H A E M O R R H A G I C S H O C K
I N P R E G N A N C Y

by

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Thesis submitted for the degree of M.D.
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PREFACE

This study was undertaken in the wards and Research Department of the Glasgow Royal Maternity and Women's Hospital during the 4 year period 1948-1952. The work was performed while the candidate was the holder of the W.G.Gardiner Research Scholarship from 1946-1950 and as University assistant in the Department of Midwifery from 1950-1952.

Through the co-operation of Professor R.A.Lennie, Professor D.F.Anderson, and Dr. J. Hewitt all cases of shock occurring at the above hospital were available for study. I wish to express my gratitude for the facilities they have provided. I also wish to express my indebtedness to Dr. A.D.T. Govan, Director of Research, for his unfailing encouragement and help in the course of these investigations and in the preparation of this thesis.

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INTRODUCTION

Haemorrhage is the most important major complication with which the obstetrician has to deal. The syndrome following loss of blood is clinically diagnosed as "shock" but there has been considerable controversy over this matter and some observers make a clear distinction between the effects of haemorrhage and shock. A fairly clear picture has been established for the pathological changes in shock of traumatic origin (Grant and Reeve, 1941; Moon, 1942; Beecher, 1949; and Wiggers, 1950), and a similarly definite pattern has been shown to exist in the sequence of biochemical changes occurring in the various phases of this condition.

Of the pathological changes great attention has been paid to the part played by the liver in shock. Both functional and anatomical studies have been made (Blalock and Mason, 1936; Davidson, 1946; and Bywaters, 1946) and the results would appear to indicate that hepatic derangement is of primary importance in deciding the outcome of the condition.

In the biochemical field changes in protein and

and carbohydrate metabolism have been the main subjects of fruitful study. An altered nitrogen metabolism has been known to exist in shock for some considerable time (Lurge, 1936; Cuthbertson, 1942) but changes in blood glucose were noted from a much earlier date. Bernard in 1877 reported hyperglycaemia in shocked patients and this has been confirmed on many occasions since. Recently an excellent field study has been made by Beecher (1949) in regard to shock in wounded personnel.

Apart from metabolic changes considerable investigation has centred around changes in electrolytes, particularly sodium and potassium. McIntosh (1930) and later Gutmann et al (1941) reported marked alteration in the levels of these ions in traumatic shock and more recently Beecher (1949) has confirmed this work. Closely associated with changes in blood electrolytes are the marked alterations in blood volume which of themselves must influence the metabolic changes by virtue of their effect on circulation.

No similar study has been made of the changes following severe haemorrhage in pregnancy. It is

obviously important to study these changes and to determine whether they follow the same pattern as those found in shock due to other causes.

A further complicating factor exists in relation to haemorrhagic shock in pregnancy. Many of these patients have, in addition, been suffering from hypertensive toxaemia during the ante-natal period. In a large number of cases this hypertensive toxaemia is the precipitating factor leading to the haemorrhage. The general consensus of opinion among obstetricians is that patients suffering from hypertensive toxaemia are more prone to develop shock and the degree of shock is likely to be more severe. There has however been no serious attempt made to analyse this possibility and at present it remains in the form of a clinical impression.

The present thesis is an attempt to study the various problems implicit in the above brief survey. One of the objects of the thesis is to determine whether the changes following haemorrhage in pregnancy are at all comparable with those occurring in traumatic shock. For this reason the investigation relates largely to the points touched upon in the previous

paragraphs. The first part of the thesis deals with metabolic changes noted during the phase of shock and subsequently in the period of recovery or deterioration. That there must be a marked change in metabolism is obvious from the clinical condition of the patient in a state of shock. These changes, however, are, of necessity, of rapid onset and relatively short duration. It was therefore thought reasonable to assume that any upset in metabolism would be reflected by alterations in the substance most easily and rapidly utilised, that is carbohydrate. The changes in blood sugar following shock in pregnancy have been studied. In addition, in an attempt to determine the underlying metabolic changes, a study has been made of the intermediate products of carbohydrate metabolism such as pyruvic acid. As phosphates are closely linked to carbohydrate metabolism in the process of phosphorylation, the inorganic phosphate in the blood was estimated. At the same time, in view of the close relationship between carbohydrate and nitrogen metabolism and also the subsequent changes in renal failure following shock, it was felt that it was necessary to investigate

possible changes in nitrogen metabolism.

In traumatic shock there are marked changes in fluid and electrolyte balance due partly to local circulatory changes and partly to the more general reaction. With loss of blood as the main feature in cases of obstetric shock, changes in fluid and electrolytes are bound to follow but these may not parallel the alterations found in traumatic shock.

Changes in blood volume are bound to be associated with alterations in the concentrations of ions in the body fluids. In addition anoxia will influence the movement of certain ions, particularly the bases. For these reasons it was felt that an investigation of sodium, potassium and chlorides would provide interesting material.

Apart from a comparison of the metabolic changes in traumatic and haemorrhagic shock there are other factors of more immediate importance in obstetrics. As previously stated there is a general impression current among obstetricians that toxaemia aggravates the condition of any pregnant patient suffering from the effects of haemorrhage. An attempt has been made to translate this clinical impression into more exact

terms.

Finally, in view of the importance attributed to liver function by the many observers who have studied traumatic shock, a study of the function of the liver was undertaken in cases with haemorrhage. In addition, the anatomical changes occurring in the liver in fatal cases were studied.

This study is not, obviously, a complete investigation into the aetiological factors and pathological changes occurring in the shock syndrome. It is hoped, however, from this study to establish whether haemorrhage produces the same syndrome as trauma. In addition, some insight into the pathological changes occurring in this syndrome may be obtained and, if possible, the fundamental changes which take place may be determined.

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GENERAL CONSIDERATIONS

No attempt will be made in this study to consider the different types of "shock" and it is necessary, therefore, to define the types of cases which have been included in the present study.

The cases were ones of post-partum haemorrhage, placenta praevia, Caesarean Section, abortion or accidental haemorrhage and the common factor in all was haemorrhage. The study then is one of haemorrhagic shock occurring in obstetric practice. It has been argued by some (Coonse et al 1935; Moon 1938) that differences exist between shock and haemorrhage. Moon believes that shock involves damages to capillary endothelium generally and represents a state in which fluid leaves the blood stream, whereas, haemorrhage causes no such damage to capillaries.

Despite these differences the clinical condition of the patient in both instances is very similar. In the present study an attempt has been made to compare the findings following haemorrhage with those occurring in traumatic shock. For convenience the condition

will be termed haemorrhagic shock.

In a few other cases there was trauma associated with haemorrhage. These cases were ones with dystocia or rupture of the uterus.

The clinical picture of shock in the pregnant woman differs little from that seen in non-pregnant individuals. In the most severe cases the patient loses consciousness but in the majority the patient is mentally clear and often apprehensive. Restlessness may be quite a marked feature in the more severe cases but other patients lie quietly.

There is marked pallor of the skin and mucous membranes but an underlying cyanosis is often noted especially of the lips and nail beds. The skin is cold but perspiration is frequently present. Thirst is a common complaint of these patients. The respirations are shallow and rapid, the pulse rate is usually rapid and the volume is poor although the pulse rate may be occasionally slower than normal. The systolic and diastolic blood pressures are markedly depressed and the temperature is usually subnormal.

An elaborate description of the shock state has

not been given as several writers including Grant and Reeve (1941); Moon (1942); Beecher (1949); and Wiggers (1950), have already adequately described it. The clinical picture given above agrees with that of the shock state described by these writers.

In these cases the body temperature is frequently in the region of 96°F. or even lower. According to Best and Taylor (1950) body temperature varies directly with the metabolic rate. This lowering of the metabolic rate is not a new conception. As long ago as 1834 Declasse stated that a general depression of vitality occurred in shock and Meltzer (1908) was also of this opinion. Experimental confirmation of this was obtained by Aub (1920) who found that the degree of fall in the basal metabolism of cats following haemorrhage was roughly proportional to the severity of the shock produced and that recovery after transfusion was usually associated with a prompt return of the metabolic rate to normal.

This lowering of basal metabolism in shock is obviously an important phenomenon and it is necessary to determine whether this is a protective mechanism or whether it is due to a pathological change. Some

attempt must also be made to determine in what manner the change is brought about and whether all or only some of the aspects of metabolism are affected. The main substances involved in metabolism are nitrogen, carbohydrate, and fat and not only is it necessary to determine which are involved in the alteration of metabolism but also the nature of the change and the effects which such a change will bring about in the body.

In the present thesis some of these points have been considered in a general fashion while others have been investigated in some detail. Obviously it would be impossible to study all aspects of shock in great detail and the main emphasis has been laid on changes in nitrogen and carbohydrate metabolism.

NITROGEN METABOLISM

Alterations in the nitrogen values in the blood in cases of shock due to tissue destruction have been reported by several workers, (Lurge 1936; Cuthbertson 1942; Engel et al 1944; Hoar and Haist 1944; McShan et al 1945; Kline 1946; Allison et al 1947; and Beecher 1949). It is possible that the rise in such cases is due to a liberation of nitrogenous products from the damaged tissues.

Similar changes have been demonstrated in cases of haemorrhage involving the digestive tract by Alsted (1936). The increase in blood urea in those cases was assumed to be due to resorption of blood in the intestines.

In our cases, however, there is neither trauma to the tissues nor resorption of blood to cause any change in the nitrogen values, and they provide an uncomplicated picture for comparison with that found in traumatic shock.

In the study of nitrogen metabolism in shock it was decided to investigate changes in those nitrogenous constituents of the blood which might

give information in regard to nitrogen metabolism in general, to liver function in relation to nitrogen and to catabolic changes occurring in the tissues. For this reason a study was made of the changes in values for urea, uric acid and amino acid nitrogen. At the same time, where possible the excretion of urea in the urine was also studied. In many cases of shock, however, temporary suppression of urine occurs and the factor of renal excretion of nitrogen is eliminated.

Methods

Urea - The Urease-Nesslerisation method of Archer and Robb (1925) was used, the readings being made on the photo-electric colorimeter.

Uric Acid - Harrison's (1947) modification of Folin and Trimble's (1924) method using phosphotungstic acid and sodium cyanide in a protein free filtrate was employed.

Amino-acid Nitrogen - Hawk's (1947) modification of Danielson's (1933) method was used.

Blood Urea - Estimations of the blood urea were made in 40 cases of shock complicating pregnancy. Owing to the natural difficulty of forecasting which

cases were likely to develop shock the blood urea was estimated in only 5 cases before the occurrence of the incident leading to shock. The values for these 5 cases fell within normal limits for non-pregnant patients. The range of values was 15.0 mg.% to 38.0 mg.% with an average of 27.5 mg.%. The value for urea in normal pregnancy is lower than in the non-pregnant, however. Crawford (1939) found a range of 16 mg.% - 21 mg.% with a mean of 18 mg.% in the blood urea of pregnant patients.

It will be noted from Table 1 that some of the values in the 5 patients before the occurrence of shock are high (see Cases 1, 2 and 5).

Table 1.

Blood Urea values before shock occurred.

Case No.	Condition	Blood Urea
1	P.P.H.	38.0 mg.%
2	Dystocia:forceps	29.4 "
3	Caes. Sect.	26.0 "
4	Caes. Sect.	15.0 "
5	P.P.H.	29.3 "

P.P.H. - post partum haemorrhage: Caes. Sect. - Caesarean Section with haemorrhage.

In these 3 cases, however, the patients were in

labour or had completed their labour, which is in itself sufficient to account for the rise as it has been shown by Crawford (1939) that the blood urea rises during labour.

To confirm this finding the blood urea was estimated during labour in 22 normal patients. The duration of labour varied from 3 hours to 48 hours. According to the Royal College of Obstetricians and Gynaecologists (1948) the limit of duration of normal labour is 48 hours. The range of urea values in normal labour in this series is 17.7 mg.% to 44.8 mg.% with an average of 28.9 mg.% (Table 2).

Table 2.

Blood Urea in normal patients during labour.

Duration of Labour	Blood Urea mg.%.	Duration of Labour	Blood Urea mg.%.
3	27.5	8	22
22	38	33	20.8
6	32	33	34
10	32.5	48	20.8
6	23.2	47	44.8
9	18.2	24	31.4
10	17.7	42	19.5
3	33.0	36	36
5	33.0	33	32
19	31.4	41	25.5
8	29.5	24	34

These intrapartum values are useful since almost all cases of shock occur either during or just after labour and they therefore provide a true basis for comparison.

Subsequently the 5 cases with blood urea estimations before shock were studied in the shock phase before any form of therapy was commenced and the changes in blood urea are noted in Table 3.

Table 3.

Case No.	Condition	Duration of Shock	Blood Urea during Shock	Rise in Blood Urea per hour
1	P.P.H.	2½ hrs.	46 mg.%	3.2 mg.%
2	Dystocia: forceps	2 "	38.8 "	4.7 "
3	Caes. Sect.	½ hr.	33.3 "	14.6 "
4	Caes. Sect.	½ "	15.5 "	0.25 "
5	P.P.H.	1 "	34.2 "	4.9 "

P.P.H. - post-partum haemorrhage: Caes. Sect. - Caesarean Section with haemorrhage.

The average value of blood urea in these cases was 33.6 mg.%.

It can be seen that the blood urea rises in all cases before blood transfusion is administered.

It is known, however, that oliguria occurs

occurs during shock and it is therefore necessary to try to determine whether the rise in blood urea noted in these cases was due to increased protein catabolism or to urinary suppression or to a combination of the two. Personal observations were made on the duration of shock and of oliguria in 60 cases of shock. It is admittedly difficult to determine when clinical recovery from shock occurs but the duration of shock was estimated as the time from the occurrence of the accident causing shock until the patient's appearance, blood pressure, and pulse rate were normal. The duration of shock and of oliguria are noted in Table 4.

In all cases the duration of oliguria exceeded the duration of shock. The mere fall in blood pressure is not sufficient to account for the low urinary output and some functional disturbance of the kidneys appears to occur which persists for a varying period and is longer than usual in cases of accidental haemorrhage.

The relationship of the oliguria to the levels of blood urea will now be considered.

Table 4.

Showing duration of shock and oliguria.

Case No.	Condition	Duration of Shock	Oliguria ozs.	Oliguria hrs.
2	Dystocia:P.P.H.	8 hrs.	0	in 12
6	P.P.H.	3 "	6	" 9
7	P.P.H.	12 "	10	" 21
8	Abortion	10 "	6	" 17
9	Caes.Sect.	5½ "	12	" 24
1	P.P.H.	4 "	0	" 12
10	P.P.H.	7½ "	0	" 12
11	Acc.Haem.	5½ "	0	" 12
12	P.P.H.	4 "	3	" 12
13	P.P.H.	1 hr.	6	" 12
14	P.P.H.	5 hrs.	2	" 12
15	P.P.H.	2 "	0	" 12
16	P.P.H.	7 "	2	" 12
17	P.P.H.	4 "	0	" 12
18	P.P.H.	4 "	0	" 12
19	A.P.H.:(Hydramnios)	2 "	0	" 12
20	Acc.Haem.	18 "	3	days
21	Acc.Haem.	18 "	2½	"
22	Acc.Haem.	5 "	0	in 16
23	Acc.Haem.	20 "	2	days
24	P.E.T.:P.P.H.	12 "	4	"
25	Acc.Haem.	5 "	0	in 24
26	Acc.Haem.	24 "	4	days
27	Acc.Haem.	12 "	2	"
3	Placenta Praevia	3 "	0	in 12
4	Caes.Sect.	3 "	4	" 12
28	Caesarean Hysterectomy	24 "	4	days
5	P.P.H.	3 "	8	in 24
29	P.P.H.	6 "	3	in 24
30	P.P.H.	5 "	0	" 12
31	Acc.Haem.	18 "	0	" 20
32	Acc.Haem.	8 "	2	" 24
33	P.P.H.	4 "	2	" 24
34	Acc.Haem.	8 "	3	days
35	P.E.T.:Dystocia	6 "	0	in 12
36	P.P.H.	4 "	0	" 12
37	P.P.H.	5 "	0	" 12
38	Abortion	7 "	4	" 12
39	P.P.H.	8 "	2	" 12
40	A.P.H.:Hydramnios	4 "	9	" 12

Table 4 (Cont'd.)

