RENAL CORTICAL NECROSIS

RENAL CORTICAL NECROSIS AND THE KIDNEY OF CONCEALED ACCIDENTAL HAEMORRHAGE

by

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PREFACE

THIS account of the renal lesions which follow concealed accidental haemorrhage is based to a great extent on the study of a series of cases at Glasgow Royal Maternity Hospital during the years 1935 to 1945. Very sincere thanks are due to my assistants there (Dr. M. D. Crawford and Dr. A. M. Stewart) who carried out some of these autopsies, and to all the clinical staff of the Hospital for their friendly and willing co-operation.

Though the analysis of these cases was primarily directed to the understanding of renal cortical necrosis, it has raised many problems on the broader subject of ischaemic damage to tissues. We have found that our own previous ideas on various aspects of general pathology were in need of considerable clarification, and sometimes of revision. Among these aspects may be mentioned the autolytic changes that occur in dead tissues, the factors which control that autolysis, and the development of the different types of thrombosis. The conclusions reached here on these questions of general pathology are founded essentially on the study of the human material, but they are strongly supported by the results of a large series of animal experiments which we have carried out and which will be reported elsewhere.

The literature has been reviewed as fully as possible up to March 1952. Since the completion of this book, two excellent general textbooks on the kidney have been published: one by H. W. Smith, *The Kidney, Structure and Function in Health and Disease*, New York, 1951; the other by A. C. Allen, *The Kidney, Medical and Surgical Diseases*, London, 1952. These two authors do not deal in great detail with renal cortical necrosis nor with the histological effects of ischaemia on the kidney, but they give a full discussion of various other aspects of acute renal failure, and their conclusions merit serious study.

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CHAPTER I

SCOPE OF THE INVESTIGATION

Though occasional cases of renal cortical necrosis were reported from 1883 onwards, the condition became widely recognised as a result of the work of Jardine, Teacher and Kennedy between 1906 and 1920. Since then many more cases have been reported, and good recent reviews of the subject have been given by Ash (1933), Gáspár (1938), Duff and More (1941), Dunn and Montgomery (1941), and Polayes (1941). The precise aetiology is still a matter of much debate, and there has been relatively little study of the early stages of the development of the lesion.

Most cases of renal cortical necrosis follow the obstetric catastrophe which is known by various names: — concealed or mixed accidental haemorrhage, premature separation of the placenta, abruptio placentae, or uteroplacental apoplexy: (from this point on, the obstetric condition will be referred to as U.P.A., and renal cortical necrosis will be abbreviated to R.C.N.). The patients who develop R.C.N. usually die several days later, when the kidney lesion is in an advanced stage. In order to find the early histological stages of R.C.N., it is necessary to search among the kidneys of patients who die within the first day or two after the U.P.A., i.e. before there is any clinical evidence to indicate whether or not the renal cortex has been severely damaged.

From such a study of the kidneys of a number of patients who have died at intervals from a few hours to several days after the U.P.A., it is not difficult to recognise the early and the late examples of R.C.N., and to identify the various stages of the development of this lesion.

In addition, such a study reveals that, in those patients who do not develop classical R.C.N., there are a number of other acute renal lesions; the various stages of development of each of these lesions can also be identified. These form the lesser grades of a series of lesions, which ascends in severity from the mildest tubular damage up to the full picture of R.C.N.. The existence of these various grades provides good evidence about the aetiological factor of ischaemia which is common to the entire series.

The present analysis of the pathology is based mainly on 67 patients who died following U.P.A.. In addition, for purposes of general analysis, the records of 700 clinical cases of U.P.A. have been studied. The deaths among these 700 cases overlap to a great extent with the 67 autopsied cases, but it is important that the two series should not be confused.

CHAPTER II

CONCEALED ACCIDENTAL HAEMORRHAGE; (U.P.A.)

GENERAL CLINICAL CONSIDERATIONS

It is necessary to give here a short summary of what is meant in this paper by the term U.P.A.. This condition varies greatly in incidence in different countries, and, in places where it is uncommon, some of the obstetricians do not distinguish it very clearly from "external accidental haemorrhage". Recent reviews have been given by Irving (1938), Young (1942a), McCain and Poliakoff (1949), Sexton et al. (1950), and Crichton (1950). A historical review was made by Holmes (1901).

