Sir,

I have the honour to present this essay in competition for the Lister (Victoria Jubilee) Prize in Surgery.

The title of the essay is, Bilateral Cortical Necrosis of the Kidneys, a review of the literature with a report of four cases occurring during pregnancy.

Yours faithfully,
The investigation and treatment of cases of bilateral cortical necrosis of the kidneys has chiefly fallen to the lot of the obstetrician. There are now, however, an appreciable number of recorded cases which have occurred without the common association of pregnancy and indeed several cases have occurred in men.

The total number of authentic cases which has been recorded in the literature is about forty-two. Last year Kellar and Arnott (1) reported three cases, Johnstone (1) one, Baird and Dunn (2) one which now brings the total number to forty-seven. The condition can no longer be regarded as a rarity although very uncommon, and indeed most pathologists and obstetricians of experience will have met with one or more examples. Professor F.J. Browne of University College told me that he had met with a case very recently. The total number of recorded cases of a disease rarity is not by any means an accurate index of its actual occurrence.

Clinically the condition is characterised by a profound or total anuria and with the striking pathological picture of almost complete necrosis of the renal cortex it forms an entity which is readily recognisable.

It is interesting to note that during the past twenty-seven years no less than fourteen cases of this type have been reported to the Edinburgh Obstetrical Society. Jardine and Kennedy (3), Davidson and Turner (4), Kellar and Arnott (1). It is probable that this has a direct relationship to the high incidence of toxaemia in Scotland.
In this short essay I shall first detail the four cases of this condition which I have studied and then proceed to a short discussion with reference to the literature on the subject.

All the kidney sections were stained haematoxylin and eosin and also with azan. In one case the alizarin stain for calcium was also employed. In case one a whole block section of the kidney was made but it was found after staining that there was no great contrast in the colour between the necrotic and the non-necrotic portions of the kidney and the striking naked eye appearance was to a great extent lost.
CASE: Mrs. F., aged 26, i-para. Patient was admitted with a history of not having passed urine for a fortnight. She was five months pregnant. From the second month of her pregnancy she had suffered severely from morning sickness. A fortnight before admission vomiting became much more severe and she retained but little food. From that time till admission she stated that she passed no urine whatsoever. During that time the sickness was still very severe and was accompanied by vague abdominal pain. For the two days prior to admission she had suffered from severe backache, lumbar in situation. The bowels had been constipated, so much so that for four days there had been no motion. On the day of admission she stated that she had been feeling hot and thirsty and had had some difficulty in swallowing. She noticed for the first time that her ankles were swollen.

Previous History: No history of scarlet fever, tonsillitis, or urinary trouble.

Previous Obstetrical History: First child, aged 5, was full-time and the delivery was spontaneous. No miscarriages.

On Admission: Patient was a well-nourished, well-developed young woman. Beyond slight pallor of the lips and mucous membranes there was no obvious morbid characteristic. Temp. 97.4°; P.R. 88; Resp. 16. There was slight oedema of both lower extremities, especially marked over the dorsum of the feet. The heart was not enlarged. The sounds were pure. B.P. 110/60. The respiratory system presented no abnormality. Mouth and tongue were dry.

Examination of the abdomen showed a uterus of a size consistent with a five-months' pregnancy. There was some vague abdominal tenderness over the uterus. Bimanual examination of the lumbar regions revealed pronounced tenderness over both posterior renal points. The kidneys were not palpable. Vaginal examination: Os one finger; membranes intact.

Nervous System: No tremor or convulsions. No disturbance of motor or sensory function. Reflexes normal.

Urinary System: Patient strongly adhered to her story that she had not passed urine for a fortnight and further she had had no desire to do so. Passage of the catheter both before and after admission failed to remove one drop of urine.

History of Further Progress: On the evening of admission patient received abundant fluid by the mouth and 400 c.c. of glucose saline intravenously. Free action of the skin was promoted by the use of the electric bath. Next morning a further attempt to remove some urine by catheter was made but without success. She felt quite comfortable and there was no material change in her condition. During this day a further intravenous glucose saline was given but still no urine was secreted.
9.8.32: Professor Johnstone was called in consultation with Dr. Matthew and it was decided that immediate termination of the pregnancy offered her the best chances of survival. On the afternoon of this day an abdominal hysterotomy was performed by Professor Johnstone under gas and oxygen anaesthesia. The uterus and the placenta were normal, a special search being made for any signs of retroplacental haemorrhage. Palpation of the kidneys showed them to be slightly enlarged and tense. Apart from some vomiting patient made an excellent recovery from the immediate effects of the operation.

We do not propose to record her condition from day to day but merely to present a summary. She survived for sixteen days after operation and during this time a full record of fluid intake, blood pressure, urinary secretion, and many of the biochemical features was made.

Her clinical condition may be summarised as follows:- For the first five days following operation she felt quite comfortable but she was very drowsy and slept a great deal. Indeed, on the 14th she was in frank coma. There was a certain amount of vomiting during this period which diminished in severity. Two days after operation she began to show sporadic twitchings of the face and hands and there was very evident muscular hyper-excitability as evidenced by repeated observations of the supinator reflexes and Chvostek's sign. Oedema also became apparent two days after operation. It was first noticed on the vulva, but within two days it had spread to the face, hands, arms and legs. From the day after operation a small daily quantity of urine was obtained by catheterisation. This never amounted to more than six drachms during this period. The specimens contained a negligible quantity of urea; indeed, the addition of sodium hypobromite to a specimen of the urine obtained on the 10th produced no effervescence at all. Apart from this the urine was crowded with pus cells with a few red blood cells. Bacteriologically there were present *E. coli* and *staphylococci*. No casts were seen.

On the 15th, after being quite unconscious on the previous day, patient was rational and the oedema had subsided to some extent. The twitchings were less evident. However, a new complication was introduced. There began to appear some oozeing from the wound. On the 16th there was a moderately severe secondary haemorrhage necessitating the operation of secondary suture. No anaesthetic was required and it was remarkable how insensitive the patient was to the introduction of large needles.

For the next four days the picture was one of drowsiness alternating with periods of fretfulness. The oedema was variable. The condition of the wound was now satisfactory. On the 19th patient passed urine herself for the first time during her stay in hospital. This, however, only amounted to some 4 czs. The
evening of this day saw the commencement of the closing phase of
the condition. Vomiting became severe and there was continuous
retching. She was almost continuously delirious and required
sedatives. On the 21st the oedema once more became very pronounced.
Twitchings were not now in evidence.

On the 23rd it was evident that broncho-pneumonia was
present, and from a condition of continuous uncontrollable delirium
patient sank into coma and died on the 25th of August, eighteen days
after entering hospital. During this period the amount of urine
secreted showed an increase and on the day before death an output
of 16 ozs. was recorded.

During the whole of this period the skin had been very
active, and it was by this route that patient was eliminating the
major portion of the large quantities of fluid that were given both
orally and rectally. B.P. during this period varied between
140/80 and 110/70. Occasional blood counts showed a progressive
secondary anaemia with a moderate leucocytic reaction. No
reticulocytosis was present. There was never at any stage any
febrile reaction.

Bilateral cortical necrosis of the kidneys.

The body was that of a moderately well-nourished young
woman. Post-mortem lividity and rigidity were present. A right
paramedial abdominal incision was present and was partly broken
down. Between the gaping edges of the wound there was liquefying
blood clot. On opening the abdomen a quantity of thick pus was
present. This was greatest in amount in the pelvis but was also
found around the kidneys and in the subphrenic space.

