will be discussed under "Eclampsia without Convulsions."

Edema: Zangemeister has shown that slight edema of the ankles especially, is found at times in practically all pregnant women. It is apparently due to retention of water by the tissues and not to passive congestion. In general, a moderate edema without albuminuria or other preëclamptic symptoms is not of serious import. Albuminuria is usually present with severe edema. In many instances of eclampsia and preëclampsia, edema is inconspicuous or absent. Edema is apparently not due to renal injury, since it commonly precedes albuminuria. Zangemeister believes that generalized capillary injury with increased permeability is the underlying cause of this form of edema. However, there is no direct evidence of generalized capillary injury. The retention of fluid may be due to injury of the tissues with increased affinity for water.

The Urine: Albumin is found in the urine in practically all instances of eclampsia. Usually it is found in large amounts, but occa-

sionally there is only a trace. In rare instances it first appears late in the illness after the convulsions (Theobald), and then only in small amounts. Cases have also been reported in which no albumin was found at any time either before or after the convulsions (Goedecke, Hiess and Beckmann, Austin, Meyer-Wirz, and Breuning). Albumin may appear in the urine or increase greatly in amount within a short time, so that repeated examinations are necessary to exclude its presence. However, it is well established that convulsions and hypertension may precede albuminuria.

There is usually a moderate oliguria during eclampsia. Sometimes only a little urine is excreted. In the rare form with cortical necrosis of the kidneys there is marked oliguria or anuria.

Erythrocytes are often found in the urine in increased numbers, but they are seldom as numerous as in acute glomerulonephritis. Gross hematuria is not often seen except in association with cortical necrosis. The presence of blood in the urine is, however, not inconsistent with the eclamptic kidney.

Blood Pressure: Hypertension is an almost constant symptom of eclampsia. Schwarz states that he has never seen an instance of eclampsia or preëclampsia without hypertension. Seitz, however, found 13 per cent of his patients with a systolic pressure below 130 mm. Hg. He found the systolic pressure over 150 mm. Hg. in 64 of 98 instances of eclampsia, and 30 of 35 instances of preeclampsia. Hiess and Beckmann reported 13 cases with no elevation of blood pressure on repeated examinations.

Heynemann calls attention to the marked lability of the blood pressure in eclampsia. A temporary hypertension is easily overlooked, especially when the patient is first seen late in the illness. Severe cases, particularly patients in coma, are apt to show a fall of blood pressure. In 8 of 56 cases which he studied carefully, the systolic blood pressure was not above 135 mm. Hg. The usual systolic pressure is 150 to 180 mm. Hg. Heynemann states that he has not seen a patient with pronounced preëclamptic symptoms who did not have hypertension.

Hypertension precedes the convulsions in a vast majority of instances, but not invariably. Seitz cites 3 cases where convulsions preceded the rise of blood pressure.

Kidney Function: The retention of water and sodium chloride in eclampsia is well known. A good discussion of the literature of

nitrogen retention in eclampsia is given by Heynemann. It is clear that the non-protein nitrogen of the blood is nearly always normal or only slightly elevated. Hüssy never found it above 50 mg. Seitz found the non-protein nitrogen above 40 mg. in about half his cases, and above 60 mg. in 10 per cent. Plass reports a slight rise in the non-protein nitrogen after delivery in normal patients, most marked during the first twenty-four hours after delivery. In the late toxemias of pregnancy this postpartum increase is accentuated. Plass is inclined to attribute the nitrogen increase to tissue retention rather than to renal insufficiency. However, as will be emphasized later, the glomerular lesions are sufficiently marked to account for some renal insufficiency.

Case Reports

The following 14 cases are examples of typical eclampsia.

Case 1. (21–477) A woman apparently 35 to 40 years of age registered at a hotel and asked for a physician, who could not be located that evening. She was found unconscious in her room the next afternoon, November 5. The records of the hospital to which she was taken show high blood pressure and convulsions. A dead fetus 48 cm. long was born without operative interference. Death Nov. 5, 1926, at 8 P.M.

Postmortem Report: No edema; moderate jaundice; no excess fluid in serous cavities; small hemorrhages in the serous membranes; heart, weight 332 gm.; lungs normal; liver, extensive subcapsular hemorrhages, and many small hemorrhages on section.

The kidneys weighed, together, 285 gm. The external surfaces were smooth. On section, the cortices were cloudy and of light yellowish brown color.

Microscopically the glomeruli are slightly enlarged, and the capillaries are very narrow. There is a marked thickening of the capillary basement membrane.

Case 2. (25–120) Gravida I. 31 years of age. Admitted Feb. 15, 1925. Duration of pregnancy, about five and a half months. She was seen by a physician early in her pregnancy, and he told her that her kidneys were normal. Edema of the feet from time to time during the five weeks preceding admission. February 1, albumin +; blood pressure 120/80; no edema. February 5, blood pressure 125/92. February 15, admitted in coma; blood pressure 184/90; slight edema of the legs and ankles; faint yellowish tinge to the skin. Urine: albumin ++++, many hyaline and granular casts. Definite oliguria. Four ounces of urine removed by catheter showed a specific gravity of 1034. Temperature ranged from 99 to 103° F. Spontaneous abortion shortly after admission.

She did not recover from the coma. She had three convulsions while in the hospital. Blood sugar 0.15 per cent; blood urea nitrogen 27 mg.; creatinin 1.5 mg.; van Slyke 46. Death February 18.

Postmortem Report: Edema of ankles; 100 cc. of clear fluid in each pleural cavity; 150 cc. in the pericardial cavity; no ascites; edema of lungs; heart, weight 300 gm.; liver, weight 1900 gm., subcapsular hemorrhages.

The kidneys, together, weighed 300 gm. On section the cortices were very cloudy. The external surfaces were smooth.

Microscopic examination shows anemic glomeruli, small capillaries, marked thickening of the glomerular basement membrane of all glomerular capillaries and some increase of endothelial nuclei in a few tufts.

CASE 3. (25–289) Gravida III. 41 years of age. Admitted April 20, 1925, in the eighth month of pregnancy. She was clear mentally on admission and stated that she had been well until April 17, 1925, when she developed a severe headache. She had one convulsion April 20, before entering the hospital. She stated that she had had convulsions seven years ago during pregnancy. Respirations were 50 per minute, and pulse 120. Blood pressure 165/115. The urine showed a specific gravity of 1037, albumin ++++, no sugar. She went into a convulsion about three hours after reaching the hospital and died a few minutes later.

Postmortem Report: No edema; no jaundice; moderate excess of fluid in the serous cavities; heart, weight 390 gm.; moderate left ventricular hypertrophy, no endocarditis, normal valves; edema of lungs; liver, weight 2180 gm., fatty, many hemorrhagic necroses; uterus contained a 2660 gm. fetus; multiple adenomas of thyroid.

The kidneys weighed 200 gm. and 190 gm. respectively. The external surfaces were smooth, the cortices cloudy.

Microscopically the kidneys show changes of unusual interest. The most impressive feature is tubular atrophy which involves over four-fifths of all the tubules. The atrophy varies from a slight decrease in size to almost complete disappearance of the tubules. The glomeruli associated with normal-sized tubules show only the acute changes of eclampsia, that is, thickening of the capillary basement membrane, but all the other glomeruli show various degrees of obliteration. Fully 20 per cent of the glomeruli are completely hyalinized and their tubules have almost disappeared (Fig. 2). The most common glomerular lesion is a focal hyalinization (Figs. 3 and 4), which is somewhat similar to healed embolic glomerulonephritis. The

tubules associated with these partly obliterated glomeruli are atrophic, but not so small as those belonging to completely hyalinized glomeruli. There is some hyaline degeneration of the afferent arterioles, but this is not marked and is not responsible for the glomerular changes.

The lesion does not resemble ordinary glomerulonephritis. The hyalinization is focal, there are no epithelial crescents and no leucocytes. There are also no enlarged glomeruli with endothelial proliferation such as one finds in chronic glomerulonephritis.

There is no basis for a diagnosis of healed embolic glomerulonephritis since the heart valves and mural endocardium are entirely normal.

All transitions are easily found between capillaries with thickening of the capillary basement membrane and those that are completely hyalinized. The process consists simply in progressive increase in the thickness of the basement membrane.

The hyaline glomerular lesions are in all probability the result of the eclampsia seven years before death.

Unfortunately there was no clinical study during the seven-year interval between the attacks of eclampsia, and consequently we do not know if this was clinically chronic renal disease. However, the left ventricular hypertrophy strongly suggests that hypertension was present, and the extensive atrophy of the tubules of the kidney makes it certain that some renal insufficiency was present.

CASE 4. (25–771) Gravida I. 40 years of age. Unmarried. Admitted Sept. 21, 1925, about eight and a half months pregnant. Nausea and vomiting throughout pregnancy, some headache for several months, edema of feet and hands past two or three weeks, almost total blindness past two or three days. September 21, blood pressure 226/150; scanty urine with heavy albuminuria; hemoglobin 75 per cent. September 22, vomiting; blood pressure 184/110; edema of legs, hands and eyelids; eyegrounds edematous; scanty urine which boiled solid; no convulsions; dilatation of cervix. September 23, fetus delivered by craniotomy; patient very restless; one convulsion during night. Death 12.15 A.M., Sept. 24, 1925.

Postmortem Report: Very obese, weight 250 lbs.; edema of legs, hands and eyelids; heart, weight 410 gm.; liver, weight 1970 gm., a few hemorrhagic necroses; no endometritis.

The kidneys weighed 175 and 150 gm. respectively. The external surfaces were smooth, the cortices very cloudy.

Microscopically erythrocytes are found in many tubules, having

escaped from deeply congested glomeruli. In general there is only a slight increase of endothelial nuclei, but a few tufts are occluded by endothelial cells. There is a moderate thickening of the capillary basement membrane in most of the glomeruli, but it is much less pronounced than in Case 14 (Fig. 5).

CASE 5. (26–145) Gravida I. 18 years of age. Admitted Feb. 12, 1926, about six and a half months pregnant. Had morning sickness during the early months of pregnancy. About one week before admission she developed vomiting and headache. Vomited eight or nine times a day for the past five days. Had a slight convulsion at 8 P.M., February 11. Two hours after entrance she began having convulsions which soon became almost continuous. February 12, blood pressure 148/98; pulse 108; temperature 99.4° F.; edema of eyelids. Urine: specific gravity 1018, albumin ++++, sugar ++, many casts, erythrocytes and leucocytes, no acetone or diacetic acid. Blood: hemoglobin 80 per cent, erythrocytes 4,560,000, leucocytes 24,000, 95 per cent polymorphonuclears. Blood urea nitrogen 24.3 mg.; creatinin 1.87 mg. February 13, induced labor with delivery of a premature dead fetus. Coma. Death 6.20 P.M.