In the present paper, the term is used in a strict sense. At some time during the last third of gestation, or very rarely a little earlier, the patient has a sudden onset of lower abdominal pain with a tense "woody" tender uterus. In most cases there is subsequently some external haemorrhage, which may be either bloody fluid or pure blood; the amount varies. The patient becomes shocked. There is a partial or complete suppression of urine, usually for only a short time but sometimes lasting several hours and occasionally much longer. The first urine which is secreted after the U.P.A. is heavily loaded with albumen. The foetus is stillborn, and there is massive retroplacental clot. Subperitoneal haemorrhages are present over the surface of the uterus, varying from small areas near the cornua up to gross lesions meriting the description of a "Couvelaire" uterus.

As with any disease process, there can be minor degrees which show less than the full picture. Such lesser cases are usually associated with only partial abruption of the placenta. They are basically similar to severe U.P.A., and differ from it only in quantitative aspects. However, for the present study, no case has been accepted unless the clinical history followed the typical course and three pathological criteria were satisfied: — the death of the foetus, the occurrence of gross retroplacental clot, and, in all cases examined pathologically, the presence of subperitoneal haemorrhages over the uterus. In addition, every case where there was anything to suggest placenta praevia or rupture of the lower segment has been rejected.

Shock and haemorrhage. The "shock" is severe and is quite commonly fatal. It is associated with considerable ante-partum blood loss; some of these patients have over 1000 gm. of retroplacental clot, which would correspond to 2 litres of whole blood. Atonic post-partum haemorrhage occurs in some of the cases, and can be a fatal complication. In the present series of autopsied cases (a)

15 patients died undelivered; (b) 23 patients died within the first 12 hours after delivery, and among these there were 4 cases of moderate and 3 of very severe post-partum haemorrhage; this blood loss probably played some part in the fatal issue; (c) 29 patients died later in the puerperium; one of these patients had had a severe post-partum haemorrhage but had recovered from this blood loss. Sexton et al. (1950) did not have any deaths from atonic post-partum haemorrhage in their series of 476 cases of premature separation of "toxic" and "non-toxic" types.

It is of interest that the blood pressure is usually well maintained during the stage of shock. Records are available in 38 cases from the present series; most of these cases were fatal within a few hours after the readings were taken. The blood pressure of these patients, while they were in a clinical condition of shock, ranged from 230/130 to 90/60, with a mean of 137/88. Dieckmann (1936) noted similar levels in non-fatal cases.

Aetiology and effects. In nearly all the cases, the U.P.A. has a sudden clinical onset without any local exciting factor. The condition is commonly treated by artificial rupture of the membranes, but this procedure does not appear to influence the pathological changes in the kidney in any way.

It is not clear how the U.P.A. is related to the renal disturbance. It has been suggested (Browne, 1931; Young, 1942a) that the retention of retroplacental clot may be the direct cause. There are so many variable factors that it is difficult to get reliable evidence bearing on this explanation. An analysis of the present series of cases does not show any clear relation of the severity of the renal lesions to the duration of the retention of the retroplacental clot (the period from the onset of clinical symptoms to the delivery), nor to the amount of the retroplacental clot or of the other uterine haemorrhages. These negative findings can however not be accepted as of great significance.

There are occasional cases where the retroplacental haemorrhage appears to be produced purely by trauma and yet leads to severe renal damage. In the present series there were 3 patients who had version or bougie induction for oedema and slight hypertension. These three patients developed U.P.A. after the obstetric interference and, though the clinical symptoms were relatively slight, there was retroplacental clot and subperitoneal haemorrhage over the uterus in all of them. The kidney lesions were indistinguishable from those following spontaneous U.P.A.; one case had albuminuria casts and the other two had R.C.N.. The U.P.A. in these cases may have been caused directly by the interference, or may have been merely precipitated by the trauma. No definite deductions can be drawn from these three cases as to the possible role of retroplacental clot in causing renal damage.