Stomach and Intestines:- These were healthy apart from a congestion
of the overlying peritoneum. There were no intestinal ulcers
present. Liver: This was slightly enlarged and pale in colour.
It was easily broken up with the fingers. Spleen: This was en-
larged but remarkably firm. Lungs: There was some blood-stained
fluid in the pleural sacs. On section both lungs presented the signs
of a broncho-pneumonia with a good deal of basal congestion.
Heart: The pericardial sac contained no excess of fluid. There
was slight enlargement of the left ventricle. The heart muscle
was pale in colour. Uterus and Appendages: The uterine wound had
broken down and there was some degree of infection. The bladder
contained a few drops of blood-stained urine. The mucosa was
slightly congested, especially in the region of the trigone. The
ureters were not thickened. Kidneys: These were slightly larger
than normal. The capsule stripped easily. The subjacent surface
showed numerous pale yellow areas, some as large as a postage stamp.
These areas tended to be recessed. The intervening kidney tissue
was slightly congested. On section the cortex showed a number of
similar yellow areas, some of which extended down into the pyramids. On section these yellow areas presented a firm surface, there being no tendency to central liquefactive necrosis. The non-necrotic areas varied between a pale cloudy appearance and red congestion. The medulla showed some streaky congestion. The pelves of the kidneys showed a moderate degree of congestion.

Kidney - Microscopic Appearances: - The cortex resolves itself into two well-defined areas. **Area 1:** In this, the zone of necrosis, the tubular epithelium has undergone complete hyaline necrosis, the epithelial nuclei have ceased to stain, the lumina of the tubules contain granular debris surrounded by annular bands of homogeneous pink material, in which all trace of individual cells has been lost. The glomeruli show some swelling and oedema. There is no evidence of endothelial proliferation of the lining cells of Bowman's capsule. The interstitial tissue is very oedematous and it shows a considerable amount of cellular infiltration, most of these cells being polymorphonuclear leucocytes. The intralobular vessels contain thrombi. Sections stained by the Azan method show a certain amount of fibrin in these thrombi. At the periphery of the necrotic areas tubules and glomeruli show scattered among them irregular aggregations of purple granules. Indeed, some of the glomeruli show up as a homogeneous purple disc. This indicates calcification. To a less extent calcification is to be found in the centres of the necrosed areas. There is no marked congestion of the vessels at the periphery of the necrosed areas.

**Area 2:** The surrounding renal tissue presents a confused picture because of the changes due to pyelo-nephritis. The tubular epithelium shows a pronounced cloudy swelling with, in many cases, complete disintegration. The tubules show a pronounced degree of dilatation. The nuclei in most tubules stain well although they are sometimes lying free in the lumen. The glomeruli show some slight congestion, the endothelial nuclei stain well, and Bowman's capsule presents no abnormality. The interstitial tissue is extremely oedematous and in places there are appearances strongly suggestive of fibroblastic proliferation. There is also in some areas an intense round-celled infiltration and here and there frank abscess formation. The vessels do not contain thrombi. There is no evidence of arterio-sclerotic change in the vessel walls. Sections stained by Weigert's method for elastin show no pronounced degree of fragmentation of the internal elastic lamina.

**Medulla:** The tubular epithelium shows cloudy swelling. The lumina contain plugs of cellular debris, these being mostly pus cells. The interstitial tissue shows oedema and round-celled infiltration.

Sections stained for fat with sudan III show fat globules in the vessels. The glomeruli stand out prominently in virtue of
these globules in the capillaries. There is only very slight fatty degeneration in the renal epithelium.

Liver:— There was present in the hepatic cells an intense cloudy swelling and but little fatty degeneration. These changes are more marked at the periphery of the lobules.

History of Recent Remonancy: L.D.F. September 21st. Up till one day before admission there had been no untoward symptoms. There had been no previous illness. The abdomen had been doing regularly. She had never suffered any swellings of her feet or ankles. Years had been free from disturbances of vision. On the afternoon before admission she had severe pain in the small of the back. The gait was comfortable and there is character, it was totally unlike the pain experienced by her back at the commencement of labor. At about the same time she began to be aware of a headache which rapidly became more severe. It was present in the situation. She did not go to bed but walked as much as her household duties would permit. Later in the afternoon, to our surprise, she found that she was feeling very much more than that of an ordinary infection. Her doctor was called in and he referred her to the Royal Maternity Hospital, where she arrived at 10.30 p.m. on 22. 4. 32.

Condition on Admission: The marked pallor of the face constricted strongly with the symmetrical of the lips. There was no jaundice. General examination failed to elicit the slightest trace of jaundice. The heart was not enlarged and the heart sounds were absent. There was some ascension of the second sound in the aortic area. The blood pressure was 105/120. The pulse was 90. There were no abnormal physical signs in the abdomen. Examination of the abdomen showed the uterus to be three fingers-breadth above the umbilicus. It was hard and tender to the touch.

April 22. 1.40 a.m. The patient was being prepared for a vaginal examination under chloroform. She was seized with a typical eclamptic convulsion. She was unconscious with chloroform and a vaginal examination made. The cervix was neither thinned out nor taken up. The index finger and exploration revealed that the membranes were intact and that no placenta occupied the lower uterine segment. Cystoscopy failed to remove any urines from the bladder.

Patient now very ragged conscious. During the next seven hours she had over fifteen severe eclamptic convulsions, remaining in deep sleep between the fits. The blood pressure gradually fell, being 30/40 two hours before death. The pulse increased to rate rising to 190. The temperature fell to 95°. Death occurred at 3:00 a.m. during an eclamptic convulsion. Chloroform had been administered at such time and three injections of morphia had been given.
CASE: Mrs. W., aged 30, ii-pars. Admitted: 29. 4.32. Complaint: Bleeding. Previous Health: There is no history obtainable on this point.

Previous Obstetric History: Has had two children. Last born spontaneously in July 1930.

History of Present Pregnancy: L.M.P. September 1931. Up till one day before admission there had been no untoward symptoms. There had been no undue sickness. The bowels had been moving regularly. She had never noticed any swellings of her feet or ankles. There had been no disturbance of vision. On the afternoon before admission she had severe pain in the "small of the back". The pain was continuous and sharp in character. It was totally unlike the pain experienced in the back at the commencement of labour. At about the same time she began to be aware of a headache which rapidly became more severe. It was frontal in its situation. She did not go to bed but rested as much as her household duties would permit. Later in the afternoon, to her surprise, she found that she was bleeding vaginally. The blood loss was fairly copious and in amount was much more than that of an ordinary period. Her doctor was called in and he referred her to the Royal Maternity Hospital, where she arrived at 10.45 p.m. on 29. 4.32.

Condition on Admission: The marked pallor of the face contrasted strongly with the cyanosis of the lips. There was no jaundice. Careful examination failed to elicit the faintest trace of oedema. The heart was not enlarged and the heart sounds were closed. There was some accentuation of the second sound in the aortic area. The blood pressure was 185/135. The pulse was 90. There were no abnormal physical signs in the chest. Examination of the abdomen showed the fundus to be three finger-breadths above the umbilicus. It was hard and tender to the touch.