Postmortem Report: Slight edema of the legs; no jaundice; no excess of fluid in the serous cavities; heart, weight 260 gm.; liver, cloudy, no gross areas of necrosis; multiple thromboses of the dural sinuses; purulent ethmoiditis.

The kidneys weighed 120 and 125 gm. respectively. There was a slight dilatation of both pelves and both ureters. The external surfaces were smooth, the cortices cloudy.

Microscopically there is a slight enlargement of the glomeruli with a moderate narrowing of the capillaries, which is caused mainly by an increase of endothelial cells. There is only a slight thickening of the capillary basement membrane. The glomerular structure is similar to that shown in Fig. 6. The associated infection may be responsible for the endothelial proliferation.

CASE 6. (26–283) Gravida I. 17 years of age. First seen by a physician at 8 A.M., March 22, 1926, in the first stage of labor. Her blood pressure was 150/110. She was delivered of a normal baby at 1.15 P.M. the same day and appeared normal at 3 P.M. At 4 P.M. she developed attacks of muscular twitching with cyanosis and retraction of the head, and passed into coma. At 5 P.M. the blood pressure was 180 systolic. 4 ounces of urine removed by catheter showed a heavy deposit of albumin. At 9 P.M. 6 ounces of urine were removed by catheter. Death, which occurred at 3 A.M. March 23, was preceded by a typical convulsion.

Postmortem Report: No edema; 200 cc. of clear fluid in the peritoneal cavity; heart, weight 300 gm.; liver, weight 1300 gm., multiple small hemorrhagic necroses.

The kidneys weighed 150 gm. each. There was moderate dilatation of the right pelvis and ureter. The external surfaces were smooth, the cortices cloudy.

Microscopically there is moderate enlargement of the glomeruli with narrowing and occlusion of the capillaries, caused chiefly by increase of the endothelial cells, but partly by thickening of the capillary basement membrane.

CASE 7. (26–725) Gravida I. 37 years of age. Admitted Aug. 4, 1926, in coma, about six and a half months pregnant. Said to have been well until early in the morning of August 4. She had three or four convulsions before admission. Blood pressure 195/130. Urine: specific gravity 1016, albumin ++++, a few hyaline and granular casts, no sugar, a few red cells and many leucocytes. Leucocytes 22,900. Blood urea nitrogen 22.9 mg. Blood sugar 0.30 per cent. A bag was inserted to induce delivery, but the patient died undelivered within three hours after admission without regaining consciousness.

Postmortem Report: No edema; slight icterus; 100 cc. of thin blood-tinged ascitic fluid; heart, weight 430 gm.; liver, weight 1910 gm., fatty, many large hemorrhagic necroses; uterus contained a fetus weighing 840 gm.

The kidneys weighed 190 and 185 gm. respectively. The external surfaces were smooth, the cortices pale with a yellowish tint.

Microscopically the glomeruli are enlarged and anemic. There is a very marked narrowing of the capillaries produced by thickening of the capillary basement membrane.

CASE 8. (26–965) Multipara. 40 years of age. Under observation during the latter part of her pregnancy. Her blood pressure was elevated, as high as 150 mm. Hg. at one time, and there was albumin in the urine. Labor started suddenly on Nov. 5, 1926, and the baby was born on the way to the hospital. The placenta was delivered in the hospital shortly after admission, at about 4 P.M. At 7 P.M., November 5, she began to complain of abdominal pain and backache. About 9 P.M. she vomited undigested food and was very restless and uncomfortable. At 11 P.M. she complained of severe pain in the chest and dyspnea. At 11:30 P.M. muscular twitchings and rigidity of the muscles of the face were noted. There were four such attacks, each of which lasted about thirty seconds. These attacks were followed by severe convulsions and coma. Systolic blood pressure at this time was 220 mm. Hg. At 6 A.M. November 6, she seemed conscious at intervals. Systolic blood pressure 135 mm. Hg. Ten ounces of urine removed by catheter at noon, November 6, showed albumin ++++, many casts and erythrocytes. About 2 P.M. November 6, she went into coma again. Systolic blood pressure 200 mm. Hg. Death in coma 7:30 A.M., Nov. 7, 1926.

Postmortem Report: No edema; no jaundice; no excess of fluid in

the serous cavities except the pericardial, which contained 150 cc.; heart not enlarged; liver, extensive subcapsular hemorrhages.

The kidneys showed smooth external surfaces and cloudy cortices.

Microscopically the glomeruli are enlarged. There is a marked narrowing of the glomerular capillaries produced chiefly by thickening of the capillary basement membrane. There is a slight increase of endothelial cells.

CASE 9. (28–383) Gravida I. 18 years of age. Admitted March 11, 1928, near full term. No symptoms until March 10, 1928, when she complained of epigastric pain. On this date her systolic blood pressure was 170 mm. Hg., and the urine showed a large amount of albumin. On March 11, labor pains began. On March 12, noon, blood pressure 188/120; heavy albuminuria and casts. Labor began in the early afternoon. One convulsion at 6 P.M., and another at 8 P.M. Forceps delivery of dead infant. Death at 10:15 P.M., thirty minutes after completion of labor.

Postmortem Report: Moderate edema of legs and labia; no fluid in serous cavities; heart, weight 300 gm.; liver, weight 2150 gm., numerous small hemorrhagic necroses.

Each kidney weighed 150 gm. The external surfaces were smooth, the cortices soft and cloudy.

Microscopically the glomeruli are enlarged and anemic. The narrowing of the capillaries is due to a marked thickening of the capillary basement membrane.

CASE 10. (28–526) Gravida I. 38 years of age. Admitted April 12, 1928. Well until April 12, 4 A.M., when she suddenly developed a convulsion. No examination before this date. A catheterized specimen of urine boiled solid. Nine convulsions before admission. In coma when admitted. Pregnancy estimated at seventh month, slight edema, cervix moderately dilated. Blood pressure 200/80; one convulsion shortly after entrance to hospital. Blood pressure fell to 125/80. Urine: large amount of albumin and many casts. Hemoglobin 85 per cent; erythrocytes 4,200,000; leucocytes 16,800. Blood urea nitrogen 17.7 mg. On April 13, blood pressure could not be obtained, but after stimulation it rose to 230/110. Vorhees bag inserted. Dead fetus delivered spontaneously at 9 P.M. Partial recovery of consciousness. April 14, marked oliguria, rapid fall of blood pressure. Death April 14, 1926.

Postmortem Report: Achondrodysplasia; no edema; 750 cc. of ascitic fluid; heart, weight 220 gm.; terminal bronchopneumonia; liver, weight 1725 gm., fatty, multiple hemorrhagic necroses.

The kidneys weighed 140 gm. each. The external surfaces were smooth, the cortices cloudy.

Microscopically the glomeruli show narrow capillaries and very little blood. The narrowing is due chiefly to thickening of the capil-

lary basement membrane, but there is some increase of endothelial cells.

CASE 11. (28–533) Gravida I. 25 years of age. Always in excellent health. Confinement expected April 20, 1928. Under constant observation during pregnancy, and nothing abnormal found until April 12, when routine urine examination revealed a moderate albuminuria. On this date no casts were found, and the systolic blood pressure was 120 mm. Hg. The patient was put to bed on a restricted diet. April 14, heavy albuminuria; puffiness about the eyes. On April 15, a severe headache developed and she was taken to a hospital. The first convulsion developed shortly after admission. Blood pressure 160 mm. Hg. systolic. There were five more convulsions within the next twenty-four hours, in spite of large doses of sedatives. Caesarian section was performed at 10:30 A.M., April 16. Living child. Mother never regained consciousness. Death 6:20 A.M., April 17, 1928.

Postmortem Report: No edema; 500 cc. of blood-tinged peritoneal fluid; 1000 cc. of clear fluid in each pleural cavity and 500 cc. in the pericardial cavity; marked edema of the lungs; distention of the stomach; heart, weight 350 gm.; no hemorrhages or necroses in the liver, cloudy swelling.

The kidneys weighed 200 gm. and 175 gm. respectively. The external surfaces were smooth. On section the cortices were cloudy and pale.

Microscopically, the glomeruli are slightly enlarged and anemic. There is a marked increase of endothelial nuclei in the glomerular capillaries which is the chief cause of the narrowing (Fig. 6). However, in some loops the thickening of the basement membrane is the main cause of the reduced caliber of the capillaries.

This lesion bears a striking resemblance to acute glomerulonephritis, but there are very few intracapillary fibers, no leucocytes, and no epithelial crescents.

CASE 12. (28–1228) Gravida VII. 39 years of age. According to her husband's statement, she had been fairly well during this pregnancy, except for occasional headaches. When he left home in the morning she said that she did not feel well. When he returned from work that evening he found her unconscious. A little later there was a precipitate spontaneous delivery of a dead infant. About eighteen hours after labor she was brought to the hospital. Upon admission she was in deep coma. Death occurred about ten minutes after admission.

Postmortem Report: Slight edema of legs; no jaundice; 500 cc. of clear fluid in the right pleural cavity; heart, weight 420 gm.; edema of right lung; liver, weight 2950 gm., fatty, numerous hemorrhagic necroses on section; no endometritis.

Kidneys weighed 200 and 205 gm. respectively. The external surfaces were smooth, the cortices cloudy.

Microscopically the glomeruli are moderately enlarged, and their capillaries are markedly narrowed. There is a marked thickening of the capillary basement membrane and some increase of endothelial cells. The changes are due chiefly to thickening of the basement membrane.

CASE 13. (30–318) 28 years of age. Confinement expected March 22, 1930. She had been under the constant care of a physician since Sept. 6, 1929. Numerous readings showed a range of the systolic blood pressure from 124 to 138 mm. Hg. The last reading, on February 21, was 138/80. Many examinations of the urine had been made, and occasionally a trace of albumin was found, but there was no albumin at the last test on February 21. She was visiting with friends on the evening of February 27, and was apparently well, but was found dead on Feb. 28, 1930.

Postmortem Report: No edema; no jaundice; the tongue was protruding and caught between the teeth; no excess of fluid in the serous cavities; heart, weight 355 gm.; liver, weight 1950 gm., fatty, numerous hemorrhagic necroses; 44 cm. fetus in the uterus; postmortem urine specimen showed abundant albumin.

The kidneys weighed 145 and 120 gm. respectively. The external surfaces were smooth, the cortices cloudy.

Microscopically, the glomeruli are slightly enlarged and the glomerular capillaries are very small. The narrowing of the capillaries is caused by a marked thickening of the capillary basement membrane.