Case No.	Condition	Duration of Shock	Oliguria ozs.	hrs.
41	P.P.H.	3 hrs.	0	in 7
42	Acc.Haem.	20 "	5½	" 24
43	Acc.Haem.	7 "	0	" 24
44	P.P.H.	2 "	9	" 12
45	Acc.Haem.	7 "	2	days
46	Acc.Haem.	18 "	1	in 24
47	Acc.Haem.	10 "	0	" 24
48	P.P.H.	20 "	5	" 24
49	Acc.Haem.	11 "	2	days
50	Acc.Haem.	9 "	2	"
51	P.P.H.	9 "	10	in 24
52	Acc.Haem.	12 "	6	" 24
53	Acc.Haem.	5 "	3	" 24
54	Caes.Sect.	5 "	12	" 24
55	Abortion	3 "	3	" 12
56	Abortion	7 "	0	" 12
57	Ruptured Rudimentary Uterine Horn	9 "	2	days
58	P.P.H.	2 "	0	in 12
59	Placenta praevia	8 "	8	" 12
60	Acc.Haem.	6 "	0	" 24

P.P.H. - Post-partum haemorrhage: Caes.Sect. - Caesarean Section with haemorrhage: Acc.Haem. - Accidental haemorrhage: A.P.H. - ante-partum haemorrhage: P.E.T. - Pre-eclamptic toxaemia.

The duration of shock before the estimation of the blood urea was noted and also the rise in blood urea per hour (Table 3.). The average rise in these cases was 5.53 mg.% in one hour. The presumed rise in blood urea due to non-functioning of the kidneys

in a patient with normal metabolism was therefore calculated as follows:-

The total body water is given as 70% of body weight (Best and Taylor, 1950). For the purposes of argument an arbitrary weight of 70 Kg.may be assumed. In such a patient the amount of body water would be $70 \times \frac{70}{100} = 49$ litres. The normal amount of urine excreted per day is 1500 cc. with a urea content of 2gms./100 cc. The normal amount of urea excreted in 24 hours is therefore 30 gms.or 1.25 gms.per hour. If this urea is retained it is distributed throughout 49 litres of fluid as urea is able to traverse all membranes and is distributed evenly by diffusion throughout all the media of the body (Peters, 1935).

The rise in blood urea in one hour in a patient weighing 70 Kg. with non-functioning kidneys would therefore be $\frac{1250}{49000} \times \frac{100}{1}$ mg.per 100 cc. = 2.55 mg.%. On the other hand if the body weight were 60 Kg.the rise in blood urea would be 3 mg.% per hour while in a patient weighing 80 Kg.the rise would be 2.23 mg.% per hour. The range of 60-80 Kg.gives very conservative results. Many pregnant women are heavier

than 80 Kg. In these cases the estimated increase in blood urea resulting from urinary suppression would be less than 2.23 mg.% per hour. It appears then that in many cases the increase in blood urea is greater than would be expected with renal dysfunction alone.

In the remaining 35 cases the patients were not seen until the onset of shock and therefore only those values for blood urea subsequent to shock were obtained. Again the values were obtained before blood transfusion or any other therapy was commenced. The results are shown in Table 5. The range of urea values was 16 mg.% to 53.3 mg.% with an average of 31.4 mg.%. These values are within normal limits for patients in labour (Table 2) but are raised compared with values for patients not in labour.

The cases were therefore divided into those in labour or recently delivered (Table 6) and those not in labour (Table 7).

From Table 6 it will be noted that the average urea values come within the range found in normal patients during labour (cf. Table 2) so that any increase in individual cases above this range is slight and might be accounted for by labour or renal dysfunction.

Consideration of the cases in Table 7 shows that the values recorded are well above those found in normal pregnancy. With the exception of five cases all of the patients in this group suffered from accidental haemorrhage and if this condition is considered separately it is found that the values are greatly increased, ranging from 22 mg.per cent. to 53.3 mg.per cent. with an average of 36.6 mg.per cent. It is generally agreed that accidental haemorrhage is associated with pre-eclamptic toxaemia and it is therefore necessary to subject the figures of all cases to a further analysis on the basis of whether the patients were suffering from toxaemia prior to the occurrence of haemorrhage. This has been done in Table 5 where it will be noted that the cases have been divided into 2 groups.

The values in the 17 cases in the toxaemic group ranged from 22 mg.% to 53.3 mg.% with a mean of 35 mg.% while in the 18 cases in the non-toxaemic group the range was 16 mg.% to 40.5 mg.% with a mean of 28 mg.%. There are therefore higher urea levels in the patients with pre-eclamptic toxaemia who suffer shock.

Table 5.

Showing the blood urea values during shock before blood transfusion.

Case No.	Condition	Blood Urea	
61	*Acc.Haem.	43 mg.%	
28	*Acc.Haem.	28 "	
42	*Acc.Haem.	38 "	
50	*Acc.Haem.	32 "	
26	*Acc.Haem.	43 "	Toxaemic
43	*Acc.Haem.	53.3 "	
24	*P.E.T.: P.P.H.	24 "	Average
23	*Acc.Haem.	31.5 "	35 mg.%
27	*Acc.Haem.	42 "	
22	*Acc.Haem.	31 "	
32	*Acc.Haem.	30 "	
49	*Acc.Haem.	27 "	
21	*Acc.Haem.	40.5 "	
20	*Acc.Haem.	42 "	
13	*P.E.T.:P.P.H.	32.5 "	
52	*Acc.Haem.	22 "	
47	*Acc.Haem.	36 "	
10	P.P.H.	16 mg.%	
62	Caes.Sect.	23 "	
63	P.P.H.	23.5 "	
16	P.P.H.	31.7 "	
17	P.P.H.	17 "	Non-toxaemic
30	P.P.H.	29.5 "	
59	P.P.H.	28 "	
64	P.P.H.	32 "	Average
65	P.P.H.	35.8 "	28 mg.%
66	Placenta praevia	40.5 "	
67	P.P.H.	18 "	
48	P.P.H.	37 "	
9	Caes.Sect.	23 "	
51	P.P.H.	37 "	
29	P.P.H.	30 "	
51	Ruptured Uterus	24 "	
7	P.P.H.	31 "	
8	Abortion	27 "	

*Cases complicated by pre-eclamptic toxaemia. P.P.H. - Post-partum haemorrhage: Acc.Haem. - Accidental haemorrhage: Caes.Sect. - Caesarean Section with haemorrhage: P.E.T. - Pre-eclamptic toxaemia.

Table 6.

Patients recently delivered.

Case No.	Condition	Blood Urea mg.%
10	P.P.H.	16
63	P.P.H.	23.5
16	P.P.H.	31.7
24	P.E.T.:P.P.H.	24
17	P.P.H.	17
30	P.P.H.	29.5
15	P.P.H.	28
64	P.P.H.	32
13	P.E.T.:P.P.H.	32.5
65	P.P.H.	35.8
67	P.P.H.	18
48	P.P.H.	37
51	P.P.H.	37
29	P.P.H.	30
7	P.P.H.	31

Range 16 mg.% - 35.8 mg.%: Average 28.2 mg.%.
P.P.H. - Post-partum haemorrhage: P.E.T. - Pre-eclamptic toxaemia.

Table 7.

Patients not in labour.

Case No.	Condition	Blood Urea mg.%
61	Acc.Haem.	43
28	Acc.Haem.	28
42	Acc.Haem.	38
50	Acc.Haem.	32
26	Acc.Haem.	43
43	Acc.Haem.	53.3
23	Acc.Haem.	31.5
27	Acc.Haem.	42
22	Acc.Haem.	31
32	Acc.Haem.	30
49	Acc.Haem.	27
21	Acc.Haem.	40.5
20	Acc.Haem.	42
52	Acc.Haem.	22
47	Acc.Haem.	36
62	Caes.Sect.	23
9	Caes.Sect.	23
66	Placenta Praevia	40.5
57	Ruptured uterus	24
8	Abortion	27

Range 22mg.% - 53.3 mg.%: Average 33.8 mg.%.

Acc.Haem. - Accidental haemorrhage: Caes.Sect.- Caesarean Section with haemorrhage.

All the patients in the present series received therapy in the form of blood transfusion.

In the present section only the changes occurring in the first 24 hours following the onset of shock are being considered. This routine was adopted since urinary suppression in the average case only lasted for this period. It was only possible, for clinical reasons, to study subsequent changes in the blood urea in 10 cases (Table 8).

Even after adequate blood transfusion therapy it will be noted that the blood urea continues to rise in almost all cases. The average increase was 5.75 mg.%. In two cases, however, there was an actual decrease in the blood urea level. On calculating the expected rise in blood urea due to non-functioning of the kidneys with a normal protein catabolism, however, the true values fell very far short of the expected values except in one case (Case 24). This patient developed a hepato-renal syndrome which will be referred to later.

Excluding this one case then this means that a further alteration in protein metabolism in a direction opposite to that noted in the earliest phase of shock has occurred.

Before discussing the changes occurring in the

Table 8.

Showing blood urea values before and after blood transfusion.

Case No.	Condition	Time between estim-ations	Blood Urea Before	Blood Urea After	Change in Blood Urea	Calculated rise in Blood urea due to anuria 60Kg.B.W.	Calculated rise in Blood urea due to anuria 80Kg.B.W.
		hrs.	mg.%	mg.%	mg.%	mg.%	mg.%
61	Acc.Haem.	20	43	48.7	5.7	60	44.6
32	Acc.Haem.	15	30	36	6	45	33.4
28	Acc.Haem.	5	28	32	4	15	11.15
24	P.E.T.:	7	24	52.5	28.5	21	15.6
22	Acc.Haem.	9	31	36	5	27	20.0
17	P.P.H.	8	17	25	8	24	17.8
16	P.P.H.	4	31.7	29	- 2.7	12	8.9
65	P.P.H.	4½	35.8	36.8	1	13.5	10.0
30	P.P.H.	2	29.5	32	2.5	6	4.5
48	P.P.H.	9	37	32	- 5	27	20.0

P.P.H. - Post-partum haemorrhage: Acc.Haem. - Accidental Haemorrhage:

P.E.T. - Pre-eclamptic toxaemia.

blood urea the alterations in uric acid and amino-acid nitrogen will be considered.

Uric Acid

The uric acid was estimated in 29 cases of obstetric shock before blood transfusion was administered. Unfortunately it was possible to make an estimation of the blood uric acid before shock occurred in only one case. This was a patient (Case 3) who subsequently developed shock following haemorrhage complicating Caesarean Section. In this case the blood uric acid level was 3.2 mg.%. According to Davis (1935) the blood uric acid in normal pregnancy is 2-4 mg.%.

Following the development of shock the blood uric acid in this patient rose to 4.1 mg.%. In the 29 patients estimations were made prior to blood transfusion. In all cases the values were high and in many instances well above normal values (Table 9). The range of values was 3.0 mg.% to 14.7 mg.% with an average of 6.35 mg.%. It should be remembered however that there is a rise in the level of blood uric acid in pre-eclamptic toxaemia. (Best and Taylor, 1950, and Crawford 1940).

Table 9.

Blood uric acid values before transfusion.

Case No.	Condition	Blood Uric Acid		
61	*Acc.Haem.	6	mg.%	
28	*Acc.Haem.	8	"	
42	*Acc.Haem.	4.9	"	
26	*Acc.Haem.	6.0	"	Toxaemic
23	*Acc.Haem.	7.3	"	
43	*Acc.Haem.	14.7	"	
27	*Acc.Haem.	7.75	"	Average
22	*Acc.Haem.	6.25	"	7.1 mg.%
32	*Acc.Haem.	7.07	"	
68	*Acc.Haem.	6.3	"	
49	*Acc.Haem.	12.4	"	
21	*Acc.Haem.	6.6	"	
20	*Acc.Haem.	3.9	"	
13	*P.E.T.:P.P.H.	4.3	"	
35	*P.E.T.:Forceps	4.55	"	
10	P.P.H.	11	"	
2	Dystocia: forceps	5.55	"	
41	P.P.H.	7.0	"	
55	Abortion	5.7	"	
17	P.P.H.	3.2	"	Non-toxaemic
30	P.P.H.	3.0	"	
19	A.P.H. (Hydramnios)	4.2	"	Average
18	P.P.H.	8.9	"	5.55 mg.%
16	P.P.H.	4.3	"	
15	P.P.H.	4.1	"	
64	P.P.H.	4.15	"	
3	Caes.Sect.	4.1	"	
63	P.P.H.	8.45	"	
5	P.P.H.	4.10	"	

* Cases complicated by pre-eclamptic toxaemia.

Acc.Haem. - Accidental haemorrhage: P.E.T. - Pre-eclamptic toxaemia: A.P.H. - Ante-partum haemorrhage;

P.P.H. - Post-partum haemorrhage: Caes. Sect. - Caesarean Section. with haemorrhage.

All cases complicated by pre-eclamptic toxaemia including cases of accidental haemorrhage were therefore considered separately from cases not complicated by this condition (Table 9). There were 15 cases associated with pre-eclamptic toxaemia and in them the uric acid level ranged from 3.90 mg.% to 14.7 mg.% with an average of 7.1 mg.%. In the other 14 cases not complicated by pre-eclamptic toxaemia the uric acid level ranged from 3.0 mg.% to 11 mg.% with an average of 5.55 mg.%. These figures indicate that there is a rise in uric acid in both toxaemic and non-toxaemic patients, but the levels are higher in the toxaemic group. This may possibly be due to a pre-existing high uric acid level in these patients.

As labour may produce a rise in uric acid it was considered advisable to make estimations in a series of normal patients. Estimations were made in 22 normal patients in labour and the results are shown in Table 10. The range of values was 2.25 mg.% to 6.3 mg.% with an average of 3.80 mg.% showing that both toxaemic and non-toxaemic patients suffering from

shock have raised uric acid values greater than can be accounted for. by labour.

Table 10.

Normal uric acid values in labour.

Duration of Labour	Blood Uric Acid
3 hours	2.7 mg.%
22 "	5.8 "
6 "	5.05 "
10 "	3.2 "
6 "	3.7 "
9 "	3.60 "
10 "	2.80 "
3 "	2.45 "
5 "	4.05 "
19 "	3.20 "
8 "	4.0 "
8 "	5.4 "
33 "	3.1 "
33 "	3.25 "
48 "	3.32 "
47 "	5.55 "
24 "	3.10 "
42 "	4.0 "
36 "	2.25 "
33 "	2.5 "
41 "	6.3 "
24 "	4.4 "

The blood uric acid was again estimated in 12 cases after blood transfusion had been given but

while the kidneys were still inactive. These values have been tabulated in Table 11 and at the same time the actual changes in uric acid have been noted and also the calculated changes due to urinary suppression with normal protein catabolism. The calculated changes in uric acid have been calculated along the same lines as for urea (p.20) with assumed body weights of 60 Kg. and 80 Kg. According to Best and Taylor (1950) the average daily output of uric acid is from 0.5 to 1 gram. Of this the endogenous uric acid amounts to from 0.3 to 0.4 gram and the precursors of endogenous uric acid are most probably furnished by muscular tissue. During the time of shock and, in most cases, for some time before, no solid food is taken by the patient so that exogenous precursors of uric acid are minimal. The probable amount of uric acid which would be excreted in the urine by these patients if they were not in a state of shock would be 0.3 gms. in 24 hours. On this basis the calculated rise in uric acid in the blood of a patient weighing 60 Kg. with non-functioning kidneys and normal protein catabolism would be $\frac{1500}{100} \times \frac{0.3}{1} \times \frac{1}{24} \times \frac{1}{42000}$ mg.%

= 0.445 mg.%. In a patient weighing 80 Kg., however, the rise expected would be 0.334 mg.%.