30. 4.32. 1.30 a.m.: As patient was being prepared for a vaginal examination under chloroform, she was seized with a typical eclamptic convulsion. She was anaesthetised with chloroform and a vaginal examination made. The cervix was neither thinned out nor taken up. The os admitted one finger and exploration revealed that the membranes were intact and that no placenta occupied the lower uterine segment. Catheterisation failed to remove any urine from the bladder.

Patient never regained consciousness. During the next seven hours she had over fifteen severe eclamptic convulsions, remaining in deep coma between the fits. The blood pressure gradually fell, being 80/40 some two hours before death. The pulse increased in rate, rising to 180. The temperature fell to 95°. Death occurred at 6.25 a.m. during an eclamptic convulsion. Chloroform had been administered at each fit and three injections of morphine had been given.
Post-mortem Examination - Summary: Eclampsia gravidarum and early bilateral cortical necrosis of the kidneys. Cerebral haemorrhage.

The body was that of a well-nourished, normally developed female. Post-mortem rigidity and lividity present: no jaundice. There was marked oedema of the lower limbs. Serous Cavities: Nothing to note. Circulatory System - Heart was of average size. There was an average amount of sub-epicardial fat. The chambers were of average size. There was nothing abnormal to note regarding the aortic, pulmonary or tricuspid valves. Blood vessels were healthy. Respiratory System: The mucosa of the larynx and trachea was congested. The pleural surface of both lungs was smooth and glistening. All the lobes showed marked congestion. There was no evidence of pneumatic consolidation. Alimentary System - Stomach of average size. Nothing abnormal to note throughout the alimentary tract. Liver - of average size. Extensive subcapsular haemorrhages were present over the right and left caudate lobes. On section, the liver was of a reddish brown appearance, and what appeared to be the outlines of the lobules could be seen. These outlines were of a pale, greyish colour. No obvious haemorrhage was present in the deeper portions of the tissue. Spleen - was slightly enlarged. The tissue was moderately firm in consistence and dark red in colour. Pancreas: Nothing abnormal to note. Suprarenal glands - of average size and appearance.

Genito- Urinary System - Kidneys: Both were rather larger than normal. The capsules stripped, leaving a very red and congested surface. On section, the cortex was broad and well defined from the medulla. The cortex was extremely red, haemorrhagic, and structureless in appearance. There was a pale, greyish-red, structureless zone immediately at the junction with the medulla. Appearances were typical of bilateral cortical necrosis in its early stages, as the whole of the cortical tissue showed the appearances of early red infarction. The medulla was very congested. There was also congestion of the mucosa of the pelvis. In both renal veins blood clot was present. This was not adherent to the wall of the vein, but was firm and somewhat greyish-red in colour, but had the appearance of having been formed some short time before death, as definite post-mortem clot was found in relation to these hard clots.

Microscopic Examination - Liver: No evidence of actual necrosis of liver cells was present. The portal veins were moderately congested and in the subcapsular region numerous small haemorrhages were seen. The liver cells in relation to these haemorrhages showed early degenerative change. In the sections stained for fat there was marked fatty degeneration in the cells of the peripheral zones of the lobules. Although this was well defined the globules were small and appearances were indicative of early fatty change.

Kidney: There were marked degenerative changes in the subcapsular region. The lining cells of the secreting tubules showed advanced
cloudy swelling. The glomeruli were very haemorrhagic and congested and there were large areas of haemorrhage. This congestion and haemorrhage was well marked throughout the whole of the cortex and probably more towards the periphery. Here and there were small areas where there had been a disappearance of units and replacement of oedematous fibrous tissue. In the other areas, towards the medulla, the lining cells of the secreting tubules showed evidence of complete necrosis. The cytoplasm was swollen and disintegrated and there was a lack of nuclei. What remained of the tubules were filled with coagulated fluid. The glomeruli showed marked congestion and haemorrhage and there was no abnormal thickening of the capsule. A large number of blood vessels showed fibrous tissue thickening of the intima. Sections stained for fat showed a very profound fatty degeneration occurring in the glomeruli. There was some slight fatty change in the secreting and distal convoluted tubules, but this was not well marked.

Spleen: Markedly congested and haemorrhagic. In the Malpighian bodies there were masses of hyaline eosinophile tissue, which had the appearance of hyaline degeneration.

Previous Health: This had been very good. Has had no serious illnesses. No history of repeated sore throats or of swelling of face at any time.

Previous Obstetric History: September, 1926; full-time child; spontaneous delivery; alive and well. April, 1930; full-time; spontaneous delivery.


For the first four months of her pregnancy patient felt in good health. She had some slight morning sickness on rising, but never after meals. About four weeks before admission patient noticed that her ankles were becoming swollen, and a few days later she found that the backs of her hands and also her face were becoming puffy. On the day of admission she had found on awakening that she was unable to see clearly and also that there was a great increase in the swelling of her face and ankles. She had a severe pain in the "pit of the stomach". Later in the day she was troubled by an intense headache in the frontal region. Although she did not actually volunteer the information, on being questioned she stated that she had noticed that for the previous fortnight she had not been passing as much water as usual.

Condition on Admission: (From antenatal clinic where she had reported) Patient was obviously ill. The face was swollen and of a marked pallor. The ankles and the lower legs were markedly oedematous. So also were the hands and arms. The mouth was dry and the tongue furred. The breath was foetid. The bowels had not moved for a day or two. Examination of the abdomen showed a swelling rising up to a point just below the umbilicus. This corresponded roughly to a pregnant uterus at the fifth month of gestation. The uterus was not tender. The foetal heart was not heard.

The heart was not found to be enlarged but on auscultation there was found to be an accentuation of the second sound in the aortic area. The blood pressure on admission was 158/100. Pulse 76. Patient complained of a slight cough, but there were no physical signs in the lungs. Respirations 20. There is no record of any retin-scopy. No muscular twitchings were present. In the antenatal department patient had been unable to pass any urine, but three ounces were obtained by the catheter. On examination this was found to be loaded with albumin and boiled solid.

Patient was placed at rest in bed and encouraged to drink large quantities of glucose and orange juice. Late on the night of
admission she complained bitterly of intense headache, and aspirin and phenacetin were given to help this.

27. 5.32.- At about 5 a.m. patient complained of intense abdominal pain of a continuous nature. This pain was situated over the uterus and was quite different to the epigastric pain which had previously troubled her. About one hour after the onset of this pain the membranes ruptured. She was examined vaginally and the os found to be one finger dilated. The presentation was cephalic. She received morphia gr. 1 one hour after the onset of this pain. A catheter was passed during the morning and only one drachm of urine was removed. This boiled solid. Colonic lavage was performed and continued till the result was clear. The pain continued to be severe, and on examination later in the day showed that the fundus of the uterus had risen above the umbilicus and that the uterus was tense and firm and very tender. Concealed accidental haemorrhage was suspected.

It was decided to carry out an abdominal hysterotomy. At 4.30 this operation was performed by Dr. Douglas Miller under stovaine as a spinal anaesthetic. On opening the abdomen the bluish motting of the uterus denoted that there was some haemorrhage. The muscle was incised and a five months' fetus together with a placenta and a large amount of black blood clot was removed. The typical ploughing up of uterine muscle was present. During the operation the blood pressure had dropped to 70/50 and this necessitated the use of ephedrine. From this time the blood pressure never rose again above 120 systolic.

Five hours after the operation a transfusion of one pint of blood was carried out. At this point the patient's condition was as follows, pulse 120, respirations 32, B.P. 110/70.