In 4 of the patients, a slight external haemorrhage had occurred 10 to 26 days before the sudden onset of the U.P.A.. It seems possible that this may have had the same basis as the ultimate haemorrhage. It was however not

accompanied by any significant clinical symptoms, and the kidneys in these cases showed no lesions sufficiently advanced to suggest an origin at the time of the preliminary haemorrhage.

CLINICAL STATISTICS OF U.P.A.

INCIDENCE

There were 700 cases of U.P.A. admitted to the hospital during the 12 year period 1932 to 1943. The total deliveries inside the hospital during that period numbered 38,600. The hospital admitted as emergencies all the complicated obstetric cases from its own district practice and very many of those from other parts of the town; calculations about various other obstetric complications indicate that each delivery in the hospital corresponded to about three deliveries in the region as a whole. The 700 cases of U.P.A. may therefore be taken as occurring in a gross total of about 115,000 deliveries; an incidence of 0.6 per cent in the region. Sexton et al. (1950) record an incidence of 0.5 per cent of "toxic placental separation" in 40,000 deliveries in Boston.

The cases of U.P.A. showed a high incidence among multiparae, as will be seen from Table 1. This is in agreement with most previous observations in the literature. Batizfalvy (1937) recorded that 20 per cent of his cases occurred in the first pregnancy, 24 per cent in the second to the fourth, and 56 per cent in the fifth or subsequent pregnancy. The corresponding percentages in the present series are 19, 32 and 49. The same aspect is reflected in the age of the patients, which in the present cases averaged 36 years. This is considerably higher than that of the general admissions to the hospital.

TABLE 1. *Relation of U.P.A. to parity*

Pregnancy	Total deliveries in hospital	Cases of U.P.A.	Percentage with U.P.A.
1	15,300	132	0.87
2 and 3	12,600	177	1.40
4 and 5	5,600	121	2.16
6 and over	5,100	270	5.30

The period of gestation at which the U.P.A. occurred is shown in Table 2. There is a high incidence as early as 28 to 31 weeks.

MATERNAL MORTALITY

There were 75 maternal deaths among these 700 cases; a maternal mortality of 10.7 per cent. As has been indicated earlier, all the foetuses died.

TABLE 2. *Relation of U.P.A. to gestation*

Weeks gestation	Cases of U.P.A.
23 to 27	10
28 to 31	123
32 to 35	189
36 to 39	236
Term	142

In the literature on accidental haemorrhage, the maternal mortality given by various authors ranges from 3 to 60 per cent. The discrepancy in the figures is the result of two factors:

(a) There are differences in the criteria of what constitutes U.P.A. or premature separation of the placenta. Some authors, as in the present paper, accept for analysis only those cases where the foetus dies; Crichton (1950) recorded a maternal mortality of 10.8 per cent in 120 cases of this type. Other authors include in their calculations not only cases of severe U.P.A. as defined here, but also milder examples of this complication, and even a number of cases which would commonly be classed as external or revealed accidental haemorrhage; a condition which carries a negligible maternal mortality and a relatively low foetal mortality. Thus Bland and Rakoff (1938) analysed 2319 cases of various types of accidental haemorrhage with 1539 foetal deaths and 146 maternal deaths; Crichton (1950) tabulated 807 cases by other authors with 468 foetal deaths and 48 maternal deaths; Sexton et al. (1950) recorded 200 cases of toxic placental separation with 104 foetal deaths and 12 maternal deaths; Browne (1951) analysed 655 cases at the Rotunda Hospital with 508 foetal deaths and 42 maternal deaths. If the maternal mortalities in each of these series are calculated against the foetal deaths, figures of 9.5, 10.3, 11.5 and 8.3 per cent are obtained. The average (9.5 per cent) is in reasonable agreement with the maternal mortality in the present series.

(b) Drastic surgery considerably increased the maternal mortality in the period before modern methods of treatment were introduced, as is shown by Crichton (1950). This accounts for the high death rates given by some authors reporting small series of cases. There are however not sufficient Caesarean section or hysterectomy deaths from that period to produce a significant alteration of the statistics from large series of cases.