However, in view of the uncertainty of the amount of uric acid which would have been excreted it was considered advisable to base the calculations also on the maximum amount of uric acid likely to be excreted, that is, 1 gm.in 24 hours. In this instance the calculated rise in uric acid in a patient weighing 60 Kg. would be 1.49 mg.% and in a patient weighing 80 Kg. 1.12 mg.%. The calculated rise in blood uric acid under these various conditions are noted in Table 11.

In only 3 cases (Nos. 10,30 and 5) is there a resemblance between the actual rise in blood uric acid and the minimal calculated rise. In all the other cases the actual rise is much less than would be expected. Indeed, in some cases there is a slight decrease in the amount of uric acid. It may be concluded then that after the initial rise in uric acid there is only a slight rise, if any, despite the fact that the kidneys are not functioning.

To recapitulate, immediately following shock there is a rise in both urea and uric acid greater than

Table 11.

Actual and calculated changes in uric acid levels.

Case No.	Condition	Time between Estimations	Blood Uric Acid Bef. Trans. mg.%	Blood Uric Acid Aft. Trans. mg.%	Act. Rise in Uric Acid mg.%	Calculated rise due to anuria. 0.3 gm. normal excretion 60Kg. B.W.	0.3 gm. normal excretion 80Kg. B.W.	1 gm. normal excretion 60Kg. B.W.	1 gm. normal excretion 80Kg. B.W.
61	Acc.Haem.	20 hrs.	6	6.2	0.2	0.89	0.68	2.98	2.24
28	Acc.Haem.	5 "	8	8	0	2.22	1.67	7.45	5.60
10	P.P.H.	2 "	11	12.1	1.1	0.89	0.67	3.0	2.24
66	Acc.Haem.	9 "	6.25	8.5	2.25	4.0	3.0	13.5	10.0
17	P.P.H.	8 "	3.2	3.2	0	3.56	2.67	12.0	8.96
30	P.P.H.	2 "	3.0	4.2	1.2	0.89	0.67	3.0	2.24
19	A.P.H. Hydramnios	1 "	4.2	4.25	0.05	0.45	0.33	1.49	1.12
16	P.P.H.	4 "	4.3	4.2	-0.1	1.78	1.33	6.0	4.48
15	P.P.H.	1½ "	4.1	4.1	0	0.67	0.5	2.25	1.68
64	P.P.H.	3 "	4.15	4.0	-0.15	1.33	1.00	4.5	3.36
3	Caes.Sect.	1 "	4.1	4.0	-1	0.45	0.33	1.49	1.12
5	P.P.H.	2 "	4.1	4.2	1	0.89	0.67	3.0	2.24

P.P.H. - Post-partum haemorrhage: Acc.Haem. - Accidental haemorrhage: A.P.H. - Ante-partum haemorrhage: Caes.Sect. - Caesarean Section. with haemorrhage.

could be accounted for by the suppression of urinary function occurring in these patients. The increase is greater in these patients who were previously hypertensive but it is to be remembered that the blood uric acid is usually raised in such patients before shock occurs and this may also happen in some cases in regard to the blood urea.

After this initial rise in urea and uric acid the values tend to remain at about the same level or to rise slightly. The rise, however, is not as great as would be expected with urinary suppression. There is, then, an initial rise in urea and uric acid greater than could be caused by anuria followed by a slight rise which is less than could be accounted for by anuria.

To complete the investigation of protein catabolism the changes occurring in amino-acid nitrogen will now be considered.

Amino-Acid Nitrogen

The values of amino-acid nitrogen were estimated in 36 patients while in a state of shock before blood transfusion had been administered. These values are noted in Table 12. The range of levels is 3.3 mg.% to

Table 12.

Blood amino-acid nitrogen levels during shock.

Case No.	Condition.	Amino-Acid Nitrogen mg.%	
61	*Acc.Haem.	3.5	
28	*Acc.Haem.	8.7	
42	*Acc.Haem.	5.9	
50	*Acc.Haem.	6.3	Toxaemic
26	*Acc.Haem.	6.6	
24	*P.E.T.:P.P.H.	7.4	
23	*Acc.Haem.	6.5	Average
43	*Acc.Haem.	10.3	
27	*Acc.Haem.	5.85	6.81 mg.%
22	*Acc.Haem.	6.0	
32	*Acc.Haem.	10.05	
68	*Acc.Haem.	10.3	
49	*Acc.Haem.	6.0	
21	*Acc.Haem.	6.35	
20	*Acc.Haem.	7.5	
13	*P.E.T.:P.P.H.	4.8	
11	*Acc.Haem.	7.3	
52	*Acc.Haem.	3.3	
10	P.P.H.	8.7	
2	Dystocia: forceps	4.38	
41	P.P.H.	7.4	Non-Toxaemic
17	P.P.H.	5.7	
30	P.P.H.	6.4	
19	A.P.H.Hydramnios	4.2	Average
18	P.P.H.	10.0	6.19 mg.%
16	P.P.H.	4.3	
15	P.P.H.	7.8	
64	P.P.H.	4.24	
3	Caes.Sect.	9.45	
63	P.P.H.	6.5	
5	P.P.H.	5.4	
9	Caes.Sect.	4.7	
69	Caes.Sect.	7.12	
7	P.P.H.	5.3	
57	Ruptured uterus	6.0	
67	P.P.H.	4.0	

* Hypertensive cases.

P.P.H. - Post-partum haemorrhage: Acc.Haem. - Accidental haemorrhage: A.P.H. - Ante-partum haemorrhage: P.E.T. - Pre-eclamptic toxaemia: Caes.Sect. - Caesarean section with haemorrhage.

to 10.3 mg.% with an average of 6.5 mg.%. Unfortunately, it was not possible to estimate the amino-acid nitrogen in any of the cases before shock ensued.

The normal level of amino-acid nitrogen in pregnancy is slightly lower than in the non-pregnant. The level in pregnancy is given as 3.5 mg.% (Bonsnes, 1947) while in the non-pregnant Cramer and Winnick (1943) give 4.1 $\pm$ 1.2 and Farr, McCarthy and Francis (1942) give 4.5 mg. $\pm$ 0.46 as the normal value.

The majority of shock cases therefore have amino-acid nitrogen values greater than normal. In order to determine whether cases with previous hypertension have higher values than non-hypertensives the cases have been divided accordingly (Table 12).

In 18 of the cases there was some evidence of previous hypertension and the range of values of amino-acid nitrogen in these cases is 3.3 mg.% to 10.3 mg.% with an average of 6.81 mg.%. In the other 18

non-hypertensive cases the range is from 4.0 mg.% to 10.0 mg.% with an average of 6.19 mg.%.

The average values in hypertension are therefore some 9 per cent. above those found in non-hypertensive cases but on comparing the uric acid values in these two groups it is found that the increase is 28 per cent. in favour of the hypertensive cases. It would appear that the slightly higher values for amino acids in the hypertensive group are not significant.

It has been found that in traumatic shock there is a greater rise in the amino acid nitrogen levels than in haemorrhagic shock due to the destruction of protein in the damaged tissues (Engel et al., 1944; Hoar and Haist, 1944; McShan et al.1945; and Kline, 1946). It is of interest at this point to determine whether there is a greater rise of amino acid nitrogen in cases of mixed and concealed accidental than in other cases of haemorrhage and from this to deduce whether tissue destruction occurs in these cases of accidental haemorrhage or not. Fourteen cases of post-partum haemorrhage were selected for comparison with the 16 cases of accidental haemorrhage (Table 12). The range of values in the cases of accidental haemorrhage

was 3.3 mg.% to 10.3 mg.% with a mean of 6.28 mg.%. While in the cases of post-partum haemorrhage the range was 4.3 mg.% to 10.0 mg.% again with a mean of 6.28 mg.%. From these figures it is concluded that there is no evidence of destruction of tissues in cases of accidental haemorrhage.

In order to determine whether labour has any influence in producing a rise in amino-acid nitrogen the levels were estimated in 22 normal cases during labour (Table 13).

Table 13.

Amino-acid nitrogen values of normal patients in labour.

Duration of Labour	Blood Amino-acid Nitrogen.
3 hours	2.8 mg.%
22 "	4.51 "
6 "	4.51 "
10 "	6.4 "
6 "	5.36 "
9 "	4.20 "
10 "	4.24 "
3 "	4.93 "
5 "	3.70 "
19 "	3.50 "
8 "	4.51 "
8 "	6.2 "
33 "	4.2 "
33 "	6.6 "
48 "	3.89 "
47 "	7.0 "
24 "	4.52 "
42 "	4.0 "
36 "	6.4 "
33 "	7.0 "
41 "	4.52 "
24 "	4.39 "

The range of normal values of amino-acid nitrogen in labour is 2.8 mg.% to 7.0 mg.% with an average of 4.9 mg.%. Although the amino-acid nitrogen is raised during labour this is not sufficient to account for the rise occurring in amino-acid nitrogen in shock.

In 12 cases the amino-acid nitrogen level was measured after blood transfusion had been administered but while the kidneys were still inactive. The results are tabulated in Table 14.

After the initial rise in the early stage of shock there is a fall in the level of amino-acid nitrogen in half of the cases while there is a very slight rise in the other cases except in one instance. In this case (No.24), with the continued increase in level of amino-acid nitrogen, jaundice developed and this was considered to be sufficient to explain the rise.

The changes which occur in amino-acid nitrogen in shock, then, are a rise in the early stages followed soon after by a maintenance of the level or an actual fall. These changes are paralleled by the ones occurring in urea and uric acid in which there is an initial rise greater than could be accounted for by urinary

Table 14.

Amino-acid nitrogen values after blood transfusion.

Case No.	Condition	Time between Estim-ations	Amino-Acid Nitrogen Before Trans. mg.%	Amino-Acid Nitrogen After Trans. mg.%	Change in A.A.N. mg.%
61	Acc.Haem.	20 hrs.	3.5	3.68	+ 0.18
28	Acc.Haem.	5 "	8.7	6.5	- 2.2
10	P.P.H.	2 "	8.7	8.1	- 0.6
24	P.E.T.: P.P.H.	7 "	7.4	8.65	+ 1.25
22	Acc.Haem.	9 "	6	5.8	- 0.2
19	A.P.H. Hydramnios	1 "	4.2	4.4	+ 0.2
18	P.P.H.	3 "	10.0	6.2	- 3.8
16	P.P.H.	4 "	4.3	4.3	0
15	P.P.H.	1½ "	7.8	5.0	- 2.8
64	P.P.H.	3 "	4.24	4.74	+ 0.5
3	Caes.Sect.	1 "	9.45	9.75	+ 0.3
5	P.P.H.	2 "	5.4	4.65	- 0.75

P.P.H. - Post-partum haemorrhage: A.P.H. - Ante-partum haemorrhage: Acc.Haem. - Accidental haemorrhage: P.E.T. - Pre-eclamptic toxaemia: Caes.Sect. - Caesarean section.

suppression. This is followed by a maintenance of the level or a slight rise but not as great as would be expected from urinary suppression in an otherwise normal patient. There is no greater rise in amino

acid nitrogen in cases of accidental haemorrhage as compared with other cases of haemorrhage.

Discussion of Nitrogen Metabolism in Haemorrhagic Shock.

The changes occurring in the nitrogenous constituents of the blood in shock may be divided into two phases (a) The early phase of increase greater than can be accounted for by urinary suppression and (b) the later phase of relative decrease. In this second phase there may be an actual increase but it is less than could be accounted for by urinary suppression.

The rise in the nitrogenous constituents in the initial phase would seem to indicate some increase in protein catabolism. As has been shown the increases are greater than can be accounted for by absence of renal excretion alone. The possibility of a non-utilisation of nitrogen allowing these substances to accumulate in the blood must, however, be considered. While such an explanation might be possible in the case of uric acid and amino-acids it is difficult to see how it is compatible with a rise in blood urea as urea can only be formed by utilisation of proteins. Although the changes in these individual substances

might possibly be independent of each other it seems reasonable to assume that they are closely related particularly in view of the fact that they follow a similar pattern.

This rise in the nitrogenous constituents of the blood has been found by many workers in shock produced by various causes. It has been noted in haemorrhagic shock by Taylor and Lewis (1915) and Engel and others (1943); in traumatic shock by Lurge (1936), Engel et al (1944), McShan et al (1945), and Kline et al (1946); and in tourniquet shock by Hoar and Haist (1944).

The rise in nitrogen substances in the blood may be due to an increased formation or to reduced excretion. As we have shown, the reduced excretion due to renal dysfunction is not sufficient to account for the rise and it is, therefore, concluded that there is an excessive formation of nitrogenous breakdown products which can only occur through an increase in protein catabolism. This accelerated protein catabolism may be a direct result of the shock stimulus or it may be mediated through some body process. It has been suggested by Selye (1950) that there is a state of "alarm reaction" after stress and this is associated with increased protein catabolism. It is

not clear why this breakdown should occur but as will be shown in a later part of the thesis shock is also associated with an increase in blood sugar levels. In this respect it is interesting to note that Evans (1936) and Long et al (1940) have suggested that the protein catabolism is related to adrenal activity and in particular to gluco-corticoid secretion. If this is so it may be that the breakdown of protein is related to this apparent demand for carbohydrate and in this way the liberation of corticoids from the adrenals in shock would account for the raised blood urea, uric acid and amino acid nitrogen levels in our cases.

However, following this initial stage with increase in the nitrogenous constituents in the blood, there is a stage in which the nitrogenous substances are not as great as would be expected even if protein catabolism remained at a normal level and this occurs in spite of oliguria and a low urinary urea content. All available references quote only the increased levels in the nitrogenous constituents in the blood and, so far as we are aware, this second phase with the relatively low levels of urea, uric acid and amino-acid nitrogen has not previously been noted.

Several factors may be involved in this reduced production of nitrogenous substances in the second phase of shock. The possible explanations are (a) some degree of starvation; (b) some liver dysfunction; or (c) a decrease in protein catabolism.

It has been shown by Benedict (1915) and again by Gamble, Ross and Tisdall (1923) that there is a decrease in blood urea in cases of starvation but it would seem very doubtful if this had any part to play in the present series of cases as the observations in the blood chemistry were made over a comparatively short space of time.

The second factor to be considered is liver dysfunction. It is necessary to determine whether liver dysfunction alone without any alterations in protein catabolism would explain the changes in the nitrogen levels. An association of deficient liver function with normal protein catabolism would produce a rise in the amino-acid nitrogen while the blood urea would remain normal. As we have shown, the blood urea was raised in the initial phase of shock and it was concluded that, in this phase the main feature was one of increased protein catabolism. In the succeeding

phase of shock, however, there was practically no rise in the level of blood urea even though the kidneys were inactive. At the same time the level of amino-acid nitrogen was maintained. If liver function were normal at this period it would be reasonable to expect that the amino-acids would be converted to urea and the amino acid level of the blood would return to normal. In these cases the amino acid values remained high. It would seem then that at this phase liver dysfunction becomes more evident. Similarly, if protein catabolism had been maintained at its previously high level or even at a normal level one would expect a continuous rise in the nitrogenous constituents of the blood. This does not occur and one must therefore conclude that nitrogen metabolism is depressed at this stage.

As has been stated previously the raised levels of nitrogen substances in the initial phase of shock can be accounted for by excessive secretion of glucocorticoids from the adrenal cortex causing increased protein catabolism. In the succeeding phase of shock, however, there is a reduction in protein catabolism. Selye (1950) postulated three phases

(a) the alarm reaction with increased protein catabolism, (b) the stage of resistance with normal or reduced protein catabolism and (c) the stage of exhaustion with increased protein catabolism.