28. 5.32.- Patient's condition was not good. The pulse was very rapid and its rate was 132. The temperature was over 100°. The skin was excreting moderately well. She was vomiting occasionally but drinking plenty. The catheter obtained one drachm of urine. B.P. 118/70.

29. 5.32.- Condition the same. About twelve drachms of urine obtained by catheter. Solid with albumin. B.P. 118/70.

30. 5.32.- Since admission the exhibition of thyroid had been carried out. It was decided to try the effect of pilocarpine and accordingly this was given as the nitrate gr. 1/12. The skin had been acting, but not very well. With the application of the shock cage and the administration of pilocarpine the skin was stimulated to secrete more. No urine was obtainable by the bladder, however. B.P. 120/80. Condition moderate. There were no muscular twitchings and the patient could co-operate in treatment, etc.
31. 5.32. - Similar condition. B.P. 120/80. No urine obtained by catheter. Previously the bowels had only been moved by enemata, but on this day there was incontinence with frequent small motions. Patient drinking plenty.

1. 6.32. - A secondary suture was required in the wound and this was performed under a local anaesthetic. 500 c.c. of glucose saline given intravenously. One and a half drachms of urine obtained.

2. 6.32. - Transferred to Deaconess Hospital under the care of Mr. Duncan Morison. The total amount of urine passed during her stay in hospital was therefore 4 oz. 5 drs. during a period of seven days. There is no exact record of the fluid intake during this time but patient drank freely nearly all the time she was in hospital.

2. 6.32. - (4.30). - A cystoscopic examination was carried out. A few drops of mucopurulent material were present in the bladder. No urine was obtained by the ureteral catheters.

Under gas and oxygen anaesthesia the left kidney was exposed by an incision through the loin. The following interesting observations were made: "The renal capsule appeared pale and semi-translucent, and through it one could see that the kidney substance was of a pale greyish-yellow colour with haemorrhagic stippling here and there. The contour of the surface did not suggest any unusual elevations other than that suggested by the normal unevenness due to lobulation. The capsule was incised over the convex outer surface of the kidney in its longitudinal axis and was stripped back more easily than normal, all round, down to the hilum. During this process it was observed that the renal capsule was exerting no pressure on the contained kidney substance and there was no increase in size of the kidney tissue as by engorgement following the stripping of its capsule." Patient was treated by shock cage and magnesium sulphate enemata in order to promote excretion. She died, however, some ten hours after operation.

Post-mortem Report: Mrs. C., aged 27, 4.6.32. Complete cortical necrosis of kidneys. Cloudy swelling of liver and myocardium. Hypostatic congestion and oedema of lungs. The body was that of a well-developed, well-nourished adult female. The superficial tissues were the seat of generalised oedema. Two recently-made surgical incisions were present, one in the middle line below the umbilicus and one in the left lumbar region.

Serous Sacs: Both pleural sacs, the pericardial sac, and the peritoneal cavity contained considerable quantities of pale yellow serous fluid.

Genito-Urinary System: The kidneys were of normal shape, but
abnormally soft and somewhat increased in size. It was found on section that the entire cortex of each organ had undergone complete necrosis. The cortex was decreased in depth and bright yellow in colour. It was completely structureless. The medulla was deep reddish-brown in colour and at the margin of the boundary zone just subjacent to the cortex the tissue was very congested and haemorrhagic. The capsule stripped from the non-decapsulated kidney with ease and exposed a smooth yellow surface. The capsule had already been stripped from the other (left) kidney. Pelvis, ureters and bladder were healthy.

Uterus was about the size of a coconut. A median incision was present in its anterior wall. The uterus was not opened. Its appendages were healthy.

Alimentary System: Oesophagus, stomach and intestines were healthy. Liver was slightly increased in size and abnormally soft. On section it presented a very pale surface. The liver was clearly the seat of advanced fatty change. Gall bladder was healthy. Spleen was of normal size, shape and consistence. On section it presented a surface which was only slightly congested. Pancreas was abnormally firm and oedematous, but otherwise healthy.

Respiratory System: Larynx and trachea were healthy. The bronchi and their branches were moderately congested.

Lungs: Pleural surfaces were smooth, glistening, and transparent. Lungs were of normal size, shape, and consistence. On section they presented moderate degrees of hypostatic congestion. Their tissue was the seat of fairly marked oedema. There was no broncho-pneumonia.

Cardio-Vascular System - Heart: Pericardial surface was smooth, glistening, and transparent. Subepicardial fat normal in amount and coronary vessels healthy. Heart was of average size, but was tending to be globular in shape. All its chambers were dilated but the valves were of normal dimensions. The myocardium was pale and soft; it was clearly the seat of advanced cloudy swelling. Aorta was healthy.

Microscopical Examination: On examining a typical N.E. area of necrosis the following changes were observed: Kidneys: Subjacent to the capsule there was a narrow area of intense congestion. Beneath this the epithelium of the convoluted tubules was observed to be swollen, with hazy outlines, the cytoplasm granular, and in most cases the nuclei were quite unstained. In some tubules the epithelium was completely disintegrated and was represented by a mass of granular detritus surrounded by the basement membrane. The glomeruli stained poorly and in most instances were swollen. There was no proliferation of the epithelial cells of Bowman's membrane.
Interstitial tissue was oedematous and there was a moderate amount of round-celled infiltration, these being mostly lymphocytes. There were occasional small haemorrhages to be observed. Some tubules showed a finely granular lilac colour indicative of calcification. In the centre of the necrotic area the tubular epithelium was almost completely necrosed, it being impossible to distinguish either cells or nuclei. The oedema of the interstitial tissue was very pronounced, widely separating the adjacent tubules. The glomeruli were very congested and in most cases the glomerular tuft completely obliterated the capsular space. Again failure of nuclear staining indicated cellular death. The intralobular vessels had oedematous walls, there being no indication of any cellular proliferation. In each case a thrombus was present. In some instances, in which the afferent glomeruli vessels could be seen taking origin from the intralobular vessels, a continuous thrombus extended into the glomerulus.

At the edge of the necrotic area there was present an intense congestion, the vessels containing thrombi. There was gross haemorrhage into the tissues. In the non-necrotic areas of the cortex there was advanced cloudy swelling of the tubular epithelium, the nuclei being well-stained and in some cases pyknotic. Again the interstitial tissue was oedematous, round-celled infiltration being prominent especially surrounding the glomeruli. The glomeruli showed but little change. The vessels were slightly congested but there was no thrombosis. In the medulla the tubules again showed cloudy swelling, in some instances proceeding to necrosis. The lumina of the tubules were packed with granular debris. In sections stained for fat the glomeruli were prominent because of the intracapillary fat globules. This could be traced through the afferent vessel to the thrombosed intralobular vessels. Tubular epithelium in all areas showed very little, if any, fatty degeneration.
CASE 4  Mrs. F.  Age 42.  Para...7

History of Previous Health.

This had always been excellent. There had never been any serious illness. No history of scarlet fever in childhood.

Obstetric History.

All labours had been full time and spontaneous. There had never been any trouble whatever during these pregnancies. The last child was born three years ago.

History of Present Pregnancy.

For a few days prior to admission patient had suffered from some frequency of micturition. She did not have to rise at night to pass urine however.

On the 27th. Feb. 1933 when over eight months advanced in her pregnancy she was suddenly seized with severe cramp-like pains in the abdomen followed in a short time by some vaginal bleeding. She was removed to the Royal Maternity Hospital.