It may therefore be concluded that the maternal mortality in the present group of cases is quite representative of that in cases of the same type in other clinics.

INCIDENCE OF RENAL FAILURE

An analysis of the 75 maternal deaths in the series of 700 clinical cases reveals certain points of importance. The primary division is into 52 cases dying from shock or haemorrhage during the first day after the U.P.A., and 23 cases dying later in the puerperium. The 52 early deaths may be subdivided on pathological grounds into (a) 27 where the kidneys showed no lesions or quite minor ones, (b) 25 with early but severe renal lesions. The puerperal deaths may be subdivided into (a) 17 due to renal failure, (b) 6 due to sepsis, pulmonary embolism or other cause, and in which the kidneys were not significantly damaged.

For the subdivision of the 52 early deaths, the kidneys of only 36 are available for histological examination. Half of these showed either no lesions or such minor ones that there would presumably not have been any significant renal insufficiency in the puerperium. The other half had gross destructive lesions in the renal cortex which would probably have led to serious or fatal renal insufficiency in the puerperium if the patient had survived the first day; at least 7 of these had progressed to the early stage of R.C.N.. These 36 cases have been analysed according to the parity and gestation of the patients, and the results applied to the whole group of 52 early deaths. Though the figures for these 52 cases are based only on calculations, they are believed to give a reasonably correct representation of the true state of affairs. The figures for the 23 late deaths are those actually observed, and involve no calculations.

Table 3 shows the 75 maternal deaths analysed in this manner according to parity and gestation. The parity includes the pregnancy in which the U.P.A. occurred, even if the patient died undelivered.

TABLE 3. *Relation of maternal deaths to parity and gestation*

	Total cases	Deaths			
		During first day		During puerperium	
		Little kidney damage	Severe kidney damage	Renal failure	Other causes
Parity					
1	132	3	4	2	1
2 and 3	177	4	3	8	1
4 and 5	121	5	3	5	0
6 and over	270	15	15	2	4
Gestation weeks					
23 to 31	133	3	5	9	0
32 to 35	189	6	7	5	1
36 to 39	236	8	10	3	4
Term	142	10	3	0	1

There are two salient features with regard to the *late* deaths from renal failure; i.e. after the first day of the puerperium.

(a) These deaths occurred mainly in 2 to 5 parae. The maternal mortality from this cause in primiparae was 1.5 per cent, in 2 to 5 parae was 4.4 per cent, and in 6 parae and over was 0.7 per cent.

(b) These deaths were more frequent when the U.P.A. occurred relatively early in the pregnancy than when it occurred near term. The maternal mortality in the late puerperium from this cause was 6.8 per cent when the U.P.A. occurred at 23 to 31 weeks, 2.6 per cent at 32 to 35 weeks, 1.3 per cent at 36 to 39 weeks, and fell to zero at term.

These two features require more detailed consideration.

Parity. The death rate from shock and haemorrhage during the first day after the U.P.A. is greater in the grand multiparae. The mortality on the first day is 5.3 per cent in primiparae, 4.0 per cent in 2 and 3 parae, 6.6 per cent in 4 and 5 parae, and 11.1 per cent in 6 parae and over.

As explained above, and shown in Table 3, in many of these early deaths there is pathological evidence of gross damage to the kidney, which would probably have led to death from renal failure in the puerperium if the patient had not died during the first day. When these cases are added to the actual deaths from renal failure in the puerperium, the total incidence of very severe damage to the kidney is 4.5 per cent in primiparae, and 6.2 to 6.6 per cent at all other parities.

The conclusions may therefore be reached (a) that parity has no significant influence on the incidence of gross renal damage, (b) that patients of 6 or greater parity are very liable to die of shock during the first day, and that, as a result, most of the grand multiparae who would have developed clinical evidence of R.C.N. died too early to show this, (c) that a high proportion of the patients of 2 to 5 parity, who had severe damage to the kidneys, survived the first day and thus showed renal failure in the puerperium.

It will be clear that, if all the deaths during the first day could be prevented, the overall mortality from renal failure in the puerperium, which is at present 2.4 per cent, would rise to about double that figure.