From the biochemical findings in the present series it would appear that according to Selye's theory there was an "alarm reaction" followed by a stage of resistance. Therapy was obviously adequate in our series since all recovered and the stage of exhaustion was not reached.

In terms of secretion of glucocorticoids by the adrenal glands, if this theory is correct, there appears to have been a rapid secretion of glucocorticoids from the adrenal glands in the initial phase of shock followed by a reduced secretion in the succeeding phases. The lower levels found in the second phase may, in addition, be due to liver dysfunction.

Many authorities believe that there is marked tissue destruction in the uterus in cases of concealed accidental haemorrhage and, indeed Young (1942) has suggested that the renal lesions associated with accidental haemorrhage can be explained on the same

basis as the "crush" syndrome. In this theory myohaemoglobin is supposed to escape from damaged muscles and be deposited in the renal tubules. From our studies of amino-acid nitrogen levels, however, there is no evidence that there is damage to the tissues in accidental haemorrhage.

The incidental finding of a greater rise in urea, uric acid and amino-acid nitrogen in patients with evidence of previous hypertensive disease is interesting. Unfortunately, in our series it was not established whether the levels of these substances was raised before the onset of shock. It is not, therefore, possible to determine whether a previous high level was present or whether hypertensive patients react differently to a shock stimulus. This question will be discussed further in a subsequent section of the thesis.

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CARBOHYDRATE METABOLISM.

As postulated in an earlier part of the thesis the rapid changes in metabolism indicated by the clinical condition of the patient suggest an upset in the rate of utilisation of easily catabolised substances such as carbohydrate. Obviously the initial step must be an investigation of blood sugar levels, although these values by themselves will not give a true reflection of the rate of carbohydrate metabolism. Changes in blood sugar levels during shock were reported as long ago as 1877 by Claude Bernard and more recently a similar investigation has been made by Beecher (1949). There is however no report of a similar study having been made in cases of shock complicating pregnancy.

Sugar

Method - The tungstate method of Herbert and Bourne (1930) was employed.

Patients were chosen carefully with regard to their clinical condition and specimens for estimation were withdrawn before therapy was commenced. It has been found that transfusion even of ordinary saline, alters the blood sugar values considerably and that there is some relationship between the levels of blood

sodium chloride and blood sugar (Kerpel-Fronius, 1937; Bauduin et al, 1936). Dr. Robin Murdoch (personal communication) is engaged in an extensive investigation of blood sugar levels in shock and as his results agree closely with my own it was felt that the investigation of any large series was unjustified. Nevertheless the blood sugar levels in ten patients were investigated partly for personal satisfaction, but also because further investigations of certain aspects of carbohydrate metabolism were carried out in a number of these individuals.

Results

The blood sugar levels in these 10 patients during the shock phase are shown in Table 15.

The average level of blood sugar in the 10 cases during the phase of shock was 182.7 mg.%. There is then a definite rise in the blood sugar levels well above normal limits in these cases during the phase of shock. The rise occurs rapidly; case 62 exemplifies this. It may be maintained for a considerable time as in case 7, but of course, with the present small series it is impossible to correlate the figures on a definite time basis.

Table 15.

Blood Sugar levels during Shock.

Case No.	Condition	Blood Sugar level during shock.	Duration of shock when sugar estimations were made
62	Caes. Sect.	260 mg.%	1 hour
50	Acc. Haem.	144 "	4 "
24	P.P.H.:P.E.T.	212 "	1½ "
55	Abortion	230 "	3 "
12	P.P.H.	126 "	3½ "
66	Placenta praevia	146 "	2½ "
5	P.P.H.	140 "	1½ "
7	P.P.H.	204 "	7 "
70	Ruptured Uterus	167 "	3 "
44	P.P.H.	198 "	1 "

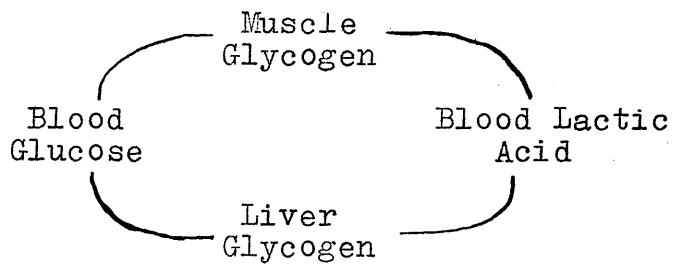
P.P.H. - Post-partum haemorrhage: P.E.T. - Pre-eclamptic toxaemia: Caes. Sect. - Caesarean Section.

One factor which always causes difficulty in assessment is the degree of shock and a more detailed investigation would be necessary to determine the various factors involved in the production of hyperglycaemia in shock. It is sufficient, however, for our purpose at the present moment to establish hyperglycaemia as a definite sequel to haemorrhagic shock in pregnancy.

A similar hyperglycaemia has been reported in relation to shock occurring in non-pregnant individuals but the mechanism of its production and the metabolic process in operation still remain obscure. The level of any particular substance in the blood does not necessarily give any indication of the process underlying its appearance. The increase in the blood glucose may be interpreted in one of several ways. For instance it may be the result of an increased demand coupled with increased utilisation. On the other hand the increase may be a result of diminished utilisation or increased demand coupled with difficulty in utilisation.

From this it is obvious that one of the main questions is that of utilisation and we must therefore try to determine whether the substance is actually being metabolised and to what extent. In the case of carbohydrate it is known that a definite metabolic cycle occurs. This was originally described by Cori and Cori (1927). According to this theory there is a breakdown of glycogen in muscles to form lactic acid which is resynthesised in the liver to glycogen. This liver glycogen is in turn converted to glucose which passes into the blood stream and is subsequently

reconverted to glycogen in the muscles. The cycle is shown graphically below:-



This, however, is an oversimplification of the processes involved in carbohydrate metabolism. There appear to be many intermediate products in the process of carbohydrate metabolism and two of these are known to be pyruvic and lactic acids. Pyruvic acid occupies a position about midway in the chain of reactions necessary before carbohydrate is finally broken down to carbon dioxide and water. Lactic acid is produced at a later phase but it appears to be rapidly reduced under normal conditions. Under conditions of oxygen lack, however, the chain of reactions occuring in the latter half of the degradation process tend to be hindered and the intermediate products accumulate in the blood. It was therefore considered that a study of these intermediate products would give some indication

of the rate and extent of carbohydrate metabolism.

Pyruvic Acid

Method - The method of Friedemann and Haugen (1943) was employed using 2,4-dinitrophenylhydrazine as indicator.

The pyruvic acid levels were estimated in a total of 28 cases during the phase of shock and prior to any treatment. Unfortunately, for clinical and administrative reasons, it was not possible to determine the levels in all cases on subsequent days but values were obtained for 11 cases on the 2nd day, 5 cases on the 3rd day, 7 cases on the 4th day and 9 cases on the 6th day. The values obtained are shown in Table 16.

In order to compare these results with normal values a series of 10 control cases late in pregnancy, in labour, or recently delivered was selected and the pyruvic acid estimated (Table 17).

The range of pyruvic acid in this control series is 1.23 mg.% - 2.88 mg.% with a mean of 1.74 mg.% Kaser and Markees (1949) found the level of pyruvic acid in normal non-pregnant patients to be 0.4-0.9 mg.%. In normal pregnancy the values were 0.8-1.8mg.% with

Table 16.

Showing pyruvic acid levels at various stages during and after shock.

Case No.	Hours of Shock	Condition	Pyruvic Acid Levels: During Shock mg.%	2nd day mg.%	3rd day mg.%	4th day mg.%	6th day mg.%
Toxaemic — Average during shock 3.0 mg.%							
42	?	*Acc.Haem.	3.60	3.68	–	–	–
50	4	*Acc.Haem.	3.58	–	–	–	2.17
26	4	*Acc.Haem.	2.14	3.77	–	1.70	–
25	4	*Acc.Haem.	2.59	–	–	–	1.50
43	3	*Acc.Haem.	2.22	–	–	1.87	–
68	3	*Acc.Haem.	2.24	–	–	–	0.66
35	½	*P.E.T.: Dystocia	2.16	–	–	0.98	–
52	2	*Acc.Haem.	2.46	0.96	–	–	–
47	5	*Acc.Haem.	7.11	–	–	–	–
45	5	*Acc.Haem.	2.06	1.36	0.90	2.42	–
Non-toxaemic — Average during shock – 2.19 mg.%							
10	2	P.P.H.	1.42	1.33	–	–	–
55	3	Abortion	1.52	–	–	–	0.74
70	3	Ruptured Uterus	3.96	0.96	–	–	–
37	3	P.P.H.	2.22	–	–	–	0.82
36	2½	P.P.H.	1.36	–	–	–	0.64
67	3	P.P.H.	6.08	6.88	–	–	–
29	3	P.P.H.	2.42	–	–	–	–
57	4	Ruptured Uterus	3.60	–	–	–	–
7	7	P.P.H.	1.88	–	–	0.56	0.64
28	5	Caesarean Hysterectomy	1.66	4.60	–	3.93	3.85
51	6	P.P.H.	1.32	1.18	–	–	–
8	3	Abortion	1.94	–	–	–	–
48	3	P.P.H.	2.92	0.84	3.28	–	1.38
9	3½	Caes. Sect.	1.44	1.24	1.04	1.80	–
56	?	Abortion	1.80	–	1.08	–	–
59	1	Placenta Praevia	1.62	0.86	–	–	–
71	?	P.P.H.	1.40	–	1.13	–	–
44	1	P.P.H.	1.38	–	–	–	–

* Cases complicated by hypertensive toxaemia.

P.P.H. - Post-partum haemorrhage: Acc.Haem. - Accidental haemorrhage: P.E.T. - Pre-eclamptic toxaemia: Caes.Sect. - Caesarean Section.

Table 17.

Pyruvic acid in normal pregnancy, labour, or post-partum.

Stage of Pregnancy	Pyruvic Acid Level
40/52	1.75 mg.%
31/52	1.75 "
40/52	1.45 "
38/52	1.90 "
40/52	1.23 "
1 hour post-partum	2.26 "
Early in labour	1.62 "
2nd stage labour	2.88 "
37/52	1.25 "
40/52	1.38 "

an average of 1.35 mg.% while the parturition values were 0.8 mg.%-2.2 mg.% with a mean of 1.32 mg.%. Our normal values in pregnancy are slightly higher than those found by the above workers. The average value of pyruvic acid in all the cases during the shock phase was 2.48 mg.% with a range of 1.36-7.11mg.%, showing that there is a rise in the level of pyruvic acid in the blood during this phase.

For purposes of comparison the average of the

cases on any particular subsequent day was related to the average value for these same cases during the shock phase. On the day following shock the average level of pyruvates in 12 cases was 2.30 mg.% while the average for these 12 cases during the shock phase was 2.51 mg.%. On the 3rd day the average value for 5 cases was 1.48 mg.%compared to 1.92 mg.% in the shock phase. On the 4th day the average value in 7 cases was 1.89 mg.% compared with 1.94 mg.% in the shock phase and on the 6th day the average value in 9 cases was 1.36 mg.% compared to 2.16 mg.% on the 1st day. The percentage variation is noted in Table 18 and is also shown in graphic form. (Graph 1).

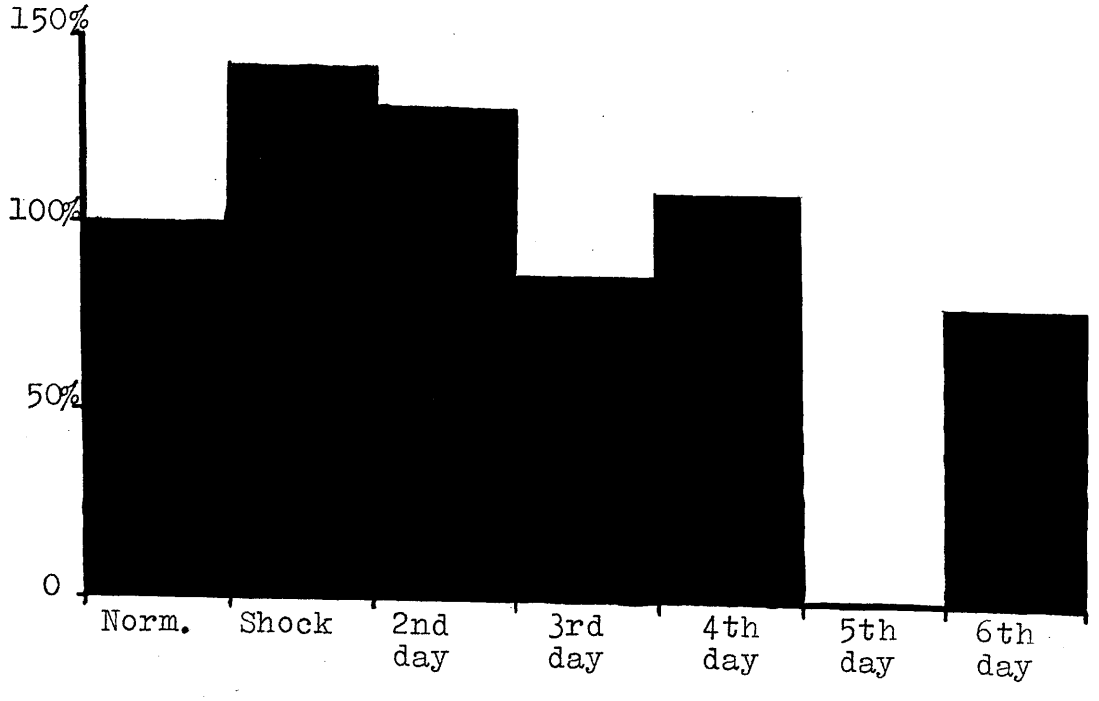
In 2 cases (Nos.9 and 29) the pyruvate values were available for the shock phase and for 3 subsequent days and the curve presented by these individual cases approximates to that shown in Graph 1 (see Graph 2), but the changes were even more dramatic.

There is a decided rise in pyruvic acid levels in the shock phase. This increase is not maintained on the day following shock but the levels are, nevertheless, still above the normal value. On the

Graph 1.

Pyruvate values shown as a percentage, the average normal (1.74 mg.%) representing 100%.

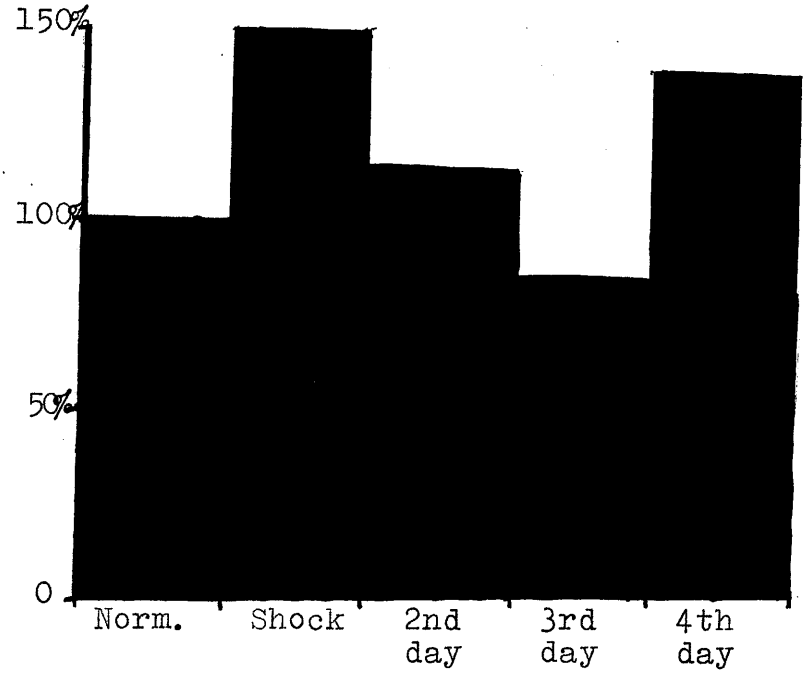
Normal - 100% (1.74)
Shock - 142% (2.48)
2nd day - 132.2% (2.30)
3rd day - 85% (1.48)
4th day - 108.6% (1.89)
6th day - 78.1% (1.36)



Graph 2.