CASE 14.* (31–476) Gravida I. 18 years of age. When first examined, June 21, the patient was at full term and labor had begun. There was moderate edema of the lower extremities, and the blood pressure was 150/100. No headache, nausea, or other toxic symptoms. The urine showed albumin +++. She was put to bed under treatment. At 4:30 P.M., June 21, she had a convulsion. Sedatives were administered. At 6 A.M., June 22, a second convulsion occurred. She became semiconscious, blood pressure 150/95. She had another convulsion during the forenoon. At 3 P.M. the cervix was fully dilated. A full term stillborn infant was delivered with low forceps. June 23, somewhat stuporous; deepening jaundice; edema slightly more pronounced; pulse 100; temperature 99 to 100° F. Glucose was given intravenously as on the previous day. Alkaline reserve 53. Hemoglobin 60 per cent. The urine, by catheter, showed albumin ++++, sugar, a few red cells, no casts, no acetone. Blood pressure 148/98. The total fluid intake from 7 A.M. June 23 to 7 A.M. June 24

* This case was made available through the courtesy of Dr. Warren C. Hunter, of Portland, Oregon.

was 2220 cc., and the total output of urine during this twenty-four hour period was 295 cc.

June 24, the patient seemed improved. There was very little stupor. Edema and jaundice unchanged. Blood pressure 148/98 to 152/64. Therapy: glucose, sodium bicarbonate, diuretin. Fluid intake 4680 cc.; urine 330 cc.; albumin++.

June 25, fluid intake 7100 cc.; urine 220 cc. Blood pressure 148/60. Temperature 101.6° F.; pulse 120.

June 26. Therapy: glucose; alkali discontinued since alkali reserve had risen to 140. Fluid intake 4600 cc.; urine 100 cc.

June 27. One hour after administration of glucose the blood sugar was 413 mg., and the alkali reserve 147. Insulin was given. Temperature 103.8° F.; pulse 120. Fluid intake 1740 cc.; urine 66 cc. The patient gradually became weaker and died at 4 A.M., June 28.

Postmortem Report: Severe jaundice; slight pitting edema of the ankles; ascites, 3000 cc.; marked bilateral hydrothorax; atelectasis of lungs; heart, weight 280 gm., no gross disease; liver, weight 2010 gm., numerous areas of hemorrhagic and anemic necrosis, fatty; cystitis; no endometritis.

The combined weight of the kidneys was 480 gm. The external surfaces were smooth. On section the cortices were pale and moist.

Microscopically the glomeruli are all moderately enlarged and anemic. There is a striking increase in the thickness of the capillary basement membrane (Fig. 5). The endothelial nuclei are not definitely increased in number. No fat is demonstrable in sections stained with Sudan III.

Anatomical Changes in Eclampsia

The Liver: A comprehensive review of the changes in the liver in eclampsia may be found in Fahr's article in Hinselmann's monograph. Only a brief summary need be given here, since this paper deals primarily with the renal lesions only. Degenerative lesions of some type are found in the liver almost constantly. The characteristic gross lesions are irregular areas of hemorrhage associated with necrosis or atrophy of the liver cords (hemorrhagic necrosis) and small areas of anemic necrosis. These macroscopic lesions are found only in eclampsia, and a diagnosis of eclampsia may be made on their presence, even in the absence of clinical signs of eclampsia. However, macroscopic necrotic lesions are not always present. Many writers report them absent in a notable percentage. In 2 of our 14 cases, no gross necroses were found. However, when a thorough microscopic examination is made, as has been emphasized by Lubarsch, Schmorl, and Fahr, necrosis and degeneration of the liver

cords are seldom entirely absent. Cloudy swelling and fatty degeneration of the hepatic cords are also found frequently. Fibrin thrombi in the small branches of the portal vein and areas of capillary ectasia with atrophy of the enclosed hepatic cords are commonly present. Thrombosis of small vessels seems sufficient to account for the areas of necrosis and hemorrhage, but the diffuse injury of the hepatic cells is best explained as the effect of a circulating toxic substance.

The Kidneys: The kidneys are affected in practically all cases of eclampsia. There are occasional reports in the literature in which the kidneys are described as normal. Seven out of 368 cases reviewed by Prutz, 1897, were considered normal. Fahr is inclined to doubt reports of normal kidneys in eclampsia, and it is evident that no such report should be accepted unless a careful macroscopic and microscopic examination has been made. However, in view of the rare instances of eclampsia without albuminuria, it seems possible that the kidneys may escape injury in exceptional instances.

The macroscopic changes are constant and easily recognized. Aside from the rare cortical necroses, which will be discussed separately, the only change is cloudy swelling. The kidneys are usually slightly enlarged and their external surfaces are smooth. On section the cortices are pale and cloudy and occasionally a yellowish tinge is noted. There is some variation in the intensity of the cloudy swelling in different instances. The macroscopic changes are therefore not pathognomonic of eclampsia, the same lesion being found in a large number of toxic and infectious processes.

On microscopic examination the tubules show the changes characteristic of cloudy swelling. The cells of the secreting tubules are usually somewhat swollen and often they contain small fat droplets. In the lumina of the tubules, casts and precipitated albumin are usually observed. Fahr emphasizes the importance of hemoglobin in the casts. In the more severe injuries there may be some evidence of necrosis and degeneration of some of the tubular epithelium. The tubular lesion is likewise not peculiar to eclampsia. It is the typical effect of toxins or toxic substances in the circulating blood, but it may also result from anemia caused by spasm of the renal arteries.

The Glomerular Lesions: Pels-Leusden, 1895, recognized clearly that the glomeruli are especially involved in eclampsia. It is true

that he regarded the lesion as acute glomerulonephritis, but he noted that the glomeruli are enlarged and pale and contain only a little blood.

Schmorl, 1902, described hyaline thromboses in the glomerular capillaries. Fahr pointed out later that this lesion occurs only infrequently. It was not found in any of our cases. Schmorl disagreed with the prevalent view at that time that the eclamptic kidney indicates glomerulonephritis.

Löhlein, 1918, gave the first concise and accurate description of the characteristic glomerular lesion in eclampsia. He noted thickening of the walls of the glomerular capillaries, decrease of erythrocytes, swelling of the glomerular epithelium and a slight increase of intracapillary cells. He stated that the lesion suggests glomerulonephritis but is different. Löhlein did not accept "nephrosis" as an entity, and it is not clear whether he regarded this glomerular change as degenerative or inflammatory.

Fahr, 1920 and 1924, has given accurate descriptions and illustrations of the glomeruli in eclampsia. He described thickening of the capillary walls with clumping and fusion of the loops, and eventually hyalinization of some of the tufts. No increase of glomerular nuclei was found as a rule, but there were some exceptions. Fahr considers this glomerular lesion peculiar to eclampsia, and calls it a glomerulonephrosis. He interprets it as a degenerative change and believes that it is best explained by the toxic theory of eclampsia.

Pohl, 1927, noted the enlargement of the glomeruli, but did not comment upon their structure.

My own observations are in almost full accord with those of Löhlein and Fahr, but I have succeeded in showing the structural changes in the glomeruli in greater detail by means of a special stain. In sections stained with hematoxylin and eosin, the glomeruli attract attention by reason of their slightly hyaline appearance and their small empty capillaries (Fig. 1). The increase in size is usually only moderate, but sometimes quite pronounced. As a rule there is no increase in the number of nuclei, but in some kidneys a definite increase is observed. Under high magnification a marked thickening of the walls of the capillaries is readily seen, as has been described by Löhlein and Fahr. No capillary thrombi were found in any of my cases.

The detailed structure of the glomerulus is brought out in a re-

markable way by the azo-carmine stain. The technique of this stain has been published by McGregor, and the reader is referred to her articles for its application to the normal glomerulus and glomerulonephritis. The great advantage of this stain is that it demonstrates the capillary basement membrane sharply and affords an easy distinction between endothelial and epithelial cells. The endothelial cells lie on the inner surface of the membrane, and the glomerular epithelial cells on its outer surface.

When the azo-carmine stain is applied to the glomerulus in eclampsia, it is easily seen that the thickening of the capillary wall is due, almost entirely, to a massive thickening of the capillary basement membrane (Fig. 5). The glomerular epithelial cells are only slightly altered. Occasionally they contain fine droplets of fat or hyaline granules, but they show no evidence of proliferation. As a rule the endothelial nuclei are slightly increased in number. The narrowing of the lumina of the capillaries is evidently due, usually, to thickening of the capillary basement membrane. The capillaries are rarely completely obstructed, but in some tufts their thickened walls are in contact and they seem to be totally occluded. Capillaries of this type appear hyaline in hematoxylin-eosin preparations.

The degree of thickening of the capillary basement membrane is fairly uniform in all the capillaries of all the glomeruli in each individual case, but it varies in different cases. In the 17 cases which showed thickening of the basement membrane, it was moderately thickened in 2 and markedly so in 15.

The thickened basement membrane is not a homogeneous structure. It is composed of parallel layers (Fig. 5). The thickening cannot be interpreted as a simple swelling (edema). It must represent an increase of substance in the membrane. There is no anatomical explanation of its increased permeability.

In 3 cases the increase of endothelial nuclei is striking (Fig. 6), and a definite but moderate increase was noted in 2 others. The endothelial nuclei lie on the inner surface of the basement membrane, and are easily distinguished from the epithelial cells. Where the endothelial nuclei are notably increased, the thickening of the basement membrane is correspondingly less pronounced.

Fahr thinks it possible that the endothelial increase is due to a complicating infectious process, and not to eclampsia *per se*. How-

ever, if a toxic substance is concerned in eclampsia there is no sound reason for believing that it cannot cause an increase of glomerular endothelium. Hyperplasia of the glomerular endothelium is by no means limited to clinical glomerulonephritis, but is found in varying degree in a wide variety of infectious processes.

There are, however, striking differences between the eclamptic glomerulus and clinical acute glomerulonephritis, even when the former shows a notable increase of endothelial nuclei. The glomeruli in eclampsia are smaller, the basement membrane is much thicker, there are no polymorphonuclear leucocytes, no intracapillary fibers and no epithelial crescents. In glomerulonephritis there is much more cytoplasm about the endothelial nuclei. The two types of glomeruli may be distinguished without difficulty.

Fahr mentions small patches of hyaline degeneration in the afferent glomerular arterioles as an occasional finding. In 2 of my cases a slight arteriolar sclerosis was found.

Symmetrical Necrosis of the Cortex of the Kidneys: The first case of this kind was described by Bradford and Lawrence in 1898, and since that time 17 similar cases have been reported: Schuppel, 1904; Lloyd, 1906; Griffith and Herringham, 1906; Klotz, 1908; Jardine and Teacher, 1911, 2 cases; Torrens, 1911; Jardine and Kennedy, 1913, 3 cases; Herzog, 1913; Rolleston, 1913; Glynn and Briggs, 1914–1915; Jardine and Kennedy, 1920; Cruickshank, 1923; Geipel, 1925; and Carson and Rockwood, 1926. Poten's case, 1906, probably belongs to this group.

The outstanding clinical features are preëclamptic symptoms with or without convulsions, followed by severe oliguria or complete anuria, and ending in death within a few days. Ten of the reported cases were in multiparae, and 6 in primiparae. Age seems to be of no significance. In 8 cases no convulsions are mentioned, an unusually large proportion of "eclampsia without convulsions." However, definite preëclamptic symptoms are described in every instance. The stage of gestation varies from three and a half months to full term. Typical uremic symptoms are commonly absent. The scanty urine contains blood, albumin and casts.