On admission I found her blanched and shocked. There was a considerable degree of uterine tenderness and the uterus on palpation was found to be hard and board like. No foetal parts could be made out. The blood pressure was 140/120 and there was some albumin in the one and a half ounces of urine obtained by catheterisation.

At first no active treatment was directed to the uterus but I transfused the patient with a pint of citrated blood which improved her general condition considerably. However later in the afternoon her condition was definitely deteriorating and
Prof. Johnstone decided to perform a Caesarian Section. This was done under local infiltration anaesthesia. Blood stained fluid was present in the peritoneal cavity. The uterus presented the typical features of a Couvelaire's uterine apoplexy. The subperitoneal haemorrhage was particularly well marked around the uterine cornua and on the posterior surface of the uterus. The child was, of course, dead and the placenta was completely detached - ablatio placenta.

The patient made an excellent recovery from her operation.

**Condition day by day.**

28.2.33. No urine passed. Patient very comfortable.

1.3.33. No urine passed. Patient comfortable. Patient was catheterised and about a half ounce of pus removed from the bladder. During this night myotonic twitchings of the face and arms were observed.

2.3.33. Patient transferred to the Royal Infirmary under the care of Mr. Henry Wade. An X-ray examination showed no calculous cause for the anuria. A cystoscopy was performed and no urine was obtained from either ureter. The blood pressure was 130/90. Two litres of sodium sulphate solution containing almost 150 Gm. of the sulphate was infused intravenously in the morning and this was repeated in the evening. Patient felt very well but tending to be somewhat drowsy.

3.3.33. Patient becoming very drowsy. Muscular twitchings noted.

4.3.33. Condition worse. Still no urinary secretion.

5-6-7-3.33. Condition gradually deteriorated until patient became comatose. Passed no urine. No fits of any sort. Died 7.3.33.
A full post mortem examination was carried out but unfortunately I have not been able to obtain the report. I will content myself with the description of the kidneys.

The Kidney.

The kidney presented the variegated appearance of a complete cortical necrosis. The cortex was of a bright yellow colour and the whole of the cortex was involved. Between the cortex and the medulla was a thin area of intense congestion. The medulla was of more or less normal appearance but streaked with very prominent vessels and small haemorrhages.

The renal capsule stripped easily and there was no evidence of any chronic process.

Microscopically.

The whole of the cortex presents the homogeneous granular appearance typical of the condition. The glomeruli are slight swollen and show no increase in cells or nuclei. They take up the stain very faintly. The tubules are devoid of all nuclear definition and present only the uniform granular appearance. Subcapsular haemorrhage is very marked. Here and there throughout the cortex and small haemorrhagic areas. There is a considerable area of congestion between the cortical zone and the more or less normal medulla. Here and there a few of the tufts are seen to be hyalinised with streaks of fibrous tissue replacing the tubules. It is by no means very extensive.
Occurring as they do in the majority of cases in association with pregnancy the age incidence naturally falls between the ages of 20 and 40. The youngest patient in the series is recorded by Apert and Bach (5) in a girl of thirteen suffering from tuberculosis. The first case of cortical necrosis which was recorded by Juhel-Renoy (6) occurred in a girl of sixteen who died of scarlatina. Zanzig recorded a case of cortical necrosis occurring in a girl of fourteen following the intravenous injection of a camphor preparation. The oldest pregnant patient was aged 48, a para seven, and is recorded by Jardine and Kennedy (3). Of the non-pregnant cases the eldest is a man aged 65 suffering and dying from carcinoma of the prostate gland and found accidentally postmortem. It is recorded by Fahr (7) in his volume on the kidney in the Henke-Lubarsch system of pathology. In the series of cases presented in this essay the ages were 26, 30, 29, and 42. We can state therefore that cortical necrosis although occurring far more commonly during the child bearing period may occur at any time of life.

Of the forty-seven or so authentic cases about six have occurred in men and we shall consider these cases again shortly. Of the remainder thirty-eight occurred in women who were pregnant. Many observers do not give details as to the parity of the patients but in those which mention this it is clearly seen that most can be classified as multiparae. We shall see later that many of these cases are associated with two conditions of pregnancy namely, eclampsia and accidental haemorrhage.
Although eclampsia occurs very frequently in the primigravid patient it occurs probably just as often in the parous woman. Accidental haemorrhage on the other hand and especially in its severer forms is essentially a condition found in the multigravid woman. Scriver has recorded a fatal case in a woman who had had fifteen children. In the present series of cases the parity was 1, 2, 2, 7. We can thus state that as the condition is so frequently associated with certain grave manifestations of toxaemias it is more likely to be found in the multipara.

As I intend to refer to the cases occurring during pregnancy almost exclusively I shall mention some of the conditions with which cortical necrosis has been associated in the male and the non-pregnant female. We have already mentioned its association with scarlatina in the case recorded by Juhel-Renoy. It is a matter of interest that cortical necrosis does not occur more often in scarlet fever as we shall see when discussing the pathogenesis. Zanzig (8) records the condition occurring after the intravenous injection of camphor in two cases. We have already mentioned the case occurring in association with carcinoma of the prostate. Lloyd (9) records a case of cortical necrosis found at autopsy on a case of malaria and Stockenius(10) on a case of diphtheria. We have mentioned the case occurring in a tuberculous individual. Lastly it has been recorded as occurring after a crushing accident to the liver by Furtwangler(11).

We see therefore that apart from pregnancy there is no constant pre-disposing factor or constant associated condition. Cases are so to speak quite sporadic occurring in
widely diverse conditions. The only poison that is recorded as having produced a complete necrosis of the renal cortex is camphor.

The Clinical Picture etc.

It is obvious that the onset of cortical necrosis will vary with the particular type of pregnancy toxaemia with which it is associated.

Case 1 is an example of an insidious onset and this of course is quite exceptional. We see that this patient was actually carrying out her household duties when, if her account be true, she was passing little or no water. She only became gradually ill and indeed was able to walk about when she was admitted to the hospital. Other observers have noted that in this type of case which is not associated with albuminuric toxaemia or haemorrhage is often surprisingly well to all appearances even when examination of the blood shows gross nitrogenous retention. Thus in this case 1 the blood urea on admission was 161 mgms per cent yet patient was able to walk about and was not feeling very ill.

Probably the most dramatic type of case is that associated with concealed or combined accidental haemorrhage. In this type of case there is the typical history of well being with a sudden and agonising abdominal pain and collapse. The usual treatment of the condition is carried out i.e. blood transfusion and caesarian section and perhaps during the day or two days after this the patient remains well. It is then noticed that she is not secreting any urine at all. Shortly after this
she begins to get a little drowsy although feeling perfectly well twitchings of the hands and of the facial muscles are seen and the patient gradually goes downhill. This is probably a fairly common type of onset and is well exemplified in case four and also in case three.

The last type of onset I would mention is that type of case which is associated with eclampsia and is exemplified by case two. Most eclamptics and many pre-eclamptics exhibit profound oliguria. Cortical necrosis therefore is not recognised quite so readily. Probably about six or seven cases are recorded as occurring in association with eclampsia.

These three modes of onset therefore are possible. Occasionally coming on insidiously, frequently coming on after concealed or combined accidental haemorrhage and lastly following on eclampsia.

There is no great interest in the clinical course. The clinical history of the cases mentioned gives a fairly composite picture. The first few days after the onset of the condition the patient although drowsy is really surprisingly well in her appearance. Gradually however the drowsiness deepens into coma and death takes place. Let us examine however more closely some of the symptoms and signs.