Pyruvate values of Cases 9 and 29 shown as a percentage, the average normal (1.74 mg.%) representing 100%.

Normal - 100% (1.74)
Shock - 150% (2.62)
2nd day - 112% (1.95)
3rd day - 83% (1.45)
4th day - 138% (2.41)



3rd day the values fall to within normal limits but on the 4th day thereis again a definite rise above the normal value. Unfortunately no estimations were made on the 5th day, but on the 6th day the levels were again back to normal.

Table 18.

	Average Pyruvic Acid Level	Average level during Shock phase	Percentage fall in Pyruvic Acid
2nd day	2.30 mg.%	2.51 mg.%	8.8%
3rd day	1.48 "	1.92 "	22.8%
4th day	1.89 "	1.94 "	2.5%
6th day	1.36 "	2.16 "	37%

It was thought that a comparison of the levels of pyruvic acid in toxaemic and non-toxaemic cases would be of interest in view of the difference in the levels of the nitrogenous constituents of the blood in these two types of cases. The values of pyruvic acid in the 10 toxaemic cases ranged from 2.14 mg.% to 7.11 mg.% with an average of 3.0 mg.% while in the 18 non-toxaemic cases the range was 1.16 mg.% - 6.08 mg.% with a mean of 2.19 mg.% (Table 16). The values of pyruvic acid in the toxaemic cases with shock are therefore higher than in the non-toxaemic cases.

It is of interest to note here that Kaser and Markees (1949) did not find any significant difference in the levels of pyruvic acid in toxaemic and non-toxaemic pregnant patients; the values being 0.8 mg.% - 1.8 mg.% with a mean of 1.35 mg.% in non-toxaemic while in the toxaemic group the range was 0.7 mg.% - 2.66 mg.% with a mean of 1.25 mg.%. These workers did, however, find a significant rise in pyruvic acid levels in eclampsia; the range being 2.38 mg.% - 6.1 mg.% with a mean of 3.75 mg.%½

Commentary

A comparable rise in pyruvic acid levels to that which we found in our series has been observed in animals subjected to haemorrhage by Russell and his co-workers (1943) and Root et al (1947) and also in non-pregnant humans by Cannon (1917), Guthrie (1918), Penfield (1919) and Cournand et al (1943). So far as we are aware a comparable study has not been made in pregnancy.

The rise is dramatic and would seem to indicate a definite upset in carbohydrate metabolism. Superficially the accumulation of pyruvic acid might indicate an increased utilisation of carbohydrate,

but equally so, as in the case of hyperglycaemia, there may be a deficient utilisation of carbohydrate with an inability on the part of the glucose breakdown products to go beyond the pyruvate stage except with difficulty.

It is obvious therefore that this study of pyruvates does not provide a complete answer to our problem in regard to the utilisation of carbohydrate. The results merely allow us to state that the process of metabolism is not halted although it may be considerably altered. Many interesting points arise regarding the behaviour of pyruvates in the period subsequent to the shock phase but these will be considered in a later part of the main discussion.

As previously stated this rise in glucose and pyruvates may be associated with increased or decreased utilisation of carbohydrate. In either case it might reasonably be expected that the fundamental change would be reflected in the behaviour of phosphorus during and following the phase of shock in the light of recent theories of phosphorylation (De Witt Stetten, 1949).

Phosphorus Metabolism.

Without going into great detail the place of phosphorus in carbohydrate metabolism may be stated as follows:-

Glucose is linked with high energy phosphate compounds and during metabolism energy is liberated by the breaking of these linkages. Associated with the utilisation of glucose there is a certain expenditure of phosphorus which is excreted as inorganic phosphate. The latter provides an indirect measure of the rate of glucose utilisation.

Inorganic Phosphates.

Method - The phosphomolybdic acid method of Briggs (1922) was employed.

The inorganic phosphates were estimated in 12 cases during the shock phase and in 4 cases on the subsequent day. The results are shown in Table 19.

There is a wide range of inorganic phosphate levels during shock - from 2.4 mg.% - 8 mg.% with an average of 4.0 mg.%.

Unfortunately no values for inorganic phosphates were obtained from these cases before the onset of shock. A series of 10 normal cases near term was

therefore selected and the phosphate values estimated. The results are shown in Table 20.

Table 19.

Case No.	Condition	Inorganic Phosphates During Shock mg.%	Inorganic Phosphates 2nd day mg%	Duration of Shock when estimations made	
50	*Acc.Haem.	8.0	-	4 hours	Toxaemic
22	*Acc.Haem.	3.1	5.7	3 "	
47	*Acc.Haem.	3.0	-	5 "	Average
46	*Acc.Haem.	8.0	-	4 "	5.12 mg.%
45	*Acc.Haem.	3.5	4.4	5 "	
9	Caes.Sect.	2.4	2.4	3½ "	
57	Ruptured Uterus	4.3	-	4 "	Non-Toxaemic
56	Abortion	2.6	-	?	
44	P.P.H.	2.8	-	1 "	Average
58	P.P.H.	2.9	-	1 "	3.17 mg.%
39	P.P.H.	3.6	4.4	5 "	
72	Ruptured Uterus	3.6	3.8	6 "	

* Cases considered to have hypertensive toxaemia.

P.P.H. - Post-partum haemorrhage: Caes.Sect. - Caesarean Section: Acc.Haem. - Accidental Haemorrhage.

The range of values in these normal patients is 2.3 mg.% - 3.6 mg.% with a mean of 3.0 mg.%. These values are higher than the ones found by Krebs and

Briggs (1923). Their range of values was 1.08 mg.% - 3.3 mg.% with an average of 2.73 mg.% but the estimations were made at different stages of pregnancy.

Table 20.

Inorganic phosphate values in blood of normal pregnant patients near term.

Inorganic Phosphates
3.4 mg.%
3.6 "
2.3 "
3.2 "
3.6 "
2.9 "
2.8 "
2.3 "
3.3 "
2.6 "

The values of phosphates in the shock patients is at or above our upper limit of normal (3.6 mg.%) in 5 instances. In no case was the value below the lower limit of normal (2.3 mg.%) although 4 cases had values below the average normal value of 3.0 mg.%. In all cases except one the values rose on the second day above the upper limit of normality. In this exceptional case the value remained unaltered near the lower limit of normality.

It is difficult to estimate accurately the duration of shock but approximate times were noted in our series. When these times are related to the values of inorganic phosphates there is some correlation. In general terms shock is present for 4 hours or more before the value of inorganic phosphate rises above the average normal value. It would seem that the inorganic phosphate level of the blood does not rise until shock has been present for some time and furthermore the inorganic phosphate level continues to rise slightly on the day after shock.

This increase in blood phosphate might indicate increased glucose utilisation but the effect of anuria in these cases must be taken into consideration. Increase of inorganic phosphate in the blood in cases of chronic nephritis is, like retention of urea and creatinine, a sign of failure of renal function (Peters and Van Slyke, 1931). The delayed rise in the inorganic phosphates supports the view that the rise is due to renal dysfunction. Whether the rise is entirely due to renal upset or is in part due to altered phosphorylation could not be determined

directly but the expected rise in phosphates due to anuria was calculated thus:-

The normal amount of phosphates in the urins is 0.2 gm.per 100 cc. (Best and Taylor, 1950) and the normal output of urine is 1500 cc. per day. In 24 hours 3 gms. of phosphates will be excreted by the normal person. This may be expressed as 125 mg.per hour. The blood volume is about 78 cc.per Kg.of body weight (Best and Taylor, 1950). In a patient weighing 60 Kg.the blood volume will, therefore, be about 4680 cc., while in a patient weighing 80 Kg.the blood volume will be 6240 cc. If there is anuria a rise of $\frac{12500}{4680}$ mg./100 cc. or 2.67 mg.% would be expected in a woman weighing 60 Kg. in one hour while in a woman weighing 80 Kg. the expected rise would be 2.0 mg.% per hour. This is assuming that phosphorylation is occurring normally.

Unfortunately no estimations of blood phosphates prior to shock were made in any of the present series of cases but estimations of blood phosphate made in normal pregnant patients gave an average of 3 mg.% which will, therefore, be assumed as the pre-shock level of the blood phosphates. On this basis the

expected rise in phosphates due to anuria has been calculated and compared with the actual rise (Table 20).

Table 20.

To show actual and calculated rises in phosphates in blood of patients in shock taking 3 mg.% as assumed pre-shock level.

Case No.	Condition	Duration of shock when estimations made.	Actual level of Phos-phates	Calculated level of phosphates	
				60 Kg.	80 Kg.
			mg.%	mg.%	mg.%
50	Acc.Haem.	4 hours	8.0	13.68	11.00
22	Acc.Haem.	3 "	3.1	11.01	8.00
9	Caes.Sect.	3½ "	2.4	12.34	10.00
57	Ruptured Uterus	4 "	4.3	13.68	11.0
47	Acc.Haem.	5 "	3.0	16.35	13.0
56	Abortion	?	2.6	?	?
44	P.P.H.	1 "	2.8	5.67	5.0
46	Acc.Haem.	4 "	8.0	13.68	11.0
58	P.P.H.	1 "	2.9	5.67	5.0
39	P.P.H.	5 "	3.6	16.35	13.0
45	Acc.Haem.	5 "	3.5	16.35	13.0
72	Ruptured Uterus	6 "	3.6	19.02	15.0

P.P.H. - Post-partum haemorrhage: Acc.Haem. - Accidental haemorrhage: Caes.Sect. - Caesarean Section.

The rise in inorganic phosphates in the blood of all the patients in shock is less than can be

accounted for by anuria.

It was considered that it would be interesting to compare the inorganic phosphate values in toxaemic and non-toxaemic cases as was done with the pyruvic acid values. There were 5 toxaemic cases (Table 19) with values ranging from 3.0 mg.% - 8.0 mg.% and a mean of 5.12 mg.%. The range of values in the 7 non-toxaemic cases was 2.4 mg.% - 4.3 mg.% with an average of 3.17 mg.%. From these figures it would appear that there is either a greater rise of inorganic phosphates in cases of pre-eclamptic toxaemia than in non-toxaemic cases or the initial level of phosphates before shock is higher in the toxaemic group. The rise in phosphates in all cases is nevertheless, smaller than could be accounted for by anuria. It is of interest to note that Mukherjee and Govan (1950) found that the phosphate in tissue fluid was increased in pre-eclampsia and they suggest that this is related to an upset in tissue carbohydrate metabolism.

Consideration of carbohydrate metabolism.

Our main problem in these cases is in relation to the mode of utilisation of the glucose which has been mobilised in the shock phase. It has been shown

that in the shock phase there is an increase in blood pyruvates. This of itself indicates that glucose is being metabolised, partially at least. According to current theories glucose passes through a long series of reactions during which it is degraded to pyruvic acid, lactic acid and finally to carbon dioxide and water. In the successive steps phosphates play an important role and it has been determined that the phosphates follow a cycle in which the various compounds fall into one or other of two main groups, known as "high-energy" and "low-energy" phosphates respectively. At any particular step in breakdown of glucose it is found that the carbohydrate moiety is linked with a "high-energy" phosphate which during the breakdown process is converted to "low-energy" phosphate with the liberation of energy. This "low-energy" phosphate under normal circumstances is subsequently transformed into "high-energy" phosphate ready to play a further part in carbohydrate breakdown. Energy is released as all these reactions occur, but De Witt Stetten (1949) states that the yield of energy as glucose is converted to pyruvates is far less than the yield obtained when pyruvic acid is further degraded

to carbon dioxide.and water.

The marked rise in blood glucose together with the increase in pyruvates indicates that carbohydrates are being metabolised and one would naturally expect a release of large amounts of energy if the metabolism is complete. It is obvious however from the clinical appearance of the patient that this is a quite unwarranted conclusion, a fact which is substantiated by the results of a study of blood phosphates. During the metabolism of carbohydrates some of the phosphate is inevitably utilised and is eventually excreted in the form of inorganic phosphates. The values for blood phosphates will naturally reflect to some extent at least the rate of carbohydrate metabolism. Our studies showed that a rise in blood phosphates occurred during the shock phase and this agrees with the findings of other workers in relation to experimental shock produced by trauma or haemorrhage. (Beal et al., 1941; Blalock and Duncan, 1942; Duncan, 1942; Bywaters and Popjack, 1942; McShan et al, 1945; Mylon and Winternitz, 1945; Darmady, 1946-47, and Root et al., 1947).

This increase in inorganic phosphates of the blood

would at first sight suggest that there was an increase in the rate of phosphorylation and therefore an increased catabolism of carbohydrate. The result of such a state of affairs would be a sudden and excessive production of energy, which in the present circumstances is obviously impossible. Some explanation other than increased carbohydrate metabolism must therefore be found for the rise in blood phosphate. In the case of traumatic shock the rise may be due to liberation of phosphates from injured muscle but this, obviously, cannot be the explanation in haemorrhagic shock.

As has been shown from a consideration of maximal and minimal values the increase in blood phosphates is entirely accounted for by the oliguria existing during the phase of shock. Indeed the increase is less than could be expected if the rate of phosphorylation was the same as that found in the normal human subject, and much less than might be expected in view of the high blood glucose levels in these patients.

On this basis our findings suggest that glucose may be metabolised but the process is far from complete

and the clinical condition of the patient certainly indicates that this is so. This in turn may account for the high blood pyruvate values. The cause of this failure to complete the metabolism of carbohydrate is obscure. It may be that there is insufficient high energy phosphate to complete the phosphorylation process. It is however, difficult to see how a purely chemical process can explain all the findings and even if there is a change in the values of one or other of the chemical substances such changes are only a reflection of more vital underlying processes which control these chemical reactions. The majority of chemical reactions in the body are completed under the influence of enzymes or catalysts and it is in these vital substances that we feel the solution to our problem must lie. Three principal enzymes have so far been recognised in relation to the metabolism of carbohydrate. These are phosphorylase, hexokinase and isomerase. Many others exist however and the close linkage between this metabolic process and the vitamins of the B group add to the complexity of the problem. It is probable, however, that since the metabolic upset is a general one affecting the whole body, the defect

will be related to the function of one or other of the main organs associated with carbohydrate metabolism and this hypothesis will be considered in a later part of the thesis.

There are various possible sources of the excess blood glucose and although this question is probably not of as great importance as that of the actual utilisation of the glucose produced the answer may nevertheless give some indication of the initial reaction phenomena occurring in shock.

The ultimate source and mode of production of the extra blood glucose are obscure. Although our data will not allow us to provide a definite answer to this question a correlation of the various findings does suggest certain possibilities which seem worthy of further consideration.

Four facts may be taken into consideration. In these cases there is a hyperglycaemia, increased blood pyruvic acid, an initial increase in nitrogenous constituents and a relative diminution of phosphates. The direct source of the increased blood glucose is liver glycogen (Cori and Cori, 1927). Dietary glucose may be ruled out in these cases and therefore

two sources of this glycogen are possible. Normally it is mainly derived from muscle glycogen which is broken down to lactic acid and transported to the liver. It may, however, be formed by a process of gluconeogenesis or transamination of amino acids in the liver (Best and Taylor, 1950). According to Riegel (1927), Gesell et al (1930), Swan (1943), Gutmann et al (1941), Cournand et al (1943) and Beatty (1945), in shock the blood contains large amounts of lactic acid and we have shown that there is a 42 per cent. increase in blood pyruvates. We have also shown that there is a marked increase in the nitrogenous constituents of the blood including a mobilisation of amino acids. Superficially, at least, these findings would support arguments in favour of both muscle glycogen and amino acids as the possible sources of liver glycogen in these cases. We have already indicated that the increase in blood pyruvates may be the result of incomplete carbohydrate metabolism. In view of the clinical condition of the patient, however, we are inclined to think that the rise in blood pyruvates cannot be fully explained by this, and much of the increase is probably related to

the attempt to provide liver glycogen from muscle. This is also suggested by the marked relative diminution of blood inorganic phosphorus. We also feel that the protein breakdown is brought about for a similar purpose. It is apparent from the rise in blood glucose that liver glycogen is being rapidly mobilised and one would therefore expect that it would be equally rapidly replenished from the sources already indicated. In these circumstances one would not expect substances such as pyruvic acid and amino acids to accumulate in the blood. We are therefore forced to conclude that soon after the initiation of the shock phase there is a diminution in the ability of the liver to utilise these substances.