Macroscopic necrosis of the liver was noted in 3 cases. In 6 cases it is clearly stated that no macroscopic necrosis was present, but in 3 of these the liver was fatty. The frequent absence of convulsions and typical necrosis of the liver raises a doubt as to whether this

group should be classified as eclampsia. They are truly not all typical eclampsia, but they may at least be grouped with pre-eclampsia on the basis of the clinical symptoms.

The kidneys in every case are similar. There is an almost complete necrosis of the cortices of both kidneys. There is thrombosis of the interlobular arteries and usually of the vasa afferentia also. Sometimes the thrombosis extends into the glomerular capillaries. The large branches of the renal arteries are free from thrombi. The prevailing opinion is that the thrombosis is primary and that the necrosis results from infarction. This interpretation is strongly supported by the finding of a thin layer of living cortex immediately under the capsule which is supplied by anastomoses with capsular arteries. Preëxisting disease of the renal arteries is described in some cases, but this is inconstant and apparently unrelated to the thrombosis. The cause of the thrombosis is not known, but it is best explained as a result of a toxic substance or a coagulant in the circulating blood.

2. Eclampsia without Convulsions

This group includes fatal toxemias, usually with some preëclamptic symptoms, but without convulsions. The diagnosis is established by the finding of typical necrosis of the liver at postmortem.

Ordinarily there is not much justification for this subgroup of eclampsia. Cases are frequently reported in which only one convulsion occurred (see Case 4); and others are reported where muscular twitchings but not true convulsions were present. The following protocol records a case which differs clinically in no way from typical eclampsia, except in the absence of convulsions.

Case 15. (30–1395) Para II. Negress, 37 years of age. Admitted Sept. 15, 1930, about seven months pregnant. Moderate nausea and vomiting during first three months. No symptoms after the third month until the day of admission, when she began to vomit. No visual disturbance. About six weeks before admission a physician took her blood pressure and told her it was high. September 15, blood pressure 266/180; slight edema of lower extremities. September 16, coma; blood pressure 170/80. Urine: large amount of albumin, large number of erythrocytes (gross hematuria), specific gravity 1020. Blood urea nitrogen 33 mg.; creatinin 3.3 mg. The eyegrounds showed some old and some recent hemorrhages, and some edema of the disc. Temperature, 104° F. No convulsions. Death Sept. 16, 1930.

Postmortem Report: Moderate edema of the lower extremities; no jaundice; a little excess of fluid in the serous cavities; heart,

weight 306 gm.; bilateral bronchopneumonia; liver, weight 1384 gm., fatty, many areas of hemorrhagic necrosis; uterus contained a 37 cm. fetus.

The kidneys weighed 180 and 164 gm. respectively. The external surfaces were smooth. The cortices were pale with a yellowish tinge.

Microscopically the glomeruli are enlarged and anemic. Small patches of hyalin are seen in the arterioles and glomeruli. There is a very marked narrowing of the glomerular capillaries produced by thickening of the capillary basement membrane. There is a slight increase of endothelial cells.

It may be contended that this is an instance of pregnancy in a woman with primary hypertension, since there is a slight renal arteriolar sclerosis, but the presence of hemorrhagic necroses in the liver establishes the disease as eclampsia. Primary hypertension as a complicating influence cannot be excluded.

The following case is, in all probability, eclampsia, although convulsions and necrosis of the liver are both absent.

CASE 16. (30–1760) Gravida I. Last menstrual period March 1, 1930. May, 1930, a trace of albumin was found in the urine. August, 1930, trace of albumin in the urine, no other signs of toxemia; blood pressure 118/70. In the next two months there was a steady increase of albumin. November 18, albumin +++, a few casts and erythrocytes; blood pressure 170/108. November 25 labor was induced, but the patient died undelivered. There were no convulsions.

Postmortem Report: Edema of one leg; no excess fluid in the serous cavities; heart, weight 350 gm., acute rheumatic mitral endocarditis; liver, weight 2665 gm., cloudy swelling, no necroses; twin pregnancy, each fetus 47 cm. long.

The kidneys weighed together 400 gm. The external surfaces were smooth. The cortices were pale and cloudy on section.

Microscopically the glomeruli are definitely enlarged, and they contain practically no blood. There are no epithelial crescents. The greater number of glomeruli show only a little endothelial increase, but in a great many the increase of endothelial cells is very prominent. There is a striking thickening of the capillary basement membrane in all the glomeruli, such as is shown in Fig. 5, a lesion which is characteristic of eclampsia and not of glomerulonephritis. A few glomeruli show intracapillary fibers.

In view of the infection which was present, namely, rheumatic endocarditis, the endothelial increase and the intracapillary fibers may be interpreted as a result of infection superimposed on an eclamptic kidney. It cannot be considered as acute glomerulonephritis complicating pregnancy, since the lesions are chiefly of the eclamptic type.

The two preceding cases are easily recognized clinically as belonging to the eclamptic group, but much more atypical cases are on record.

Schmorl, 1902, called attention to a type of toxemia which differs sharply clinically from typical eclampsia, and is only recognized with certainty as eclampsia by the finding of necrosis of the liver at postmortem. It is convenient to designate this group as "eclampsia without convulsions" or "atypical eclampsia." Over 40 cases of this type have been reported. The literature on this topic will not be reviewed here. The reader is referred to the papers of Schmorl, Schmid, Ranzel, Liebmann, Pohl, Bock, and Wronski.

The attack may develop before, during, or after labor. Usually there are some warning preëclamptic symptoms, but sometimes the patient sinks into coma or circulatory collapse without any previous signs of toxemia. In the complete absence of preëclamptic symptoms, the diagnosis can hardly be established ante mortem. Albumin may be absent until shortly before death. The blood pressure tends to fall.

The disease is recognized as eclampsia by the finding of the typical necroses of the liver. In some of the most atypical cases there is also a large intracranial hemorrhage.

The kidneys in atypical eclampsia have not been studied in detail microscopically. The reports indicate that the same macroscopic changes are present as in typical eclampsia.

It is to be noted that bilateral symmetrical necrosis of the cortex of the kidneys gives rise to an atypical clinical form of eclampsia.

3. Preëclampsia

Preëclampsia is characterized by the presence of the symptoms and signs which usually precede the eclamptic convulsion. The most important of these are hypertension, albuminuria, visual disturbances, edema, headache, nausea and vomiting, vertigo, and so

on. The individual symptoms and signs vary greatly in their prominence in different cases. When severe visual disturbances are present there is great danger that convulsions will develop. Moderate edema without other preëclamptic symptoms is not of serious significance, and is probably not a true preëclamptic sign.

Preëclampsia recurs oftener in subsequent pregnancies than typical eclampsia, and recovery from severe preëclampsia is apparently more prolonged.

The clinical phenomena indicate that the same type of lesion is present in preëclampsia as in typical eclampsia, although it is presumably less severe. Heynemann described a case of preëclampsia in which death was due to premature separation of the placenta. The characteristic changes were present in the liver and kidneys. Even the typical glomerular lesions were found. Heynemann states that 6 similar cases have been reported. This would seem to establish the essential identity of eclampsia and preëclampsia. Cases 15 and 16 might well be classified as preëclampsia rather than as eclampsia without convulsions.

Changes in the Kidneys Subsequent to an Attack of Eclampsia

What permanent damage, if any, does eclampsia produce in the kidneys? Is the acute glomerular lesion reversible or does it lead to partial or complete obliteration of glomeruli with atrophy of their corresponding tubules? Does a clinical chronic renal disease result from eclampsia; and, if so, what are its characteristic features? These are some of the questions to which we shall now direct our inquiry.

A number of clinical reports deal with the question of chronic renal disease following eclampsia. Leyden, 1886, reports one case of chronic nephritis following eclampsia. The woman was said to have been well before pregnancy, but apparently no study was made with respect to the presence of latent renal disease. The postmortem revealed contracted kidneys.

Koblanck, 1894, reëxamined 77 women who had had eclampsia (time of recheck not given): 59.7 per cent had no albumin; 16.9 per cent had a transitory trace of albumin; 15.4 per cent had catarrh of the urinary tract; and 6.5 per cent (5 cases) had nephritis. No details of the nephritis were given.

Meyer-Wirz, 1904, observed 35 postmortems in instances of eclampsia, and found 3 with chronic indurated kidneys. He also found that the great majority of eclamptics were free from albumin on dismissal from the hospital, but he mentioned 9 cases in which albumin was still present.

Zangemeister, 1913, found that a chronic nephritis remained in 7 per cent of eclamptics. He thought that the majority of these developed from the eclamptic kidney and not from a previous chronic nephritis.

Baisch, 1913, traced 110 women who had had an attack of eclampsia (60 cases) or severe preëclamptic symptoms (50 cases). Of these 110 patients, 9 were dead, and 11 were permanent invalids. Only 40 per cent were entirely well. No information is given as to the cause of death or invalidism. No evidence of renal disease was presented.

Wolff and Zade, 1914, found 2 out of 23 eclamptics, whom they reexamined some years later, with evidence of chronic nephritis. The first patient had no albumin on dismissal, and when reëxamined had hypertension without albumin. The second had no albumin on dismissal, and on reëxamination had hypertension, 200/120, and a trace of albumin. Two of seven preëclamptics had similar evidence of a chronic nephritis on reëxamination. These cases can hardly be accepted as proof that a chronic nephritis may develop from the eclamptic kidney, but such an interpretation is possible. They may represent instances of primary hypertension developing independently of eclampsia.

Sachs, 1918, found 81 of 87 eclamptics entirely well on reëxamination some years later. Four were dead (one from a recurrent eclampsia, three from intercurrent disease). Two showed signs of chronic nephritis.

Hüssy, 1921, doubts the transition of the eclamptic kidney into chronic nephritis. He did not see any instance of this in his experience.

Breuning, 1924, in a report of 88 cases of eclampsia, states that 88 per cent of those who survived were free from albumin when dismissed from the hospital.

Heynemann, 1924, gives a full account of the results of reëxamination of 45 patients who had eclampsia and 7 who had pronounced preëclamptic symptoms. His paper should be consulted for the

detailed findings in each case. He concludes that not infrequently there is evidence of renal injury not only on dismissal but on later reexamination. This is indicated by the presence of albuminuria or hypertension, or both. He interprets these findings in most instances as evidence of delayed healing, but thinks that the cases with hypertension only may be due to disease of arterioles and capillaries resulting from eclampsia. He finds no convincing evidence in his experience that chronic renal disease results from eclampsia. Patients with pronounced preëclamptic symptoms show slower healing than those with eclampsia.

Fahr, 1924, in the light of his pathological studies, expresses the opinion that it is possible for the eclamptic kidney to give rise to chronic renal disease.