The anuria.

This of course is the one important symptom. It may be relative or absolute. In the case reported by Jungano there was complete anuria for thirteen days (12). Dalrymple (13) records a case in which there was complete anuria for eleven days.
One of Clifford White's cases which recovered after decapsulation had extreme oliguria for seventeen days. Turning to our own series of cases we find that the history given to us by the patient in case 1 was that she had not passed urine for a fortnight. Although we cannot be sure about the truth of this statement there is the incontrovertible fact that the blood urea on the day of admission was 161 mgms. per cent. so that she could have been passing very little urine. During the nineteen days she was in hospital case one passed 81 ozs. of urine of which over 40 ozs. were passed on the last five days of life. The anuria in case four is also remarkable but quite understandable when the state of her kidneys is recalled. Thus in nine days only one half ounce of fluid was recovered from the bladder. Case three passed 4½ ounces of urine in eight days. The one important fact is that in case one the urinary output was increasing and that on the day prior to death she had secreted over sixteen ounces of urine. So much for the question of the anuria. As most cases die after about one weeks anuria it follows that most cases only have anuria for seven or eight days.

Oedema.

In the majority of cases there is a certain amount of oedema but this does not become very severe and is never a general anasarca. In case one we find that there was a certain amount of oedema of the legs and face and that this varied from day to day. In case three there was also considerable oedema of the superficial tissues. In case four there was hardly any oedema at all even before death. It will be noticed in case one
there was a certain upset in the albumin globulin ratio of one to one and a half.

The Blood Pressure.

It can be said that in those cases in which the blood pressure has been recorded it is usually slightly or perhaps considerably elevated. It is unusual for the systolic pressure to be low. The highest pressure recorded is that in a case reported by Carson and Rockwood (15) in which the systolic pressure was 200mm of mercury. In the present series of cases the blood pressure varies. In case one there is a slight tendency to rise the average being 130/80. In case two which was an eclamptic the blood pressure was 185/135. In case three the blood pressure was high at first 158/100 but fell gradually to 110 systolic. In case four the blood pressure was slightly high and on the last occasion on which it was taken it was 134/78. Probably if careful blood pressure readings were taken in all cases it would be found that it is only in those cases which are associated with eclampsia and the toxic haemorrhages that show any very great elevation in blood pressure. In case one where there was no such association we see only a very slightly raised pressure. It must be remembered that in a very large number of the recorded cases the blood pressure is not mentioned at all. It has been remarked by some observers that it is strange there is no compensatory rise in blood pressure and we shall discuss this point later on.

Other Symptoms and Signs.

Vomiting in cases of cortical necrosis is the
### Table—Data in Case I. (After the 15th vomiting prevented estimation of fluid intake.)

<table>
<thead>
<tr>
<th>Date</th>
<th>Blood Urea Mgrm. per cent</th>
<th>Blood Creatinine Mgrm. per cent</th>
<th>CO₂ Combining Power</th>
<th>Serum Calcium Mgrm. per cent</th>
<th>Plasma Phosphorus Mgrm. per cent</th>
<th>Calcium Phosphorus Ratio</th>
<th>Plasma Albumin Mgrm. per cent</th>
<th>Plasma Globulin Mgrm. per cent</th>
<th>A/G Ratio</th>
<th>Plasma Fibrinogen Mgrm. per cent</th>
<th>Blood Cholesterol Mgrm. per cent</th>
<th>Blood Pressure Min. Hg</th>
<th>Fluid Intake Oz.</th>
<th>Urine Output Oz.</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>161</td>
<td>5.5</td>
<td>45</td>
<td>7.4</td>
<td>7.3</td>
<td>1.01</td>
<td>2.31</td>
<td>1.80</td>
<td>1.5/1</td>
<td>94</td>
<td>120</td>
<td>110/70</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>8</td>
<td>...</td>
<td>...</td>
<td>47</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>9</td>
<td>165</td>
<td>5.5</td>
<td>54</td>
<td>7.0</td>
<td>0.64</td>
<td>1.94</td>
<td>2.00</td>
<td>1.81</td>
<td>1.1/1</td>
<td>69</td>
<td>125</td>
<td>110/70</td>
<td>96</td>
<td>...</td>
</tr>
<tr>
<td>10</td>
<td>266</td>
<td>6.6</td>
<td>6.8</td>
<td>10.5</td>
<td>0.64</td>
<td>1.94</td>
<td>1.83</td>
<td>1.2/1</td>
<td>65</td>
<td>133</td>
<td>120/80</td>
<td>86</td>
<td>0.37</td>
<td>...</td>
</tr>
<tr>
<td>11</td>
<td>255</td>
<td>5.4</td>
<td>11.7</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>2.19</td>
<td>1.38</td>
<td>1.2/1</td>
<td>65</td>
<td>127</td>
<td>120/80</td>
<td>68</td>
<td>0.5</td>
</tr>
<tr>
<td>12</td>
<td>257</td>
<td>6.7</td>
<td>3.7</td>
<td>10.2</td>
<td>...</td>
<td>...</td>
<td>2.38</td>
<td>1.94</td>
<td>1.2/1</td>
<td>65</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>72</td>
</tr>
<tr>
<td>13</td>
<td>283</td>
<td>7.4</td>
<td>0.7</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>120/75</td>
<td>62</td>
<td>0.25</td>
</tr>
<tr>
<td>14</td>
<td>366</td>
<td>8.0</td>
<td>0.9</td>
<td>11.1</td>
<td>0.67</td>
<td>2.63</td>
<td>1.63</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>72</td>
</tr>
<tr>
<td>15</td>
<td>348</td>
<td>8.8</td>
<td>7.2</td>
<td>12.5</td>
<td>0.58</td>
<td>2.43</td>
<td>2.00</td>
<td>1.2/1</td>
<td>44</td>
<td>167</td>
<td>...</td>
<td>130/80</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>16</td>
<td>377</td>
<td>9.0</td>
<td>7.2</td>
<td>13.3</td>
<td>0.54</td>
<td>1.93</td>
<td>2.43</td>
<td>1.2/3</td>
<td>44</td>
<td>160</td>
<td>...</td>
<td>130/80</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>17</td>
<td>420</td>
<td>10.0</td>
<td>7.2</td>
<td>13.6</td>
<td>0.53</td>
<td>1.16</td>
<td>3.25</td>
<td>1.2/8</td>
<td>38</td>
<td>130</td>
<td>...</td>
<td>130/75</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>439</td>
<td>11.6</td>
<td>7.2</td>
<td>14.3</td>
<td>0.50</td>
<td>2.38</td>
<td>1.94</td>
<td>1.2/1</td>
<td>69</td>
<td>126</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>5</td>
</tr>
<tr>
<td>19</td>
<td>459</td>
<td>14.0</td>
<td>6.9</td>
<td>15.4</td>
<td>0.44</td>
<td>2.63</td>
<td>1.69</td>
<td>1.6/1</td>
<td>63</td>
<td>145</td>
<td>...</td>
<td>130/80</td>
<td>...</td>
<td>4</td>
</tr>
<tr>
<td>20</td>
<td>...</td>
<td>...</td>
<td>8.4</td>
<td>15.6</td>
<td>0.54</td>
<td>2.63</td>
<td>1.44</td>
<td>1.8/1</td>
<td>69</td>
<td>143</td>
<td>125/80</td>
<td>...</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>22</td>
<td>480</td>
<td>13.3</td>
<td>9.0</td>
<td>15.6</td>
<td>0.38</td>
<td>2.06</td>
<td>1.44</td>
<td>2.1/1</td>
<td>75</td>
<td>130</td>
<td>130/80</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>544</td>
<td>13.3</td>
<td>9.3</td>
<td>16.7</td>
<td>0.55</td>
<td>2.56</td>
<td>2.50</td>
<td>1/1</td>
<td>50</td>
<td>128</td>
<td>...</td>
<td>130/80</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>589</td>
<td>12.0</td>
<td>8.2</td>
<td>14.0</td>
<td>0.39</td>
<td>2.38</td>
<td>2.38</td>
<td>1/1</td>
<td>44</td>
<td>160</td>
<td>130/80</td>
<td>...</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>484</td>
<td>11.5</td>
<td>7.9</td>
<td>15.2</td>
<td>0.46</td>
<td>2.81</td>
<td>2.31</td>
<td>1.2/1</td>
<td>69</td>
<td>150</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>
rule. It is found in the majority of cases. In case four however it was not at all marked.