Even more interesting than the slow fall of pyruvates to normal is the sudden rise on the 4th day of the puerperium. This cannot be due to a sudden failure of either liver function or carbohydrate metabolism since the patient has an uninterrupted recovery, and it is difficult to conceive that it is related to shock at all. On seeking for some reasonable explanation for this change in pyruvic acid levels one cannot but be impressed by the fact that at this time

in the puerperium the secretion of true milk begins. A large amount of lactate is required in the production of true milk. In view of the close relationship between pyruvic and lactic acids in the carbohydrate cycle it seems reasonable to assume that the rise in blood pyruvic acid is closely related to the secretion of true milk.

To summarise our findings so far we have shown that there is an excessive outpouring of glucose into the blood stream. This is undoubtedly due to a demand for glucose on the part of the body as several processes are set in motion to attain this hyperglycaemia. It occurs so rapidly and is such a constant feature one must conclude that it is not just a passive liberation of glucose from the liver.

The inability of the body to utilise glucose continues after apparent clinical recovery from shock but returns to normal about the 3rd day after although there is again a rise in the pyruvic acid levels on the 4th day which is possibly related to lactation.

The above-mentioned changes in nitrogen and carbohydrate metabolism occurring in haemorrhagic shock in pregnant patients are paralleled by changes observed

in non-pregnant patients suffering from shock due to trauma by Bernard (1877), Lurge (1936), Cuthbertson (1942), Cournand et al (1943), Engel et al (1944), McShan et al (1945), Allison et al (1947), Beecher (1947), and Root et al (1947). So far as metabolic changes are concerned the effect is the same whether shock is produced by trauma or haemorrhage. It has been argued by some (Coonse et al, 1935 and Moon, 1938) that haemorrhage and shock are different entities in spite of the similarity of the metabolic changes. Other important changes observed in traumatic shock are those concerned with electrolytes. Changes in sodium and potassium levels have been noted in traumatic shock in non-pregnant patients by several workers (Gutmann et al, 1941; Clarke and Cleghorn, 1942; Manery and Solandt, 1943; Winkler and Hoff, 1943; Beecher, 1947; McIntosh et al, 1930; and Wilson et al 1938). If similar changes can be demonstrated in pregnant patients with shock due to haemorrhage this will strengthen the view that haemorrhage does produce shock.

Acidosis is a well marked feature of all types of shock but the behaviour of the base ions has

received less attention and a study of the possible changes and relationship to the acidosis would appear profitable. A further reason for undertaking a study of the electrolytes is the likelihood of alterations occurring in their values due to altered function of the adrenal cortex which possibly occurs in shock.

An investigation of electrolytes in pregnant patients with collapse due to haemorrhage was therefore carried out. This investigation will be discussed before considering the liver function in shock as the electrolyte changes may reflect some changes in liver function.

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ELECTROLYTE CHANGES IN SHOCK.

The main electrolytes present in the body are sodium and potassium and any change occurring in electrolyte balance will be reflected by changes in these substances. At the same time, in view of the intimate relationship between these ions and chlorides in the maintenance of electrolyte balance, the levels of chlorides in the blood were also estimated. This study of electrolyte balance may also be of importance in relation to the onset of shock in these cases as Marriott (1947) has shown that a clinical picture similar to that of shock can occur in patients suffering from dehydration.

Methods

Sodium - King's (1947) modification of Noyons's (1939) method using zinc uranyl acetate was employed; the readings being made in the photo-electric colorimeter.

Potassium - King's (1947) adaptation of Jacob's and Hoffman's (1931) method using sodium cobalti-nitrite agent was employed; the readings being made in the photo-electric colorimeter.

Chlorides - The method of Schales and Schales

(1941) was employed. Titrations were made with mercuric nitrate and diphenylcarbasone was used as indicator.

PLASMA SODIUM

Thirty-five cases were studied in this investigation. In four of these it was possible to obtain values before the onset of shock. All were investigated during the shock phase prior to treatment. Subsequently estimations were carried out on 11 cases after blood transfusion, 16 cases on the day following the incident (i.e. day 2), 6 cases on the 3rd day, and 10 cases on the 4th day. The results are shown in Table 21.

The range of plasma sodium in the 4 cases before shock is 335 mg.% to 368 mg.% with an average of 348.5 mg.%. Although this average value is in accordance with the accepted limits of normal which are given as 325 mg.% to 350 mg.% (King, 1947, and Best and Taylor, 1950), the values were high in 2 of the cases (Nos.12 and 73). Both of these cases had pre-eclamptic toxaemia and further mention of this will be made in the discussion.

A study of the average values during and

Table 21.

To show levels of plasma sodium at various stages, before, during and after shock.

Case No.	Condition	Before Shock	Before Transfn	After Transfn.	2nd day	3rd day	4th day
Toxaemic - Average during shock - 317 mg.%							
53	*Acc.haem.		319 mg.%	327 mg.%			
42	*Acc.Haem.		321 "		333mg%		
50	*Acc.haem.		319 "		326 "		
26	*Acc.haem.		327 "		333 "	327mg%	
25	*Acc.haem.		321 "			327 "	
24	*P.E.T.:P.P.H.		347 "	315 "	347 "		347mg%
23	*Acc.haem.		300 "		311 "		
43	*Acc.Haem.		325 "		330 "		330 "
68	*Acc.haem.		312 "				
49	*Acc.haem.		284 "		324 "	327 "	320 "
21	*Acc.haem.		348 "		377 "		
12	*P.E.T.:P.P.H.	350mg%	310 "	306 "			345 "
73	*P.E.T.: Dystocia	368 "	325 "				350 "
35	*P.E.T.; Dystocia		300 "				306 "
52	*Acc.haem.		327 "		306 "		
47	*Acc.haem.		300 "				
45	*Acc.haem.		306 "	306 "	306 "		
Non-toxaemic - Average during shock - 306.5 mg.%							
41	P.P.H.		330 "		333 "		
55	Abortion		329 "				
17	P.P.H.		350 "	335 "	335 "	335 "	
3	Caes.Sect.	341.5"	290 "	327 "			345 "
4	Caes.Sect.	335 "	300 "	293 "			320 "
65	P.P.H.		198 "	260 "			320 "
37	P.P.H.		321 "				
36	P.P.H.		307 "				
63	P.P.H.		326 "		319 "		
67	P.P.H.		300 "				
29	P.P.H.		306 "				
57	Ruptured Uterus		300 "				
7	P.P.H.		339 "				300 "
51	P.P.H.		306 "	312 "	315 "		
8	Abortion		327 "	321 "			
48	P.P.H.		300 "			321 "	
53	Caes.Sect.		306 "		312 "	312 "	
72	Ruptured Uterus		282 "	345 "	303 "		

*Denotes hypertension preceeding shock.
P.P.H. - Post-partum haemorrhage: Acc.haem. - Accidental haemorrhage: P.E.T. - Pre-eclamptic toxaemia: Caes.Sect. - Caesarean Section.with haemorrhage.

following recovery from shock shows that there is a cyclical variation in the sodium values. This is shown graphically in Figure 3.

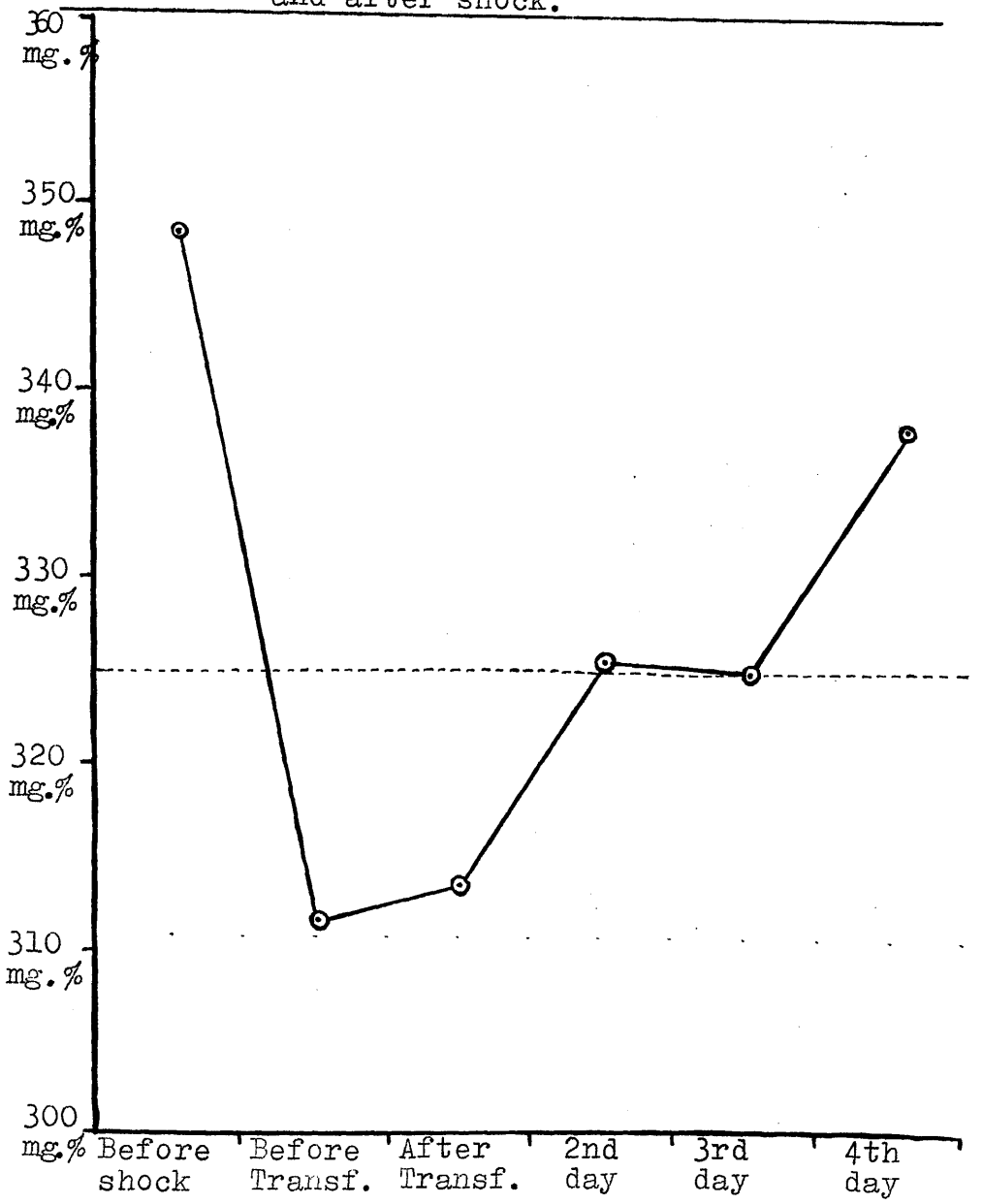
It can be seen that there is a tendency for the blood sodium level to fall during shock.

A retention of sodium has been shown to occur in patients with pre-eclamptic toxaemia (Nordenstrahl, 1952). As this may be the reason for the higher levels of sodium in some of the patients the cases have been divided into those in whom pre-eclamptic toxaemia was presumed to be present before shock ensued and those without toxaemia (Table 21). There were 17 presumed toxaemic and 18 non-toxaemic cases. The average serum sodium in the toxaemic group was 317 mg.% while in the non-toxaemic group the average was 306.5 mg.%.

The average level of plasma sodium is therefore greater in the toxaemic group during shock than in the non-toxaemic group. This may be due to higher

Figure 3.

Showing average values of sodium before, during and after shock.



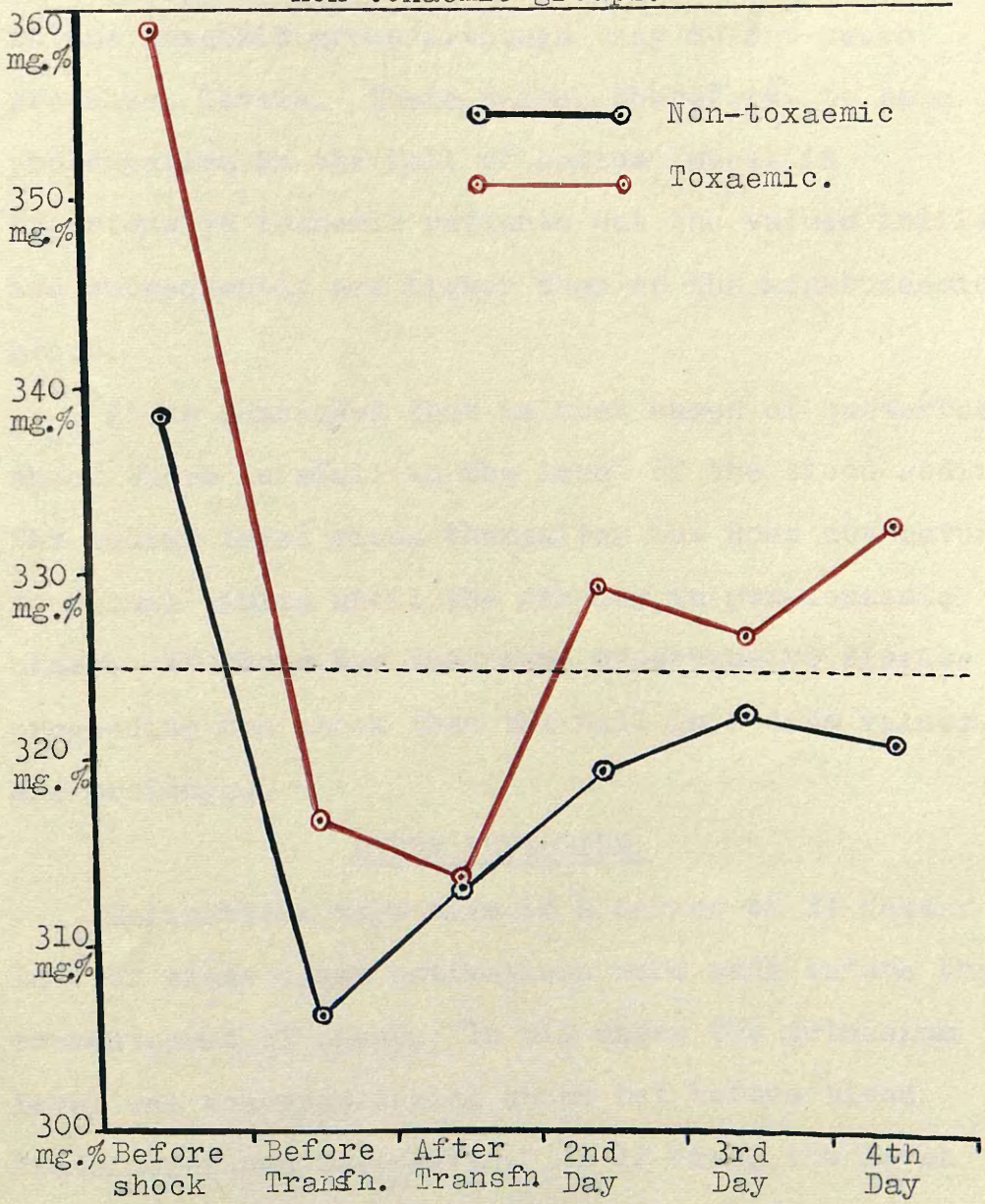
pre-shock levels in the toxaemic group. The pre-shock value of sodium was estimated in only 2 cases of pre-eclampsia (Table 21) and the average value was 359 mg.%. This is much higher than the average value in the 2 non-toxaemic cases which was 338.2 mg.% (Table 21). The number of cases is too small to be conclusive but these results agree with those reported by other observers. A comparison of the levels of the plasma sodium in the various phases was first made in the non-toxaemic group as it was considered that this would give a clearer picture of the subsequent progress of the sodium levels after shock. The comparison of the values in the non-toxaemic group is shown in Figure 4.