Zondek and Jacobowitz, 1924, reëxamined 38 patients who had had eclampsia or preëclampsia, one to seven years later. There was one case of chronic nephritis which they believe was present before the attack of eclampsia. In a few cases there was evidence of a slight renal disturbance. They conclude that it is possible that eclampsia gives rise to chronic nephritis, but it must be very rare.

Döderlein, 1925, reëxamined 26 patients eight months to fifteen years after eclampsia and 16 were entirely normal. Slight albuminuria with normal kidney function was present in 3 patients and 7 showed albumin and casts, with some evidence of decreased renal function, which he interprets as indicating a chronic nephrosis resulting from eclampsia.

Bund, 1925, partly by correspondence, followed 39 patients who had eclampsia. Four had chronic nephritis which he attributed to eclampsia.

Nevermann, 1927, reëxamined 60 patients, one to twenty-three years after eclampsia. Thirty-seven were studied more than ten years after the attack. Twenty-seven were entirely normal. The others had various complaints such as headache, poor memory, visual disturbances and edema of the legs. Eight women had hypertension (systolic pressure 140 to 170 mm. Hg.). Three had albumin and casts: (*a*) one year after eclampsia, trace of albumin, blood pressure 118 mm. Hg.; (*b*) eclampsia in 1903 and again in 1905, albuminuria on dismissal each time, since 1905 seven abortions and premature labors; in 1925, blood pressure 170 mm. Hg., large amount of albumin; (*c*) eclampsia in 1921, mild preëclampsia with abortion in

1925 (albumin), normal in 1926. There was only one patient with a persistent renal lesion. Nevermann believes that chronic nephritis rarely, if ever, develops from eclampsia.

Peckham, 1929, found 17 (23 per cent) of 77 women with chronic nephritis on reëxamination one year after eclampsia. Nephritis developed somewhat oftener in those who were albumin-free at the end of three weeks than in those who had albuminuria at that time. Peckham does not explain the criteria on which his diagnosis of chronic nephritis is based.

Schmechel, 1929, in a large experience with eclampsia, knew of only one patient who developed chronic renal disease. He thought that this patient probably had renal disease before pregnancy.

Kobes, 1930, found that 19 of 32 eclamptics had albuminuria at the end of the third week after the attack. Reëxamination of these 32 women from three to eighty-five months later showed only 3 with albuminuria (four months, seven months, ten months later).

Fourteen of 19 preëclamptics had abnormal urine when reëxamined, but 13 of these had a history of renal disease prior to pregnancy. Two women had evidence of contracted kidney. Kobes was unable to decide whether or not eclampsia causes chronic renal disease.

Seitz, 1930, found 78 eclamptics all entirely well at the end of eight weeks. The preëclamptics (27 in number) showed a little slower healing. A few were not normal after fourteen weeks.

It is difficult to draw definite conclusions from the literature, since the experience of different observers has not been uniform. However, it appears that evidence of mild renal injury is frequently found a long time after an attack of eclampsia. Whether or not the cases of definite chronic nephritis that follow eclampsia are the outcome of the eclamptic kidney cannot be decided. In order to establish such an origin for the nephritis, it must be shown by careful examination that nephritis was not present prior to the pregnancy. None of the reported cases of contracted kidneys were studied before pregnancy.

The clinical evidence indicates that the eclamptic kidney usually heals rapidly, but in some instances very slowly. There is a possibility that it may rarely pass into a definite chronic nephritis with contracted kidneys, but there is no convincing evidence that this occurs.

We may next inquire if there is any anatomical evidence of a permanent renal lesion resulting from the eclamptic kidney. Microscopic examination of kidneys from women who had eclampsia a long time previously should reveal permanent lesions if any are present, but apparently no such studies have been made. It will be interesting, therefore, to study in detail the old lesions in Case 3, in which there is a history of a previous attack of eclampsia seven years before death. In the protocol (Case 3), the histological changes are fully described (see also Figs. 2, 3 and 4). It is clear that the acute lesions of eclampsia did not heal entirely in this instance. The capillary basement membrane thickened to the point of complete obliteration of groups of glomerular capillaries. Disuse atrophy of the tubule developed to a degree proportionate to the diminished capillary bed of its glomerulus.

The clinical evidence in this case is lacking, but there is strong anatomical evidence of chronic renal disease resulting from eclampsia. It is quite different from ordinary chronic glomerulonephritis in its pathogenesis, but the end result is obstruction of glomerular capillaries and tubular atrophy. It may be said, therefore, that chronic renal disease may result from the acute lesion of eclampsia, but it is a special type differing from the known forms of chronic renal disease in its structure and pathogenesis. On the basis of the anatomical structure, one would expect to find hypertension and renal insufficiency clinically.

4. Hyperemesis Gravidarum

In general this form of toxemia is different from eclampsia, but cases occur which show some of the features of eclampsia, and raise a doubt whether these two forms of toxemia are entirely distinct entities.

The outstanding clinical feature of hyperemesis gravidarum is obstinate vomiting developing in early pregnancy, and the characteristic lesion found at postmortem is fatty degeneration of the liver. In some instances a severe anemia or a toxic myelitis dominates the clinical picture to such an extent that we seem to be dealing with a separate entity and not with hyperemesis gravidarum.

Two fairly typical cases of hyperemesis gravidarum are reported by Harbitz. The first case, a woman 25 years old, began to vomit in

the second month. The vomiting became very severe, and she became almost blind. Death occurred in the third month, forty-eight hours after the uterus was emptied. The liver and kidneys were fatty. There were no necroses in the liver. The second case, a woman 22 years old, vomited for three months and died in the fourth month. The same lesions were found at postmortem as in the first case.

The following four cases came under my observation:

CASE 17. (29–1213) Gravida I. 39 years of age. Admitted Aug. 14, 1929. About four months pregnant. Last menses in April. Vomiting more or less continuously since the latter part of May. Complains of vomiting, weakness and loss of weight. Blood pressure 100/70. No edema. Some mental disturbance. Slight icteric tint in the sclera. Moderate enlargement of the thyroid of two years' duration. Hemoglobin 85 per cent; erythrocytes 4,060,000; leucocytes 9,350. Differential count normal. Urine showed sugar, acetone and diacetic acid, no albumin. Blood urea nitrogen 14 mg. No improvement under treatment. Vaginal hysterotomy and craniotomy. August 21, collapse. Death Aug. 22, 1929.

Postmortem Report: Slight jaundice; no edema; no fluid in serous cavities; heart, weight 250 gm.; liver, weight 1150 gm., diffuse fatty metamorphosis; colloid goiter; no gross changes in pancreas.

Kidneys weighed 140 and 145 gm. respectively. Slight dilatation of right pelvis and ureter. No other gross changes.

Microscopically the glomeruli show a normal structure.

This is a typical case of hyperemesis gravidarum, showing none of the features of eclampsia, and not complicated with anemia or toxic myelitis. The kidneys were normal. The characteristic glomerular lesion of eclampsia is absent.

CASE 18. (26–238) Gravida I. 20 years of age. About Dec. 25, 1925, she first developed nausea and vomiting. She became acutely ill Jan. 1, 1926, and has vomited almost continuously since that date whenever she attempted to eat. Admitted Feb. 2, 1926, three months pregnant at this time. The vomiting improved notably under treatment. The urine showed albumin, acetone and diacetic acid. Discharged February 26, much improved. Readmitted, March 2, complaining of a sore throat and disturbances of vision. Her vision was so impaired that she could barely recognize faces. Hemorrhages were visible in the retinae. Blood pressure 114/80. Temperature ranged between 100 and 103° F. Pulse very rapid. Leucocytes 7,000. Blood urea nitrogen normal. Urine showed albumin. Death March 9, 1926.

Postmortem Report: No edema; no jaundice; 200 cc. of blood-tinged ascitic fluid; heart, weight 220 gm., soft myocardium; liver, weight 1515 gm., very fatty, no hemorrhages or necroses; uterus contained a four months' fetus; no endometritis.

Each kidney weighed 150 gm. The external surfaces were smooth. The cortices were very pale, and two small abscesses were found in the cortex of one kidney. There were many petechial hemorrhages in the pelves. Microscopically the glomeruli are practically normal.

In the foregoing case death was apparently due to bacteremia rather than to toxemia of pregnancy. The retinal hemorrhages with loss of vision suggest eclampsia, since this is a rare complication of a simple septicemia. There was no hypertension. The extreme fatty degeneration of the liver is to be referred to toxemia of pregnancy. The glomeruli do not show the distinctive lesion of eclampsia.

CASE 19. (28–197) Gravida II. 24 years of age. Admitted Jan. 28, 1928. First pregnancy three years ago terminated in abortion at three and a half months. Duration of this pregnancy about seven and a half months. Vomiting began during the third month of pregnancy. She would vomit after every meal. The vomiting then stopped for three months, but recurred in the sixth month. For the past six weeks she has retained practically nothing that was taken by mouth. About two weeks before admission she developed difficulty in swallowing, which persisted. January 28, blood pressure 100/85. The urine on two examinations showed a faint trace of albumin, many hyaline casts, and a few erythrocytes. Hemoglobin 50 per cent. Erythrocytes 2,100,000. High color index. Blood smear showed moderate poikilocytosis and anisocytosis, no nucleated reds or polychromatophilia. Blood Wassermann negative. Blood urea nitrogen 17.8 mg. The vomiting was not relieved by treatment. On February 2, she suddenly went into labor and a living child was born spontaneously. About six hours after labor she became dyspneic. There were no convulsions. Death 11:35 A.M., Feb. 3, 1928.

Postmortem Report: No edema; 100 cc. of clear fluid in the pericardial cavity, none in the other serous cavities; heart, weight 198 gm.; liver, weight 1445 gm., light brown color, no areas of necrosis, very little fat.

The left kidney weighed 125 gm., the right 110 gm. Submucosal hemorrhages in the left pelvis. The external surfaces were smooth, the cortices pale.

Microscopically the glomeruli are moderately enlarged and anemic. There is a definite narrowing of the glomerular capillaries, produced by a marked thickening of the capillary basement membrane.

On clinical grounds this case may be interpreted as hyperemesis gravidarum complicated by severe anemia. The typical liver lesion of hyperemesis is, however, not present. There was only a faint trace of albumin in the urine, and there was no hypertension, but the characteristic glomerular lesion of eclampsia is present.

CASE 20. (30–3) Gravida VI. 30 years of age. Admitted Dec. 30, 1929. She was about four months pregnant, had been ill for two months, and confined to bed for seven weeks. For the past three days she had been delirious and semiconscious, and had had a fever. Since the early part of October she had been repeatedly passing catheters into the uterus in an attempt to produce abortion. There had been slight bleeding as a result of this instrumentation, but no pain. She had been seen by a private physician ten days before admission. At that time she was excitable, but not unconscious, and had choreiform movements of the limbs. The systolic blood pressure was 155 mm. Hg., and the pulse 130. She had been vomiting after almost every attempt to eat or drink during the past six weeks, and there had been some vaginal bleeding. Five days before admission her temperature was 99° F. There had been no chills associated with the illness. The urine at that time was negative except for a few pus cells. She had some difficulty in moving her legs, and complained of severe pain when they were touched. She had had a curettement five years before, following a spontaneous abortion at five months. There was also an abortion two and a half years ago at four months. She had three living children aged 3, 5 and 7 years.