Diarrhoea has been noted in many cases and was found in case one. At post mortem 'uraemic' ulceration of the colon has not been present.

Convulsions are usually absent. In none of the cases of this series was there any convulsions apart from the eclamptic fits of course. It is exceptional to get generalised convulsions after the necrosis has been well established. Of course muscular twitchings are observed in many cases and are merely an expression of the upset in the acid-base equilibrium.

The Biochemical Data.

Very few reports contain any biochemical data. A glance at the table in which are laid out the biochemical findings in case one will show the extraordinary heights to which the blood urea rose. On the 23rd. of August the blood urea had reached the dizzy heights of 544 mgms. per cent. On the 20th. August the blood creatinine had been at 14.5 mgms per cent. There was generally a low blood calcium level and the CO2 combining power showed the tendency to acidosis. These figures are very interesting and unique as they show the behaviour of these various substances when the kidney is quite functionless. The same effect is given as the removal of a single kidney.

Cast four had some biochemical observations made and there too we see the rise of the blood urea nitrogen to 144 mgms. per cent. and the creatinine to 10 mgms. per cent.
Certain Observations on Mrs. F. Case 4.

<table>
<thead>
<tr>
<th>Date</th>
<th>Blood Urea N.</th>
<th>Creatinine</th>
<th>CO₂</th>
<th>B.P.</th>
<th>Fluid Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.3.33.</td>
<td>71</td>
<td>5.7</td>
<td>35.</td>
<td>130/80</td>
<td>370</td>
</tr>
<tr>
<td>3.3.33.</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>134/78</td>
<td>370</td>
</tr>
<tr>
<td>4.3.33.</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>334</td>
</tr>
<tr>
<td>5.3.33.</td>
<td>102</td>
<td>6.7</td>
<td>37</td>
<td>--</td>
<td>346</td>
</tr>
<tr>
<td>6.3.33.</td>
<td>122</td>
<td>7.2</td>
<td>35.5</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>7.3.33.</td>
<td>144</td>
<td>10</td>
<td>12</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>
Kellogg (16) found in his case that the non-protein nitrogen was 100 mgms per cent. In Crook's case (17) which recovered after decapsulation the blood urea nitrogen was 388 mgms. per cent. It is important to note that this case recovered even after this gross amount of nitrogenous retention had occurred. In the case of Scriven and Oertel which recovered (18) the non-protein nitrogen was 100 mgms. per cent. That this might not have been a case of cortical necrosis is of course possible. Crooks case was confirmed by biopsy at the time of decapsulation.

The biochemical data therefore simply show a progressive rise in the nitrogenous bodies, a tendency to a low calcium and a low CO2 combining power reading. There is some disturbance in the albumin globulin ratio.

The Urine.

Examination of the small quantity of urine available shows the presence of some albumin. There is a varying amount of blood and some casts and epithelial debris may be found. It is interesting to note that in case one the early specimens contained no urea at all but later urea was present in reasonable amounts.

Summing up the clinical part of our study of these cases. Bilateral cortical necrosis occurs most often in association with pregnancy and also with eclampsia and toxic haemorrhage. Extreme oliguria or anuria is the rule and there is a progressive nitrogenous retention. The patient passes into coma gradually and death occurs.

We shall now turn to a study of the pathology of the condition.
The Pathology of Bilateral Cortical Necrosis.

The Morbid Anatomy.

The naked eye appearances of the condition are very striking and cannot possibly be mistaken or missed. If the kidneys be seen at post-mortem after the condition has been present for several days they are not enlarged at all or very slightly. The capsule is removed strips readily and reveals many dilated and congested vessels on the surface. Owing to the thin rim of normal cortex immediately subjacent to the capsule the colour of the uncut kidney is more or less normal or perhaps slightly more red than usual.

On bisecting the kidney in the usual way the characteristic appearance is seen. The larger part of the cortex is seen to be converted into a bright yellow coloured area with smaller areas of bright red in it. The medulla is unchanged except for the areas of haemorrhage and the dilated vessels running through it. The renal pelvis is frequently somewhat inflamed from ascending infection from the bladder. In case one there was some degree of pyelitis.

The naked eye appearances of the other organs naturally vary. In eclamptic cases the liver may show the characteristic haemorrhages into its substance. In cases where the condition has been associated with concealed accidental haemorrhage the uterus may still show evidence of subperitoneal haemorrhages.

Occasionally there has been found antemortem clot in the renal veins and Davidson has remarked on the presence
CASE 2. Shows the intense hyperaemia of the early infarct.
of thrombi in the ovarian veins.

The Microscopic appearances.

Cortical necrosis being as it is a condition of infarction of the kidney cortex will show varying changes according as to what time in the process the case comes to post mortem.

In our series the earliest case is that of case two. It will be recalled that this case occurred in an éclamptic who died some hours after the onset of the fits. The diagnosis was made chiefly on the microscopic appearances. In this case the naked eye appearance of the cortex was not typical of the fully established condition. The cortex was broad and intensely congested and red. It was homogeneous in appearance. In this case the medulla was also very congested and there was also congestion of the renal pelves. Microscopically the tubules showed advanced cloudy swelling and in some cases necrosis. The glomeruli were swollen and the vessels engorged. Here and there there was haemorrhage into the interstitium. In this case there were present in the kidney definitely thickened vessels. The illustration shown gives a good idea of the condition present. This stage can be summarised therefore as the early stage of red infarction.

It is interesting to note that in this case the liver cells did not show any great amount of necrosis and did not present the appearance which one associates with an éclamptic liver.

Pathologically the fourth case is next in the series. Here the condition is fully established the initial hyperaemia has all passed off and the typical picture of necrosis
CASE 3  Mrs. C.

Thrombosis in an afferent glomerular vessel.

Section satined for fat. 3 intravascular fat globules.

Infarcted area (a) surrounded by congested zone (b)
Microscopically the cortex shows the usual changes. The peculiar ground glass appearance is well marked. All nuclei stain poorly and there is but little differentiation in the staining. Here were found several hyalinised glomeruli but probably not more than were normal for a woman of this age and parity.

Pathologically in case three the condition is as it were healing. In this case the extent of the infarction is not quite so extensive. One can see areas of cortex where there has been no necrosis and in those parts adjacent to infarced areas there is great congestion of the vessels. Further in infarcted areas there is seen to be here and there areas of commencing calcification.