Gestation. Similar considerations, applied to the period of gestation, show however that this factor has a real influence on the incidence of damage to the kidney.

The mortality from shock during the first day rises gradually from 6.0 per cent in patients at 23 to 31 weeks gestation up to 9.1 per cent in patients at term. When the cases with severe renal damage, whether dying in the first day or later, are taken together, it will be seen that the incidence of this renal damage is 10.5 per cent in patients at 23 to 31 weeks, 6.3 per cent at 32 to 35 weeks, 5.5 per cent at 36 to 39 weeks, and only 2.1 per cent at term. No satisfactory explanation can be offered as to why the liability of the kidney to be

damaged in cases of U.P.A. should be greater at 6 or 7 months gestation than at term.

In the literature there are about 70 maternal deaths which occurred after the first day, and in which clinical and pathological details are recorded. These cases are detailed in the subsequent chapters. The great majority of them are cases of R.C.N.. The parities and gestations of these fatal cases are given in Table 4; there is no information as to the parity and gestation of the whole series of cases of U.P.A. from which they were drawn.

The parities show a similar distribution to that among the 700 cases of U.P.A. discussed here; the high early mortality from shock among grand multiparae, which obscures this in the present series of fatal cases, appears not to have been operative. In general, the cases in the literature support the conclusion from the present series that there is no correlation between parity and kidney damage.

These cases of fatal renal failure in the literature show a very great preponderance among patients whose U.P.A. occurred at 23 to 31 weeks. This is even more marked than in the present series, and emphasises the great danger to the kidney resulting from U.P.A. at 6 or 7 months gestation.

TABLE 4. *Maternal deaths from renal failure after first day of puerperium recorded in the literature*

Parity	Number of cases
1	16
2 and 3	13
4 and 5	10
6 and over	20

Gestation, weeks	Number of cases
23 to 31	35
32 to 35	13
36 to 39	5
Term	1

PRE-EXISTENT HYPERTENSION AND TOXAEMIA

From this point onwards, consideration is given only to the autopsy group. In some of these cases there are adequate clinical records of ante-natal investigations. Many of the patients were however admitted to hospital as emergencies, and their clinical condition had not been studied before the onset of the U.P.A., though there are admission notes about the presence or absence of oedema, and of any obvious symptoms suggesting toxaemia. However, a full post-mortem examination was made in every case, so that the conclusions are in some ways more reliable than in a series based on clinical evidence alone.

CHRONIC HYPERTENSION

There was evidence of previous hypertension of some standing in 16 of the patients. The heart was increased in weight (range of 360 to 500 gm.) and

showed hypertrophy of the left ventricle. There was usually gross fibrous thickening of the intima of large and small arteries in the kidney. In 7 of these cases the blood pressure was taken during the stage of shock soon after the U.P.A. had occurred, and the systolic pressures were found to be 140, 150, 190, 200, 210, 210, and 220 mm. Hg. Most of the patients had considerable oedema on admission, and some gave a characteristic history of the recent development of dyspnoea on exertion. Four of them had some pre-eclamptic symptoms, and their livers showed small periportal lesions of eclamptic type (Sheehan, 1950). Records of urine examination during the week before the U.P.A. are available in only two of the cases; both of these patients had albuminuria at that time.

PREGNANCY TOXAEMIA

Twelve patients had definite pregnancy toxaemia without any evidence of pre-existing chronic hypertension. These patients had hearts in the normal weight-range of 230 to 330 gm., and there was no unusual thickening of arteries in the kidneys. In all of them the liver had periportal lesions of eclamptic type, though these were usually small and very scanty. Five of the patients had eclamptic convulsions; one had symptoms of pre-eclampsia; three had some hypertension and oedema and had had albuminuria during the week before the U.P.A.; the remaining two had normal blood pressures and no oedema on admission. Five of these patients had minor changes in the glomeruli of the type which is seen in eclampsia. These eclamptic lesions will not be considered any further in the present paper.

MINOR DISTURBANCES

Thirteen patients had some oedema on admission. Five of these patients had been examined within two weeks before the U.P.A. and had been found to have slight to moderate hypertension, but only one had albuminuria. None of this group of patients had any pathological evidence of hypertension or toxaemia, as judged from the heart, liver and kidney.