On admission the temperature was 99° F., and the pulse 145. Respirations 28 per minute. She was semicomatose. There was a coloboma of the right eye, with loss of vision. The left fundus showed retinal hemorrhages and edema of the disc. Blood pressure 142/94. Abdominal and knee reflexes absent. Babinski test negative. December 31, semicomatose; temperature 102° F.; rapid pulse; pale and dehydrated. She answered questions occasionally, but in a confused and delirious manner. No facial asymmetry. Biceps and triceps reflexes were equal and normal. Abdominal, patellar, hamstring and Achilles reflexes were absent. She appeared to be using the diaphragm very little and was incontinent. She was able to raise her lower extremities to some extent. Muscles of the legs were very flaccid. Spinal puncture revealed a clear fluid under normal pressure. Urine: December 30, faint trace of albumin, no sugar. December 31, large amount of albumin and sugar and large numbers of erythrocytes (catheterized specimen). Hemoglobin 65 per cent; erythrocytes 3,560,000; leucocytes 8,100 to 11,650; 80 per cent polymorphonuclears; 20 per cent lymphocytes. January 1, labored respirations; cyanosis; temperature 103 to 105° F.; death.

Postmortem Report: Slight edema of the legs; no jaundice; no fluid in the serous cavities; heart, weight 285 gm.; liver, weight 1625 gm., cloudy swelling, no necroses; four months' fetus in the uterus.

The kidneys weighed together 280 gm. The external surfaces were smooth, the cortices cloudy.

Microscopically the glomeruli show a normal structure.

Microscopic studies of the spinal cord showed extensive degeneration and necrosis of the nerve cells (toxic myelitis).

The foregoing is an illustration of hyperemesis gravidarum in which toxic myelitis dominates the clinical picture. Berkwitz has

described several cases of this type. The hypertension and eye-ground changes suggest a relationship to eclampsia, but the liver and kidney lesions peculiar to eclampsia are not present.

There seems to be some relationship between hyperemesis gravidarum and eclampsia, but there is no convincing evidence at present that they are due to the same underlying disturbance.

5. Pregnancy in Association with Preëxisting Renal Disease

Eight cases have come under my observation in which it is reasonably sure that chronic renal disease was present prior to pregnancy.

Case 21. (21–219) 26 years of age. Admitted Jan. 31, 1921. Had smallpox at age of 11 years. Frequent attacks of sore throat for many years. No history of scarlet fever or rheumatism. When she was 16 years old a physician told her she had kidney trouble. Has had headaches as long as she can remember. Her vision has been poor for years. Has noted slight pain about the heart for several years. At her first pregnancy in 1913, at the age of 18 years, she was comatose for four or five days and had convulsions. For this reason the pregnancy was terminated at the fifth month by therapeutic abortion. The second and third pregnancies ended in spontaneous abortion. The fourth pregnancy was terminated by therapeutic abortion in September, 1920. She has not menstruated since.

During her stay in the hospital the blood pressure readings were: Jan. 31, 1921, 176/140; a little later, 190/140; February 11, 122/90; February 26, 206/164; March 3, 209/160; March 14, 196/120. There was a continuous low fever. The urine was of low specific gravity, and contained a large amount of albumin. Blood urea nitrogen ranged from 89.9 to 115 mg. The phenolsulphonephthalein test was 5 per cent on February 9. Albuminuric retinitis was present. The leucocyte count varied from 25,000 to 32,000, 80 to 90 per cent polymorphonuclears. Death May 15, 1921.

Postmortem Report: No edema; one liter of thin purulent fluid in the left pleural cavity; heart, weight 375 gm., left ventricular hypertrophy; liver, no disease.

The left kidney weighed 40 gm., and the right 25 gm.

The microscopic structure is typical advanced chronic glomerulonephritis. No glomerular lesions resembling those of Case 3.

It might be argued in this instance that the chronic nephritis resulted from eclampsia in 1913, but there was evidence of nephritis before that time and the structure of the kidney is in no way different from typical glomerulonephritis.

Case 22. (18–237) 22 years of age. Admitted Nov. 1, 1918, in coma. She was having convulsions every hour. She had been under a physician's care for three or four months. A diagnosis of nephritis had been made, and a therapeutic

abortion performed about two months before admission. Abdominal paracentesis had been performed repeatedly. During the period of hospital observation there was a marked oliguria, and the urine contained a large amount of albumin, many casts and erythrocytes. The blood pressure was 200/120. Albuminuric retinitis was present. There was marked edema. She was in coma or semicomatose most of the time. On November 7, pericarditis was demonstrated. Blood urea was 33 mg. on November 8. Death Nov. 13, 1918.

Postmortem Report: Marked generalized edema; large amounts of thin purulent fluid in the peritoneal, pleural and pericardial cavities; heart, weight 300 gm., pericarditis only; liver, cloudy swelling; no infection in the uterus.

The kidneys weighed 130 gm. each. The external surfaces were smooth, the cortices pale and fatty.

Microscopically a typical chronic glomerulonephritis is present. There are numerous hyaline glomeruli with completely atrophied tubules. There can be no doubt that nephritis antedated pregnancy.

CASE 23. (23–267) 35 years of age. First seen April 17, 1923, complaining of weakness, dyspnea, palpitation, edema of the ankles and cough. No serious illness during childhood. Her first pregnancy resulted in a stillbirth at eight months. The second pregnancy terminated in miscarriage at six months (a macerated fetus). The third pregnancy also resulted in miscarriage. In the fourth pregnancy she developed albuminuria and convulsions, and a stillborn fetus was delivered spontaneously at eight months. The fifth pregnancy in the spring of 1919 resulted in a living child. There were postpartum hemorrhages at this labor.

She dated her present illness from August, 1922, when she developed weakness, vertigo and dyspnea on exertion. She became progressively weaker after that time. April 17, blood pressure 140/90; marked albuminuria with casts. Only a trace of phenolsulphonephthalein was excreted in two hours. Blood Wassermann negative. Signs of pneumonia appeared toward the last. Death April 24, 1923.

Postmortem Report: Edema of the lower extremities; ascites; lobar pneumonia; heart, weight 375 gm.

The right kidney weighed 60 gm., and the left 75 gm. The capsules were adherent and the external surfaces granular. The cortices were very thin.

Microscopically a typical advanced chronic glomerulonephritis is seen.

The history as well as the structure of the kidneys indicates that nephritis was present many years, and was responsible for the complications of all her pregnancies.

CASE 24. (23–435) 26 years of age. First pregnancy in 1915. Never well since that time. In January, 1919, the urine showed heavy albuminuria, many casts and erythrocytes. She complained of loss of appetite and insomnia. Shortly afterwards she became pregnant and went through pregnancy with some difficulty. She was seen at various times during the past three years, but the renal condition was not studied. She had albuminuria and slight hypertension during this period. Hemoglobin 16 per cent. Shortly before death she had repeated convulsions. Death July 10, 1923.

Postmortem Report: No edema; a small amount of fluid in the serous cavities; heart, weight 375 gm., left ventricular hypertrophy; edema of lungs; liver, normal.

The left kidney weighed 58 gm., and the right 68 gm. The capsules were adherent and the external surfaces deeply pitted. The cortices were thin.

Microscopically a typical advanced chronic glomerulonephritis is seen. In view of the history it is certain that chronic renal disease was present before the second pregnancy, but there is no history of eclampsia at any time.

CASE 25. (26–286) 26 years of age. Had scarlet fever in childhood. Numerous attacks of tonsillitis. The first pregnancy ended in abortion at two months, in October, 1922. She first came under medical care in April, 1923, during the fifth month of her second pregnancy. From April until her delivery, July 14, she had moderate edema and moderate albuminuria. The blood pressure ranged from 122/66 to 160/110. There were usually casts and erythrocytes in the urine. There were no visual disturbances and no convulsions.

She remained in the hospital three weeks after delivery. During this time the edema disappeared. The blood pressure ranged from 130/88 to 180/118. July 19, five days after delivery, the blood urea nitrogen was 57 mg., and creatinin 5 mg. August 7, nineteen days later, the blood urea nitrogen was 32 mg., and creatinin 3 mg. August 21, blood urea nitrogen was 72 mg., and creatinin 1.7 mg. Hemoglobin, July 19, 40 per cent.

The patient was observed from time to time during the next three years. The blood pressure gradually rose to higher levels. During 1925 it ranged from 180/106 to 210/130. There were no definite changes in the eyegrounds. The hemoglobin remained low. About March 19, 1926, she developed an upper respiratory infection and died four days later.

Postmortem Report: Moderate generalized edema, ascites and hydropericardium; heart, weight 380 gm., left ventricular hypertrophy; bronchopneumonia; cloudy swelling of the liver.

The kidneys weighed 90 gm. and 120 gm. respectively. The capsules were adherent and the external surfaces deeply pitted. The cortices were thin.

Microscopically an advanced chronic glomerulonephritis is found, which shows no unusual features.

The definite renal insufficiency which was found immediately after labor establishes the diagnosis of chronic glomerulonephritis at that time. Very probably it was present before the first pregnancy in 1922.

CASE 26. (23–635) 41 years of age. In September, 1919, when she was eight months pregnant she was admitted to another hospital in labor. She was delivered by forceps because she was having convulsions. The infant was stillborn. She stated that she was unconscious for about one month after delivery. On admission June 8, 1921, she complained of incontinence of urine. The urine contained albumin, casts and erythrocytes. Her blood pressure was 134/90. The phenolsulphonephthalein excretion in two hours was 10 per cent. Blood urea nitrogen 34 mg. She was discharged July 20, 1921, and was not seen again until her readmission Sept. 20, 1923. At this time she was irrational and delirious. The blood pressure was 185/125. Hemoglobin 55 per cent. Erythrocytes 2,700,000. Blood urea nitrogen 125 mg. and 185 mg.; phenolsulphonephthalein output 0 per cent. Urine: specific gravity about 1010, abundant albumin, casts and erythrocytes. Slight terminal edema of the ankles. Death Oct. 3, 1923.

Postmortem Report: Slight edema of the feet; no excess of fluid in the serous cavities; heart, weight 365 gm., moderate left ventricular hypertrophy; edema of the lungs; liver, normal.

The kidneys weighed 33 gm. and 30 gm. respectively. The capsules were adherent and the external surfaces finely granular. The cortices were very thin.

Microscopically a typical, very advanced chronic glomerulonephritis is found.