When the levels of the non-toxaemic group in Figure 4 are compared with those in Figure 3 it is seen that there is a fairly close correlation. Further analysis, however, shows that the sodium values remain below the lower limit of normal until the 4th Day.

A similar study of the toxaemic patients shows that the fall in sodium values is prolonged after transfusion whereas in the non-toxaemic cases the

Figure 4.

Showing average values of sodium in toxaemic and non-toxaemic groups.



sodium level has begun to rise again (See Figure 4). The values, however, on subsequent days are higher in the toxaemic group although they do not reach pre-shock levels. There tends, therefore, to be a prolongation in the fall of sodium levels in hypertensive toxaemic patients but the values initially and subsequently are higher than in the non-toxaemic group.

It is concluded that in most cases of haemorrhagic shock there is a fall in the level of the blood sodium. The sodium level rises thereafter but does not return to normal limits until the 4th day in non-toxaemic cases. If there has been some hypertensive disease preceeding the shock then the fall in sodium values are prolonged.

SERUM POTASSIUM.

Estimations were made in a series of 31 cases. In 4 of these cases estimations were made before the commencement of shock. In all cases the potassium level was measured during shock but before blood transfusion had been given. In 12 cases the level was estimated after blood transfusion had been administered; in 16 cases on the 2nd day; in 5 cases on the 3rd day; 9 cases on the 4th day. The results

are shown in Table 22.

Table 22

To show the changes in serum potassium before, during and after shock.

Case No.	Condition	Before Shock	Before Transfn.	After Transfn.	2nd day	3rd day	4th day
Toxaemic - Average during shock - 19.7 mg.%							
53	*Acc.haem.		10.3mg.%	17 mg.%			
42	*Acc.haem.		16.2 "		18.4mg%		
50	*Acc.haem.		18.4 "		14.5 "		
25	*Acc.haem.		17.6 "			19.4mg%	
24	*P.E.T.: P.P.H.		28.0 "	52 "	42.0 "		32mg%
67	*Acc.haem.		16.7 "		17.8 "		
43	*Acc.haem.		20 "		28 "		25 "
49	*Acc.haem.		17.5 "		20.4 "	22.2mg%	24.8 "
21	*Acc.haem.		13.3 "		18 "		
12	*P.E.T.: P.P.H.	18 mg%	21 "	21 "			18 "
73	*P.E.T.: Dystocia	18.5 "	24.3 "				21.0 "
55	*P.E.T.: Forceps		17 "				16 "
52	*Acc.haem.		23.0 "		24.4 "		
47	*Acc.haem.		17.7 "				
45	*Acc.haem.		34.5 "	33.4 "	36.6 "		
Non-Toxaemic - Average during shock - 24.1 mg.%.							
10	P.P.H.		24.4 "	26.7 "	28 "		
41	P.P.H.		22 "		24 "		
55	Abortion		20 "				
17	P.P.H.		21 "	22 "	18 "	20 "	
3	Caes.Sect.	19.7 "	21.4 "	21 "			19.8 "
4	Caes.Sect.	18.4 "	22.0 "	21.6 "			19.2 "
65	P.P.H.		25.6 "	22.8 "			20.2 "
37	P.P.H.		23.0 "				
63	P.P.H.		11.0 "		17.0 "		
29	P.P.H.		25.5 "				
57	Ruptured Uterus		18.8 "				
51	P.P.H.		27.0 "	23.4 "	13.3 "		
8	Abortion		19.4 "	22.2 "			
48	P.P.H.		40.0 "			22.0"	
9	Caes.Sect.		24.4 "		27.3 "	31.0"	
72	Ruptured Uterus		30.0 "	32.0 "	32.0 "		

*Denotes hypertension preceeding shock. P.P.H. - Post-partum haemorrhage: Acc.Haem. - Accidental haemorrhage: P.E.T. - Pre-eclamptic toxaemia: Caes.Sect. - Caesarean Section.

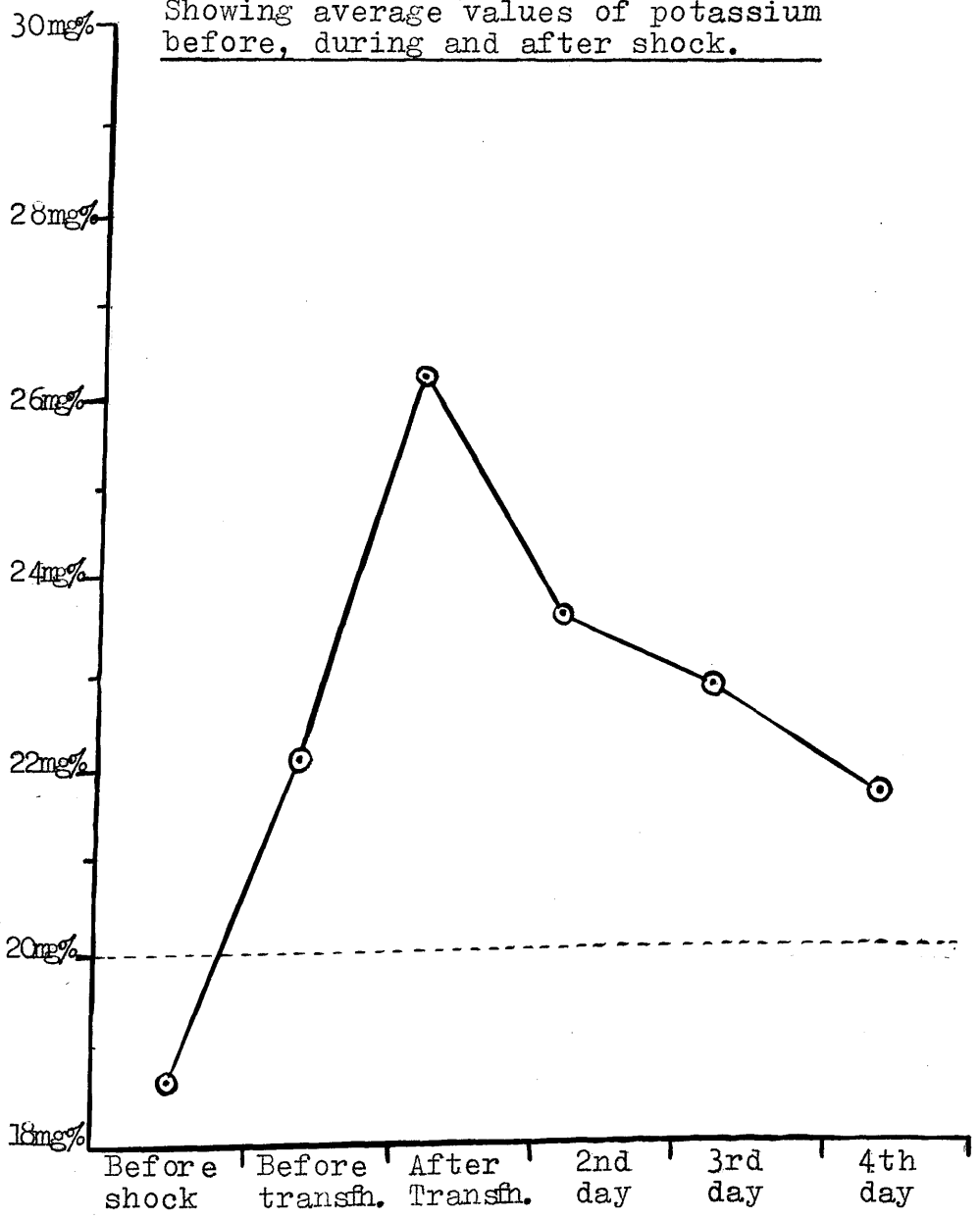
In the 4 cases in which the serum potassium was estimated before the commencement of shock the range was found to be 18 mg.% - 19.7 mg.% with a mean of 18.65 mg.% which is within the accepted limits of normal - 16 to 20 mg.% (King, 1947). During the phase of shock a rise occurred in the levels of potassium in all 4 cases, the average rise being 3.5 mg.%.

The average values of serum potassium are shown graphically (Figure 5) to compare the levels in the various stages before, during, and after recovery from shock.

It can be seen from Figure 5 that there is a definite tendency for the serum potassium levels to rise during shock.

As the plasma sodium values in hypertensive patients were found to differ from those in non-hypertensive cases a comparison of the average values of serum potassium in these two groups has

Figure 5.
Showing average values of potassium before, during and after shock.

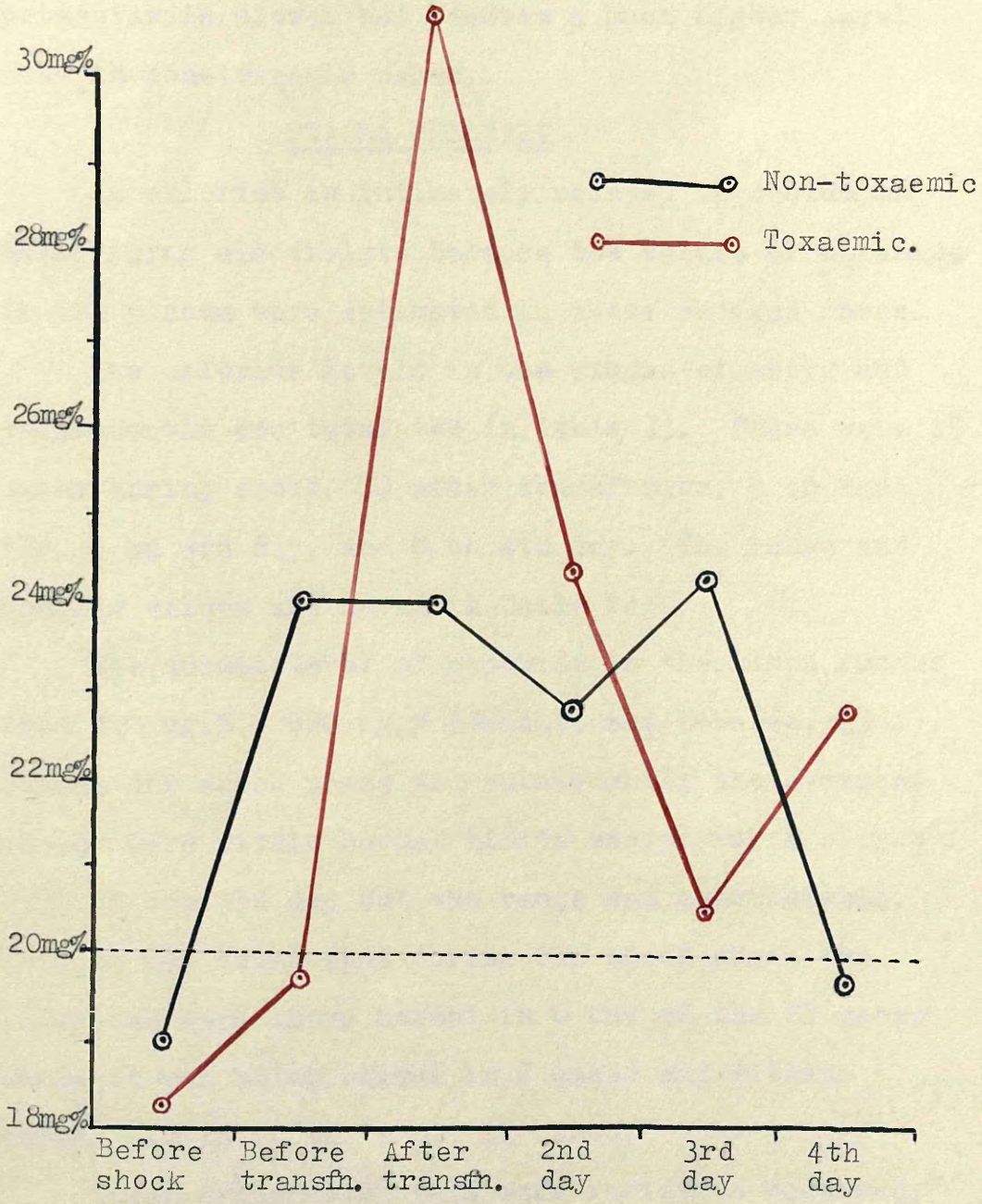


been made (Figure 6). There were 15 hypertensive and 16 non-hypertensive cases in the series (Table 22). The pre-shock levels of potassium were estimated in only 2 hypertensive cases and 2 non-hypertensive cases. All values were within normal limits but the level was slightly lower in the toxaemic cases (18.25 mg.%) as compared with non-toxaemic (19.05 mg.%). This is probably of little significance.

From Figure 6 it can be seen that there is a rise in the level of serum potassium in both groups during shock. In the toxaemic group the rise in potassium is, at first, slower than in the non-toxaemic group but the rise is prolonged and reaches a much higher level after transfusion. The increase in serum potassium is maintained for some time after recovery. In the non-toxaemic group it continues until the 4th day but in the toxaemic patients it falls rapidly and by the 3rd day is practically at a normal level although there is a second rise on the 4th day.

To summarise the findings, there is a rise in the serum potassium during shock. The levels tend to return to normal values about the 4th day after shock. If there has been hypertensive toxaemia the rise in

Figure 6.



Showing average values of potassium in toxaemic and non-toxaemic groups.

potassium is slower but reaches a much higher level than in non-toxaemic cases.

PLASMA CHLORIDE

As chloride is intimately related to sodium in maintaining electrolyte balance the values of chloride in the plasma were estimated in these shocked cases.

The chloride levels in the stages of shock and subsequently are tabulated in Table 23. There were 25 cases during shock, 10 after transfusion, 9 on 2nd day, 6 on 3rd day, and 8 on 4th day. The range and average values are noted in Table 24.

The normal level of chloride in the blood ranges from 560 mg.% - 620 mg.% (Schales and Schales, 1941). During the shock phase and subsequently the average values were within normal limits except for a slight fall on the 3rd day but the range was considerable.

It was found that during the shock phase the chlorides were above normal in 8 out of the 25 cases while it was below normal in 6 cases and within normal limits in the other 11 cases.

After transfusion this same variation occurred. There were 5 cases above normal, 2 below and the other 3 within normal limits. On the 2nd day there was no

Table 23.

Plasma chloride values during shock and on subsequent days.

Case No.	Condition	During Shock Before Transfn.	After Transfn.	2nd Day	3rd Day	4th Day
		mg.%	mg.%	mg%	mg%	mg%
53	Acc.Haem.	560	570			
24	P.E.T.: P.P.H.	585	535	555	545	545
55	Abortion	730				
23	Acc.Haem.	580		580		
27	Acc.Haem.	590				
32	Acc.Haem.	595		585		
49	Acc.Haem.	635		617	612	601
21	Acc.Haem.	524	585	570	575	
21	Acc.Haem.	525		520	470	
17	P.P.H.	500	525	525	530	
12	P.E.T.: P.P.H.	667	630			
3	Caes.Sect.	652	649			585
73	P.E.T.: Dystocia	652	666			614
4	Caes.Sect.	684	649			
65	P.P.H.	546	568			625
37	P.P.H.	631				656
36	P.P.H.	639				
35	P.E.T.: Dystocia	613				613
63	P.P.H.	525		555		
48	P.P.H.	585				602
28	Caes.Sect.			546	567	
40	Hydramnios: A.P.H.	600				
58	P.P.H.	620				
46	Acc.Haem.	547				
44	P.P.H.	620				
72	Ruptured Uterus	585	623			

P.P.H. - Post-partum haemorrhage: Acc.Haem. - Accidental haemorrhage: P.E.T. - Pre-eclamptic toxaemia: Caes.Sect. - Caesarean Section: A.P.H. - Ante-partum haemorrhage.