NORMAL

In the remaining 26 patients there was nothing to suggest any previous toxaemia or cardio-vasculo-renal disorder. A few of the clinical records have incomplete data, but as far as can be ascertained, this group were free from previous oedema or other symptoms.

From this analysis it is clear that there are a large proportion of cases with no evidence of toxaemia or hypertension before the occurrence of the U.P.A.. Nevertheless these two conditions appear to be associated with U.P.A. rather commonly. The occurrence of chronic hypertension in 16 patients out of 67

obstetric autopsies is very much higher than its incidence in routine obstetric autopsies, and must be accepted as significant.

The association of U.P.A. with pregnancy toxaemia is more debatable. The diagnosis of pregnancy toxaemia is primarily based here on the finding of periportal liver lesions of the type seen in eclampsia. It is, of course, open to argument whether these lesions do, in fact, necessarily indicate pregnancy toxaemia; this argument will not be pursued as it leads into the further discussion of the meaning of the phrase "pregnancy toxaemia". It may however be pointed out that, of the 16 cases of U.P.A. with these liver lesions, 5 had eclamptic convulsions and 5 had had previous symptoms of pre-eclampsia.

A more important consideration is whether this association of U.P.A. and pregnancy toxaemia is a chance one. In the routine obstetric autopsies of the hospital, about 8 or 10 per cent of the patients had died of eclampsia. The incidence of eclamptic convulsions in the fatal cases of U.P.A. (5 out of 67) was thus no higher than in the whole group of the fatal cases in the hospital. On the other hand the incidence of the liver lesions in U.P.A. is twice as great as in the routine obstetric autopsies. It would appear therefore that the association of pregnancy toxaemia with U.P.A. is too high to be merely coincidental. The reason for the association between the two conditions can only be a matter for speculation at present.

The relation between pregnancy toxaemia and U.P.A. has been stressed by many authors (Bartholomew et al., 1949). Premature separation was noted by Sexton et al. (1950) in 3 per cent of mild pre-eclampsias, in 14 per cent of severe pre-eclampsias, and in 37 per cent of cases of eclampsia. This raises the possibility that many of the cases of R.C.N. which are recorded as following eclampsia have, in fact, followed U.P.A. associated with eclampsia. It may be noted in this connection that many cases of eclampsia have some subperitoneal haemorrhages at the cornua of the uterus; they have presumably had a vascular disturbance in the uterus similar to that which occurs in U.P.A., even though retroplacental haemorrhage be absent. The description of the eclamptic kidney, types 2 and 3, by Lubarsch (1896) is clearly that of R.C.N. of focal, minor or patchy extent; he gives no clinical details, and it is certainly possible that these renal lesions were really from cases of U.P.A. associated with eclampsia.

In the present series, eclamptic lesions in the liver are relatively frequent in the patients who died during the first day or two after the U.P.A., and particularly in those who had early R.C.N.. The reason for this is that patients who die early do so because of a combination of factors, of which severe toxaemia is certainly a common and important one. Patients who die later in the puerperium usually do not show these eclamptic lesions in the liver; if such lesions had developed, the toxaemia would have been so severe as to render unlikely the patient's survival until the late puerperium.

CHRONIC NEPHRITIS

In the literature it is frequently maintained, on the clinical grounds of previous hypertension and albuminuria, that many of the patients with U.P.A. have an antecedent chronic nephritis.

The pathological diagnosis of chronic nephritis requires that there shall be significant focal or diffuse scarring of the renal cortex, leading to the destruction of many nephrons. For the diagnosis of chronic glomerulonephritis there should, in addition, be evidence of glomerular lesions of some standing. In the present series there was not a single case which could be accepted pathologically as an example of chronic nephritis. A detailed examination of the kidneys showed in 3 a few very small areas of reticular fibrosis in the outer cortex; this lesion was quite trivial, and could easily have been overlooked on ordinary examination. One of these three patients had a chronic hypertension, one had a toxaemia, and the other had no clinical evidence of either condition. In addition there were 12 cases with occasional minute fibrous areas immediately beneath the renal capsule, representing the scars of surface nephrons which had been lost earlier in life. These are the ordinary changes which develop in the kidney with advancing years, and are no more than would be expected in any group of adult patients such as the present series.