Very probably the convulsions that occurred during her labor in 1919 were uremic and not eclamptic. The extreme atrophy of the kidneys indicates a nephritis of many years' duration.

CASE 27. (28–906) 37 years of age. Admitted March 26, 1928. The patient stated that she had had albumin in the urine since the birth of her last child, three and one-half years previously. Her immediate illness began in January, 1928, with dyspnea, and edema of the ankles. These symptoms gradually became more severe and she became progressively weaker until she was obliged to go to bed. The blood pressure varied from 142/104 to 162/114. The urine was of low specific gravity, and contained abundant albumin and casts. Blood urea nitrogen, March 28, 38.5 mg. May 1, hemoglobin 54 per cent; erythrocytes 3,490,000. The edema progressed until it became a marked generalized anasarca. Death July 8, 1928.

Postmortem Report: Marked anasarca; ascites; hydrothorax; heart, weight 340 gm., recurrent mitral endocarditis; liver, normal.

The kidneys weighed 73 gm. and 63 gm. respectively. The capsules were adherent, and the external surfaces finely granular. The cortices were very thin.

A typical advanced chronic glomerulonephritis is found microscopically.

The patient dated her illness from her last pregnancy, but there was no history of eclampsia. The structure of the kidneys indicates a long duration of the disease.

CASE 28. (28–123) Gravida II. 38 years of age. Admitted Jan. 18, 1928. Expected date of confinement, March 22. Said to have had a few convulsions during her first pregnancy, fourteen years before. Under treatment for hypertension for the past five years. Blood pressure usually above 200 mm. Hg., during this period. She was seen by her physician shortly after the beginning of the present pregnancy, and the blood pressure was found to be 215/120. During the course of the pregnancy the blood pressure was never found below 170/110. She entered the hospital because she was beginning to have visual disturbances, edema and vomiting. For two months she had been troubled with headaches and dizziness. During her stay in the hospital the systolic blood pressure ranged from 210 to 240 mm. Hg. There was edema of the ankles. The urine contained a large amount of albumin and many casts. Blood urea nitrogen 23.3 mg.; hemoglobin 85 per cent. During the last week she vomited almost continuously. Labor was induced January 25, and a dead fetus was delivered. The patient died suddenly about two hours after the completion of labor. There were no convulsions.

Postmortem Report: Moderate edema of the ankles; no fluid in the serous cavities; heart, weight 310 gm., moderate hypertrophy of the left ventricle; liver, weight 1700 gm., chronic passive congestion and moderate fatty metamorphosis, no areas of necrosis.

The kidneys weighed 175 and 100 gm. respectively. The smaller kidney was adherent to the surrounding tissues because of an operation several years before. The cortices were slightly cloudy.

Microscopically there is a generalized arteriolar sclerosis, but no atrophy of the parenchyma. The glomeruli show a marked thickening of the capillary basement membrane, an appearance that is found both in primary hypertension and in eclampsia.

This is undoubtedly an instance of pregnancy in a woman with preëxistent hypertension.

The foregoing 8 cases (Cases 21 to 28), illustrate the course of pregnancy in women with previous chronic renal disease. There is usually a marked aggravation of the nephritic symptoms. The distinction from gestation eclampsia is difficult when the function of

the kidneys prior to pregnancy is unknown. All the symptoms of eclampsia, namely — hypertension, albuminuria, edema, headache, visual disturbances, vomiting, convulsions and coma — may occur in nephritis uncomplicated by pregnancy. However, if a definite impairment of renal function is demonstrable, the diagnosis of pre-existing chronic nephritis may be established.

Many women with chronic renal disease go through pregnancy without serious complications, but the usual effect is an increase in the intensity of the symptoms referable to nephritis. When the uterus is emptied the nephritic symptoms usually improve, but do not disappear entirely.

There is no evidence in my experience that the presence of chronic renal disease increases the danger of the development of gestation eclampsia. Heynemann expresses a similar opinion.

Discussion

In fatal cases of eclampsia and preëclampsia, a characteristic glomerular lesion is found. The glomeruli are slightly enlarged and the lumina of their capillaries are narrowed and sometimes completely closed, so that they contain very few erythrocytes. The decrease in size of the capillary lumina is caused chiefly by a marked thickening of the capillary basement membrane. Usually there is only a slight increase of endothelial cells, but sometimes the endothelial increase is prominent, and then becomes a more important factor in capillary obstruction than the thickened basement membrane.

When the increase of endothelial cells is prominent (Fig. 6), there is a definite resemblance to acute glomerulonephritis. But the more striking features of acute glomerulonephritis are absent. There are no very large glomeruli, and no epithelial crescents. Intracapillary fibers were found in only one instance, Case 16, and then in association with acute rheumatic endocarditis. Fahr noted an increase of endothelial nuclei in exceptional instances, and was inclined to attribute it to an associated infection. His view seems to be that a mild glomerulonephritis is superimposed on the eclamptic kidney in these cases. Fahr's interpretation of the endothelial increase is probably influenced to some extent by his conviction that the lesion of the eclamptic kidney is a nephrosis.

The increase of endothelial cells is surely an inflammatory phenomenon, that is, a form of glomerulonephritis. It occurs so frequently that Fahr's interpretation of superimposed infection seems doubtful. A simpler explanation is to consider it a reaction to the toxic substance responsible for the toxemia of pregnancy.

The interpretation of the thickening of the capillary basement membrane is more difficult. It is not clear whether this is a degenerative or an inflammatory phenomenon. One is tempted to explain it as a compensatory reaction to increased intravascular pressure since it occurs so regularly in primary hypertension. But it was found in one case of hyperemesis gravidarum (Case 19) in which there was no elevation of blood pressure, and I have found it in instances of lipoid nephrosis without hypertension.

Volhard's theory of arteriolar spasm does not seem adequate to explain thickening of the capillary walls. We are left with the theory that a soluble toxic substance in the blood is responsible for the thickening of the basement membrane. This view can neither be established nor disproved with our present knowledge.

The thickening of the capillary basement membrane is apparently a process of hypertrophy, similar to the thickening of the elastica interna of the arteries that occurs in advanced life. Whether this is an inflammatory process or not depends upon how inflammation is defined. It is not what one ordinarily understands as inflammation, but it probably represents a reaction to some kind of stimulus.

The glomerular lesion of eclampsia is, therefore, a distinct pathological entity. It is perhaps best classified as a special form of glomerulonephritis, although it is to be distinguished from ordinary glomerulonephritis. It is somewhat confusing to classify a disease of this type as nephrosis.

The classification of the lesion as nephritis or nephrosis is of no great importance. The essential nature of the disease is an injury of the glomerular capillaries, which allows albumin to escape and impedes the flow of blood through the kidneys.

The glomerular lesion may be the primary cause of the hypertension rather than its effect. The fact that hypertension often precedes albuminuria does not exclude this interpretation, since the narrowing of the capillaries may take place before they are permeable to albumin.

The glomerular lesions support the view that the fundamental

cause of eclampsia is a toxic substance in the circulating blood. The peculiar histological structure suggests that the poison is quite distinct from that causing glomerulonephritis.

SUMMARY

In fatal cases of eclampsia a characteristic glomerular lesion is found.

The glomeruli show a marked narrowing of all their capillaries, caused usually by an increase in thickness of the capillary basement membrane, but sometimes by an increase of endothelial cells.

One case is reported (Case 3) in which the lesions resulting from an attack of eclampsia seven years before are described. These consist of focal hyaline areas in the glomeruli with partial or complete glomerular obliteration and varying degrees of tubular atrophy. It is shown that a peculiar form of chronic renal disease may result from the eclamptic kidney.

In one case of hyperemesis gravidarum (Case 19) glomerular lesions were found which correspond entirely to those of typical eclampsia. In three other cases the glomeruli were normal. A fatty liver without necroses is characteristic of this form of toxemia.

When a woman with chronic renal disease becomes pregnant, there is usually an aggravation of all the nephritic symptoms. The condition cannot be distinguished from preëclampsia and eclampsia unless the condition of the kidneys prior to pregnancy is known, or unless there is a definite impairment of renal function. Chronic nephritics show no special tendency to develop gestation eclampsia.

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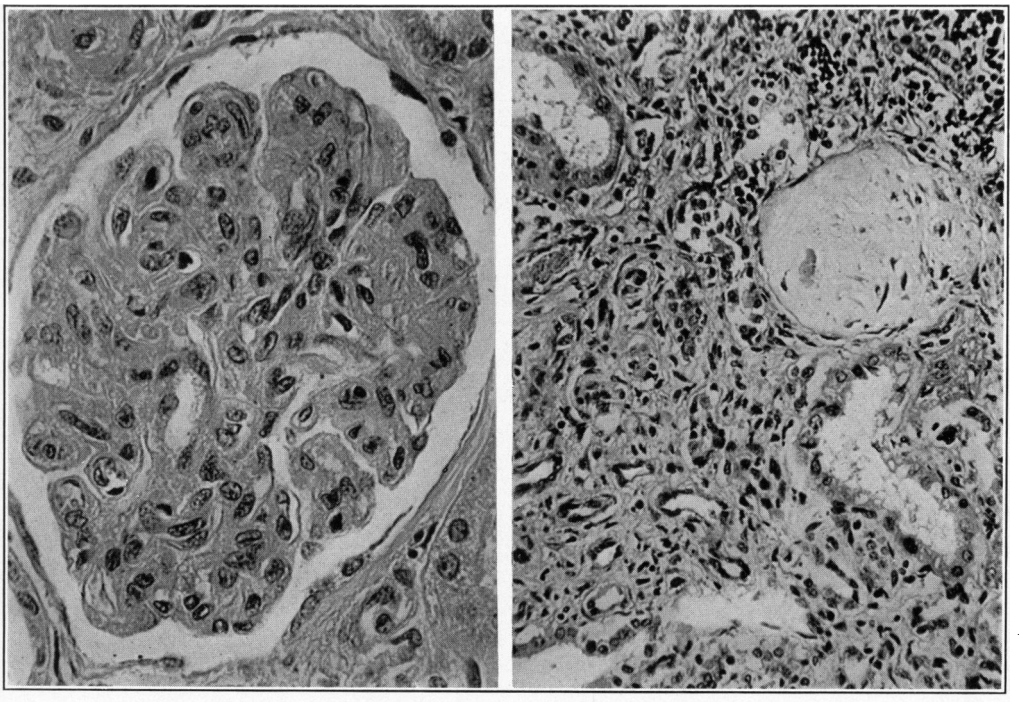
DESCRIPTION OF PLATES

PLATE 1

FIG. 1. Case 14. Photomicrograph of glomerulus under low magnification, showing extensive obstruction of the capillaries. Hematoxylin-eosin stain.

FIGS. 2, 3 and 4. Case 3. These photomicrographs illustrate the effect of an attack of eclampsia seven years before death. The hyaline glomeruli are associated with atrophic tubules (Fig. 2). Figures 3 and 4 show partially obliterated glomeruli.