Case one shows quite advanced healing. Scattered throughout the infarcted area are seen places where there is calcification and collapse of the tissue. In this case also the whole of the cortex was not infarcted and areas where there is more or less normal tissue can be seen. However it will be recalled that in this case there was an ascending infection which rather complicates the histology.

Summing up then, the condition may be defined as an infarction of the whole or part of the renal cortex. In the first stage there is intense hyperaemia and all the appearances of the red infarct. Kaufmann states that this stage of an infarct lasts only a short time perhaps fort-eight hours or so. After this the infarcted area becomes anaemic while around its margins there is still hyperaemia. Thus under the capsule there is
Fig. 1.—Case I. Showing wedge-shaped area of infarction with peripheral calcification. (Low power.)

Fig. 2.—Case I. Showing shrinkage of infarcted area with advanced calcification. (Low power.)
an area of intense congestion and also at the margins of infarcted cortical tissue with medulla or with uninfarcted cortex.
The infarcted area thereupon undergoes cell death and a deposition of lime occurs. Probably if the patient could survive long enough this would gradually shrink and become invaded by fibroblasts and ultimately from a scar.

The presence of calcium in amorphous deposits in cases one and three is interesting. The exact time in which calcium may be laid down in a tissue is difficult to say. Kaufmann believes that it may be deposited in two to three days and this is seen in sublimate poisoning. It is probably however an expression of healing. Ogilvie has seen calcification in necrotic renal tubules four days after the ingestion of corrosive sublimate.

Recently Baird and Dunn (2) have studied the renal lesion in eclampsia and have described certain changes in the glomerulus. This consists of an increase in cellularity with a thickening of the basement membrane of the glomerular capillaries. Although this was particularly looked for no such change was found in any of these cases. In the case of cortical necrosis which these two observers record there was present before the necrosis a true capillary glomerulo-nephritis.

Professor F.J. Browne together with many other obstetricians believe that accidental haemorrhage is very frequently associated with chronic nephritis. Browne showed that in rabbits with a chronic oxalate nephritis accidental haemorrhage was prone to occur. Again in this series of cases two of
the cases were associated with severe accidental haemorrhage. In neither was there any evidence of any chronic nephritis. It will be recalled that in case four some hyalinised glomeruli were four but these would not reduce the function of the kidney at all. Two cases are not many but it would be thought if Browne's thesis were correct that this is exactly the type of case one would find marked evidence of nephritis.

The Cause of Bilateral Cortical Necrosis.

It will be agreed that the cause of the condition must be intimately associated with that of the toxæmias of pregnancy.

There are several possible mechanisms which we might consider. Parkes Weber in 1909 thought that the condition was primarily a destruction of the renal tissue and that any vascular thrombosis was secondary. However since then more cases have been studied and it is obvious that the condition is due to a vascular condition. We have seen the thrombosed glomerular capillaries and have been able to trace them back to the interlobar vessels. Also the whole pathological picture is so essentially that of infarction which is known practically and experimentally to be caused by vascular conditions. The condition is due therefore to an interference with the vascular supply to the cortex.

The possibility of Embolism.

It is exceedingly unlikely that multiple small emboli could be so suddenly released into the blood stream as cause infarction of both kidneys so suddenly and without causing
the infarction of other organs. Schuppel (19) suggested that the condition might be due to fat embolism as he noticed the fact that the renal vessels are full of fat droplets. Scrivner and Oertel have recorded a high blood fat in cortical necrosis and it is probable that these droplets would be found in vessels elsewhere than the kidney. Hyperlipaemia has been found to occur also in the renal necrosis following sublimate poisoning and is probably found in many toxaemic states.

The possibility of Vaso-spasm.

Jardine and Kennedy (20) published a case of cortical necrosis which they thought might be due to vaso-spasm as the patient also suffered from Raynaud's disease. He later abandoned this view. There is much to be said for the view that spasm of the vessels might be of sufficient intensity and duration as to cut off the blood supply to the renal cortex. Vascular spasm undoubtedly plays a part in eclampsia and probably in acute nephritis. This suggestion however is very difficult to prove or disprove.

The possibility of Thrombosis.

Previously much attention was focussed on the question of venous and arterial thrombosis but it is probable that the end result is much the same. In the case of bilateral cortical necrosis the thrombosis is probably on the arterial side at first and these arterial thrombi could be seen very readily in the cases examined.

I do not propose to enter into the question of what causes the thrombosis. Presumably it is some toxin which acts on the endothelial lining of the vessels. That such a toxin
Urea in mg.\%  
Creatinine in mg.\%  
Urine in ozs.

CHART.—Graph of blood urea and creatinine and urinary output in Case I.
exists having a peculiar predilection for endothelium is of course purely speculative. It is well known however that in eclampsia there is a tendency for capillary damage, the brain, myocardium kidneys all suffering. In the uterine wall in accidental haemorrhage one can observe haemorrhages into the wall and separating the muscle bundles at a distance from the placental site.

The Question of Recovery.

It is obvious that recovery will depend on the amount of cortex destroyed. It is possible that in severe cases of eclampsia and accidental haemorrhage which recover there may have been small areas of renal substance damaged but which cause no symptoms. That recovery is possible is to my mind perfectly feasible. Apart from the cases in the literature which have been known to have cortical necrosis and recover a study of case one is at least suggestive if not convincing. In this case there was a drop in the nitrogenous retention and also a steadily increasing rise in the urinary output. I think that if this poor woman had not developed a pyelo-nephritis she would have recovered. Crook's case which we have already mentioned is a good example of a recovery. In this case a piece of tissue was actually excised and the condition shown to be that of bilateral necrosis.

The Question of Treatment.

Given a knowledge of the pathology of this condition it is easy to understand how much one requires to do in treatment. The question of decapsulation of the kidney
immediately springs to the mind. It is my own belief that all cases that have recovered after decapsulation have done so in spite of the operation rather than because of it. We saw in case three there was no bulging seen when the renal tissue was stripped of the capsule. This is easy to understand when the short duration of the congested early stage is recalled. To decapsulate the kidneys at the end of the first week is surely unnecessary.

The patient should be treated by means of intravenous fluids, hot air baths, sponging colonic lavage etc. in an endeavour to stave off the almost certain uraemia. At the end of five days it might be possible to stimulate the damaged kidney with some diuretic such as hypertonic glucose. To give a woman with a cortical necrosis 100 Gm. of sodium sulphate in order to stimulate the renal secretion strikes me as ludicrous.

If enough renal tissue has been spared the patient will in all probability recover without any treatment. When the necrosis is as extensive as it was in case four nothing could possibly help her. In all about half a dozen undoubted cases of cortical necrosis have recovered.
Bibliography.

2) Baird and Dunn. J. of Path. and Bact. 1933. No. 3.
   xxxvli1 158.
   52. 471.
8) Zanzig. Inaug. Dissert. Halle-Wittenberg. 1915 Quoted by
   Scriver and Oertel.
9) Lloyd. Lancet. 1906. 1. 156.
10) Stockenius. Beitr. z. anat undall. path. 1921. 69. 373.
18) Scriver and Oertel. J. path. and Bact. 1930. 33. 1071.
   This contains a very good bibliography and
   includes those cases not specifically referred to in the text.
20) Teacher and Jardine. J. of Path and Bact. 1911. xv. 357.