A survey of the literature does not show any acceptable histological reports of chronic nephritis in cases of U.P.A.. Ivens (1928) recorded an early case where the kidney showed some chronic fibrosis, but she gives no further details. Naked-eye reports of chronic nephritis are given by Knauer (1903, Cases 2 and 3), Pulvirenti (1908, Case 5), Frankl and Hiess (1921, Cases 4 and 5), and Crichton (1950, 4 cases). None of these accounts have any histological data to support the diagnosis.

Several authors have recorded as "acute" or "subacute nephritis" the lesions which are seen in the healing stage around an area of R.C.N., and which are described later in this paper. In some of these reports it was recognised that the lesions were purely secondary to the R.C.N.; in others it was assumed that the lesions were pre-existent (Griffith and Herringham, 1906; Cruickshank, 1923; Davidson and Turner, 1930, Case 4; Dalrymple, 1930; Dingle, 1943, Case 1). Other authors have reported what appears to be the healing stage of proximal convoluted tubule necrosis or focal R.C.N. under various titles, such as diffuse interstitial nephritis, nephrosclerosis, etc. (Jardine and Kennedy, 1920, Case 11; Batisweiler, 1933, Case 2; Batizfalvy, 1937, Case 7; Adam, 1945, Case 6). In certain of these reports the histological descriptions are very meagre, so that it is possible that an occasional case may have been misinterpreted in the present analysis. It is not inconceivable that a patient with true chronic nephritis might develop U.P.A. but, as far as pathological evidence is available, the association must be considered as an extreme rarity.

GENERAL PATHOLOGICAL LESIONS OF U.P.A.

This section does not include the renal lesions, as they are considered in detail later.

UTERUS AND APPENDAGES

In patients who were undelivered, the retroplacental clot remained *in situ*. Subperitoneal haemorrhages were observed over the uterus in every case. These haemorrhages were most marked near the cornua but, in the most extensive examples, they were scattered over any part of the upper segment. There was usually some haemorrhage into the muscle in the region of these haemorrhages, though often quite superficial. There was no relationship between the site of the retroplacental haemorrhage and that of the subperitoneal haemorrhages.

Haemorrhages had occurred into both broad ligaments in 10 cases and into one broad ligament in 5. In 4 cases subperitoneal haemorrhage was present over the Fallopian tubes and round ligaments, and in 2 cases into the substance of the ovaries. A spread of the haemorrhage under the peritoneum of the posterior wall of the pelvis had occurred in 3 cases; in 2 of these it had extended out of the pelvis into the lumbar region. In 8 patients there was a small or moderate amount of free blood in the peritoneal cavity. Multiple splits of the peritoneum over the posterior surface of the upper segment of the uterus were present in 5 cases, and over both anterior and posterior surfaces in one. Oedema fluid, which was commonly blood-stained, was present in the parametria and broad ligaments in 14 cases. There was some ascitic fluid in 8 patients.

The condition of the placenta will not be considered here, as it has been amply described by numerous other authors.

SHOCK LESIONS

When the patient had died in shock, the pathological lesions usually associated with this condition were found (Sheehan, 1948a and 1948b). The subendocardial haemorrhages were usually prominent, but the flares of congestion near the centres of the liver lobules were rather more variable in incidence. The pituitaries of 24 of these cases have been examined histologically, but only 6 were later than 12 hours after the U.P.A.; i.e. at a time when pituitary lesions are sufficiently advanced to be recognisable. Necrosis of the anterior lobe was present in 3 of them. It may be noted that R.C.N. was present in the 3 cases without pituitary necrosis, and in one of the cases that showed this lesion. Pituitary necrosis in association with R.C.N. has been noted by Young (1942b), Sheldon and Hertig (1942), Tomlinson (1945), Hügin (1946), Doniach and Walker (1946), Grasby (1947), Joekes and Bull (1948), and MacGillivray (1950). It appears to be purely a result of the shock which develops after the U.P.A.