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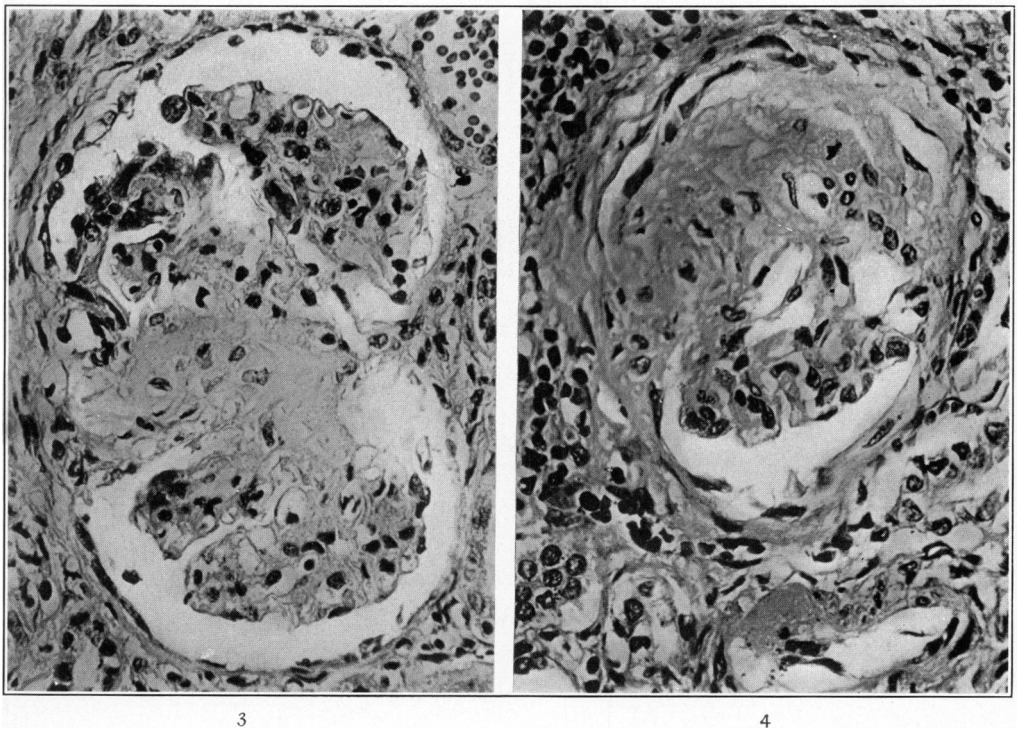

3 4

Bell Renal Lesions in Toxemias of Pregnancy

PLATE 2

FIG. 5. Case 14. Drawing showing portion of a glomerulus under high magnification. Azo-carmine stain. Note the marked thickening of the capillary basement membrane (b. m.). End., endothelial cell; ep., epithelial cell; g., hyaline granules in an epithelial cell; er., erythrocyte; l., lumen of capillary.

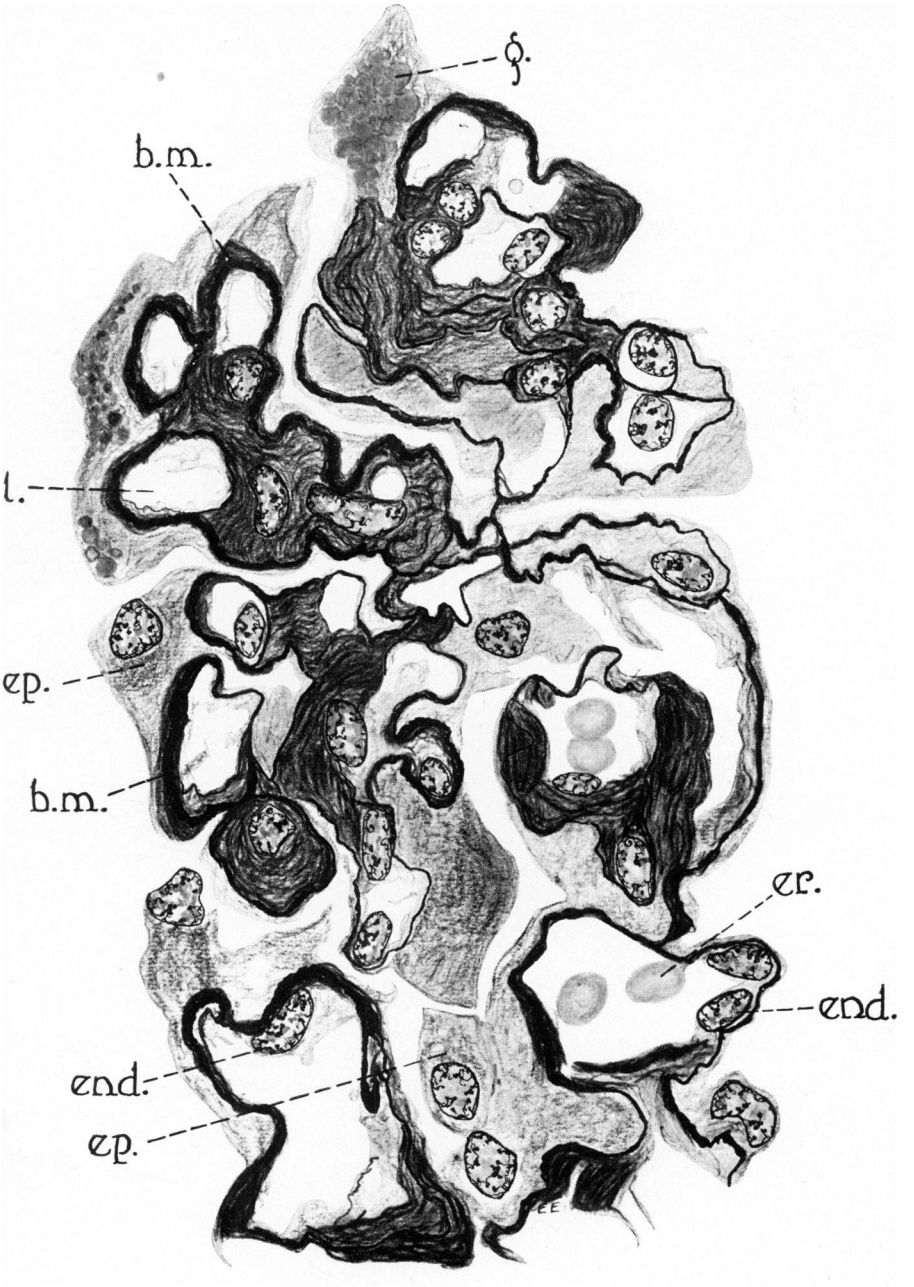

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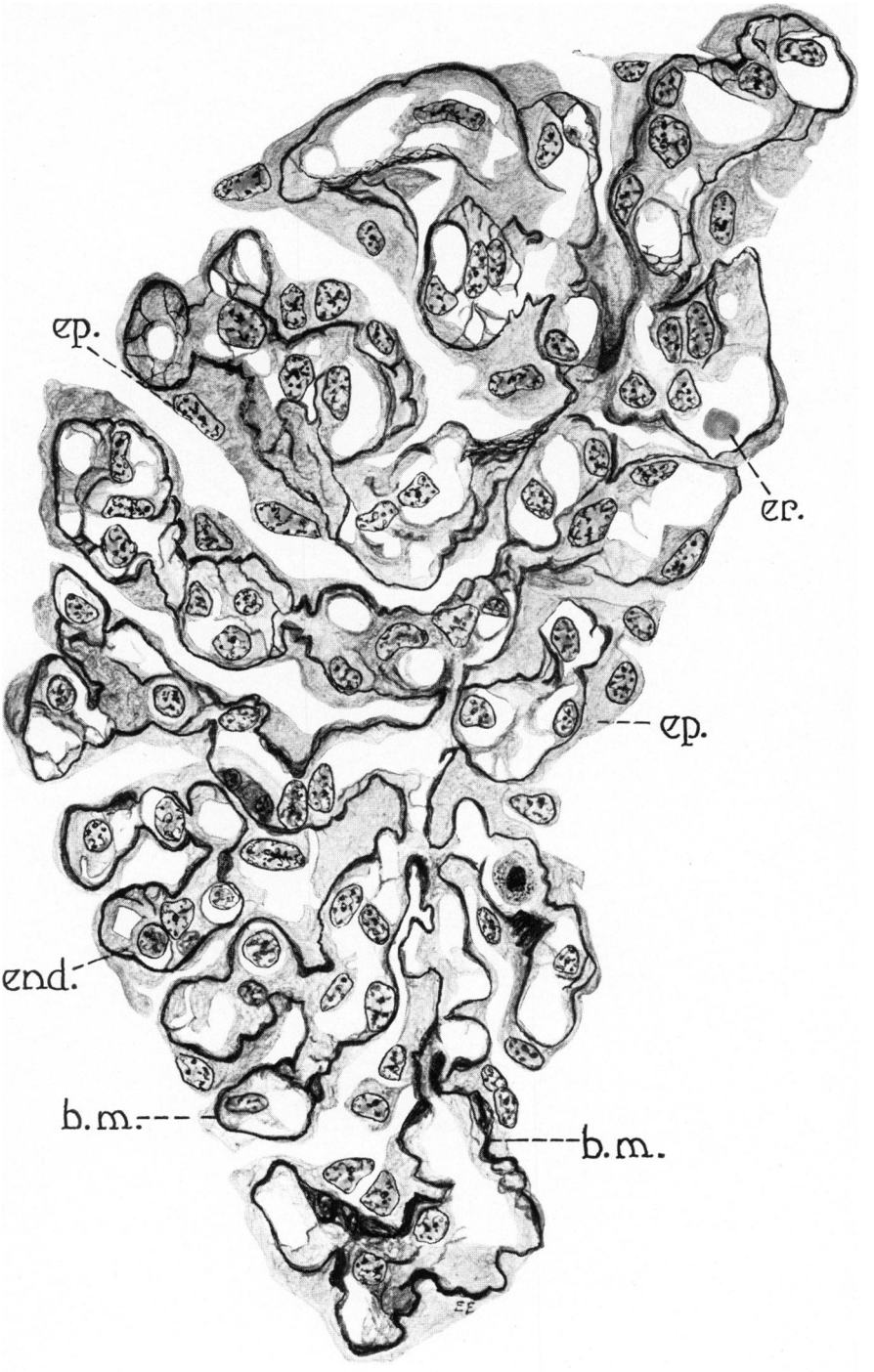
PLATE 3

FIG. 6. Case 11. Drawing showing portion of a glomerulus under high magnification. Azo-carmine stain. Note the marked increase of endothelial cells (end.). The capillary basement membrane (b. m.) shows a moderate but uneven thickening. Ep., epithelial cell; er., erythrocyte.



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