Table 24.

	Range Cl.	Average Cl.
During shock Before transfn.	500-730 mg.%	600 mg.%
During shock After transfn.	525-666 "	600 "
2nd day	520-617 "	561.4 "
3rd day	470-612 "	549.8 "
4th day	545-656 "	605 "

case above normal limits, but 5 cases below normal while the other 4 were within normal limits. Again on the 3rd day there were no cases above normal limits but 3 out of the 6 cases had values below normal. On the 4th day, however, there were 2 cases above normal limits, one below the normal limit and the other 5 were within normal limits.

As this variation in the chloride levels may be connected with an attempt on the part of the body to maintain electrolyte balance, the results of the chloride estimations have been compared with the sodium

levels. If the chloride combines with sodium to maintain electrolyte balance then we would expect to obtain some information by studying the ratio of sodium to chloride. This was done and the results are shown in Table 25. The values of sodium and chloride have been converted to milli-equivalents to give a more accurate comparison.

Table 25.

Showing Chloride: Sodium ratio.

Case No.	Condition	m.Eq.Na.	m.Eq.Na.Cl.	Ratio Na:NaCl.
53	Acc.Haem.	138.7	95.7	1.45 : 1
24	P.E.T.: P.P.H.	150.9	100	1.50 : 1
55	Abortion	143.0	124.7	1.14 : 1
23	Acc.Haem.	130.4	99.1	1.31 : 1
49	Acc.Haem.	123.5	108.5	1.14 : 1
21	Acc.Haem.	151.1	89.6	1.66 : 1
17	P.P.H.	151.5	85.4	1.72 : 1
12	P.E.T.: P.P.H.	134.6	114.0	1.18 : 1
3	Caes.Sect.	126.1	111.4	1.13 : 1
4	Caes.Sect.	130.4	116.9	1.11 : 1
65	P.P.H.	86.1	93.3	0.92 : 1
37	P.P.H.	139.6	107.8	1.29 : 1
36	P.P.H.	134.3	109.2	1.23 : 1
35	P.E.T.: Dystocia	130.4	120.2	1.09 : 1
63	P.P.H.	141.7	89.7	1.58 : 1
48	P.P.H.	130.4	100	1.30 : 1
72	Ruptured Uterus	122.6	100	1.22 : 1

P.P.H. - Post-partum haemorrhage: Acc.Haem. - Accidental haemorrhage: P.E.T. - Pre-eclamptic toxaemic: Caes.Sect. - Caesarean Section.

The normal ratio of sodium to sodium chloride expressed in milli-equivalents is from 1.33 : 1 to 1.59 : 1. The ratio of sodium to sodium chloride is below normal in 12 out of the 17 cases of shock and above normal in 2 cases. There is therefore a preponderance of chloride over sodium.

DISCUSSION OF ELECTROLYTE CHANGES IN SHOCK.

It has thus been shown that in cases of haemorrhagic shock in pregnancy there is a fall in blood sodium associated with a rise in blood potassium. These changes do not affect the level of blood chlorides to any marked extent.

Alterations in blood sodium are common in disease but they do not appear to be associated with any marked consequences for the patient unless they are extreme. Changes in the blood potassium however are usually concomitant with severe symptomatology. This is understandable since potassium is normally intra-cellular and is non-diffusible except under conditions of considerably altered metabolism or cell damage. Mobilisation of intra-cellular potassium has been shown to occur under certain well defined conditions. According to Fenn and Cobb (1934) and Black (1953) acidosis of varying origins can cause potassium to leave cells and become available for excretion. Similarly there is a mobilisation of cell potassium during glycolysis (Fenn 1939) and protein breakdown (Fenn 1940). Howard and Carey (1949) have shown that augmentation of the blood potassium from

tissue cells is a constant feature of tissue breakdown.

A definite acidosis has been observed in shock by many workers (Cannon, 1917; Guthrie, 1918; Penfield, 1919; Cournand et al, 1943). This acidosis appears to be associated with the breakdown of glucose. Riegel (1927), Gesell et al (1930), Gutmann et al (1941), Cournand et al (1943), Swan (1943), and Beatty (1945) have all shown that there is an increase in blood lactates during shock. In addition we have found an increase of pyruvates and according to Russell et al (1943) and Root et al (1947) the acidosis of shock can be attributed to carbonates, lactates and pyruvates. There is thus a ready explanation for the mobilisation of potassium. At the same time it is doubtful if this shift of potassium is a purely passive phenomenon to provide extra base in view of the fall in blood sodium. The explanation must be related to more vital processes. We have shown that there is a considerable degree of glycolysis and protein breakdown, processes which are known to be associated with liberation of potassium from cells. Buchanan, Hastings and Nesbitt (1949) have shown that potassium ions are essential for the metabolism of

glucose and Weller and Taylor (1950), from their studies have similarly come to the conclusion that there is an intimate relationship between potassium and glucose metabolism. What form this relationship takes, is not at present known but it appears to play a vital part in energy transformation.

It is possible, however, that part of this change in potassium content may be due to tissue damage secondary to the vascular upset produced by shock. This is a particularly attractive theory in view of the co-incidental changes in blood sodium. Fox and Baer (1947), by means of radio-active isotopes, have shown that, in experimental shock, damaged tissues extrude considerable amounts of potassium and take up an equivalent amount of sodium. Similarly Darrow and Engel (1945) found a 10 to 25% reduction in potassium and an appreciable increase in sodium in the livers of rats following haemorrhagic shock. This is a possibility which will have to be considered and a study of the liver in fatal cases of haemorrhagic shock in pregnancy has been made in a later part of the thesis.

The fall in blood sodium is equally pronounced.

In view of the anuria during the shock phase this fall must be due to movement of the sodium ions into the tissues. It remains to be seen whether this sodium is deposited in the tissue spaces or enters the cells. The movement of sodium ions must upset the osmotic balance both in the blood and tissues. With the loss of potassium from the cells a large accumulation of sodium in the tissue spaces would produce intense osmotic changes within the cells and the position would be untenable. The osmotic balance might be restored if a large volume of fluid migrated with the sodium ions into the tissue spaces. The volume of circulating blood would thereby be greatly reduced. This is a point which will have to be considered and a report of investigations relating to blood volume is presented in a further section of the thesis.

The osmotic pressure of the blood will be greatly altered by the loss of sodium ions but this may be counterbalanced by the movement of potassium ions into the plasma. A study of milli-equivalent values for the two ions in four patients is presented in Table 26.

Table 26.

To show the sum of sodium and potassium values expressed in milliequivalents before and during shock.

Case No.	Condition	Before Shock	During Shock
3	Caes. Sect.	153.4 m.Eq.	131.3 m.Eq.
4	Caes. Sect.	150.3 m.Eq.	136.0 m.Eq.
12	P.E.T.: P.P.H.	158.7 m.Eq.	140.3 m.Eq.
73	P.E.T.: Dystocia	164.7 m.Eq.	147.5 m.Eq.

P.P.H. - Post-partum haemorrhage: P.E.P. - Pre-eclamptic toxaemia: Caes. Sect. - Caesarean Section with haemorrhage.

The average sum of the milliequivalents of sodium and potassium before shock was 156.8 m.Eq., while during shock it was 138.8 m.Eq. It appears then that, if there is a transfer of potassium from the tissues into the serum to maintain osmotic balance, the response is poor.

It is obvious that osmotic equilibrium will be attained and one factor of considerable importance in this respect is the increase in blood glucose. Although this mobilisation of glucose is obviously not a passive phenomenon it is likely that one of its secondary actions is to restore the osmotic balance.

It remains to be seen whether the movement of sodium is accompanied by any marked change in the fluid content of the blood and on this depends the answer to the problem of whether the sodium remains in the tissue spaces or enters the cells.

A remarkable feature is the upset in the sodium-chlorine ratio. Apparently the chlorine ion does not move with the sodium. This is not what one would expect if the transfer of sodium was a purely passive osmotic phenomenon. The relative increase of chlorine will tend to enhance any existing acidosis. As has already been indicated the acidosis in shock is mainly related to accumulation of lactates and pyruvates but these relative changes in the chlorine ion will not be without their significance.

Apart from the metabolic disturbance it seems likely that the changes in these various substances are initiated by some controlling influence, probably hormonal. In any process involving alteration in the values for sodium and potassium the adrenals must be considered.

It has been known for some time that the adrenal cortex exerts some influence on the electrolyte and

fluid balances of the body and indeed one of the group of hormones secreted by the adrenal cortex has been termed the "salt-active" corticoids. The exact control of electrolytes by the adrenal cortex is not fully understood and there is still some confusion in the matter. Most of the work has been carried out on animals but some observations have been made on patients with diseases of the adrenal cortex causing either hypoactivity or hyperactivity.

The most notable physiological defect in adrenal insufficiency, as in Addison's disease, is a failure of conservation of sodium by the kidneys with the consequent loss of sodium and water from the body and a low level of plasma sodium. Loeb (1932) found a low sodium and high potassium level in the blood of patients with Addison's disease. In adrenalectomised animals also there is a decrease in the plasma concentration of sodium and chloride and a rise in potassium (Baumann and Kurland, 1927; and Loeb, 1935).

The decreases in plasma sodium in adrenalectomised animals has been shown to be due to loss of sodium through the kidneys (Loeb et al., 1933; and Harrop et al., 1933). Swingle and co-workers (1933) found that there is an associated fall in the level of chloride

in the plasma and a rise in potassium.

In our cases the low levels of plasma sodium and the high levels of serum potassium would suggest adrenal insufficiency. However, the reduction in plasma sodium levels caused by adrenal cortical insufficiency is said to be due to an increased loss of sodium in the urine. As was shown in a previous section of the thesis there was oliguria or anuria in our patients during the shock phase and for some time afterwards. Furthermore, the reduction in plasma sodium occurred rapidly and indeed so rapidly that a considerable volume of urine with a high sodium content would require to be excreted in a short space of time.

Conclusive evidence has been advanced recently, however, (Flanagan et al., 1950 and Stern et al., 1951) to show that in adrenalectomised animals the total excretory loss of sodium and chloride could not completely account for the reduction in these ions. The fall in sodium may therefore be partly explained by a transfer of sodium ions from the plasma into the tissues. This is the type of change which has occurred in our patients and on this basis one might conclude that adrenal insufficiency was responsible for the process.

As already stated, however, in adrenalectomised animals there is a fall in plasma chloride levels. On the other hand there was a relative increase of plasma chloride in our cases. We must therefore conclude that there is no definite evidence of a deficiency of the mineralo-corticoid fraction of the adrenal cortex in our cases. At the same time the changes in sodium and potassium exclude the possibility of hyperactivity of this fraction. Britton and Silvette (1934) found a decrease in the sugar content of the blood in adrenalectomised animals. In our cases there was hyperglycaemia. This is a further argument against the existence of adrenal deficiency but in addition it raises the possibility of hyperactivity of the gluco-corticoid moiety. It may be that all of the changes in electrolytes noted are related to altered carbohydrate metabolism which in turn depends on increased activity of gluco-corticoids. Noble and Collip (1942) and Swingle et al (1943), however, were unable to detect any beneficial effect from the administration of adrenal cortical extract in shock. This, of course, may have been due to the use of relatively impure extracts and now that pure gluco-

corticoids.are available fresh evidence will be forthcoming. Suffice to say that our evidence indicates that there is no deficiency of adrenal function but there may be some hyperactivity of these glands particularly in relation to their effect on carbohydrate metabolism.

It is noteworthy that the changes in electrolytes found in our cases are similar to those reported in traumatic shock by other workers (McIntosh, 1930; Wilson et al., 1936; Gutmann et al., 1941; Clarke and Cleghorn, 1942; Manery and Solandt, 1943; Winkler and Hoff, 1943; and Beecher, 1949).

SUMMARY

1. In haemorrhagic shock in pregnancy serum potassium increases, serum sodium diminishes and chloride remains unaltered.
2. It is felt that these changes must be related to the marked glycolysis and protein metabolism reported in the earlier parts of the thesis.
3. These changes may be operating under the influence of the gluco-corticoid fraction of the adrenal cortex.
4. These changes in sodium and potassium may, however,

be due to the movement of these ions into and out of damaged cells. This is a possibility which will be investigated in a later portion of the thesis.

5. The destination of the sodium ions has not been determined. The redistribution may be either into the tissue spaces or into cells. If the migration is into the tissue spaces then one would expect marked changes in blood volume and this has been made the subject of a short investigation and is reported in the subsequent section or the thesis.
6. The changes in sodium and potassium are delayed and prolonged where the condition is complicated by pre-eclamptic toxaemia. This is probably related to the diminished glycolysis already noted in these cases and it indicates that there is some pre-existing upset of carbohydrate metabolism in pre-eclamptic toxaemia.
7. The results of our studies of electrolyte changes provide a further support for the belief that the process in shock due to haemorrhage differs little from that following trauma.

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BLOOD VOLUME CHANGES IN HAEMORRHAGIC SHOCK

As indicated in the preceding part of the thesis it is necessary to study blood volume changes in these cases to determine, among other things, the fate of the sodium which is lost from the blood.

Methods.

The method employed was the estimation of haemoglobin and packed cell volumes before and during shock and after blood transfusion. Estimation of blood volume by the Evan's Blue method could not be employed since the dye is not rapidly eliminated and it was therefore impossible to make the repeated estimations necessary for comparison during the shock and recovery phases.

Results.

The levels of haemoglobin and the packed cell volumes with the amounts of blood transfused in 20 cases are shown in Table 2'/. All cases which received saline, glucose or plasma transfusions have been excluded.

There were only 3 cases (Nos.1, 2 and 3) in which the haemoglobin and packed cell volumes were known before shock. The haemoglobin fell from

Table 27.

To show haemoglobin and packed cell volumes before, during and after shock.

Case No.	Transfn. Pints	Before Shock		After Shock		Days after Transfusion 1		2	
		Hb.	P.C.V.	Hb.	P.C.V.	Hb.	P.C.V.	Hb.	P.C.V.
1	1	72	35	60	28	-	-	-	-
2	2	80	32	63	20	75	38	-	-
3	2	50	29	45	27	47	29	-	-
4	2	-	-	73	33	71	33	-	-
23	1½	-	-	50	21	-	-	34	16
26	3	-	-	78	28	-	-	67	26
27	1	-	-	53	18	-	-	34	14
31	0	-	-	58	25	-	-	55	24
32	1	-	-	45	16	-	-	50	22
33	3	-	-	62	31	72	34	56	27
41	0	-	-	60	27	-	-	55	25
42	2	-	-	59	24	-	-	44	19
43	2	-	-	57	27	-	-	49	23
48	3	-	-	55	27	67	31	-	-
49	0	-	-	60	29	-	-	45	25
51	4	-	-	50	24	68	27	45	21
52	2	-	-	62	29	-	-	56	28
53	4	-	-	66	32	-	-	60	27
66	1	-	-	54	24	40	19	-	-
67	1	-	-	78	37	-	-	60	27

73% to 60% and the P.C.V. from 35% to 28% in 1 hour in Case 1. In Case 2 the haemoglobin fell from 80% to 63% and the P.C.V. from 32% to 20% in 1 hour. In Case 3 the haemoglobin level fell from 50% to45% and the packed cell volume from 29% to 27% in ½ hour.

There can be no doubt, from these figures that

haemodilution has occurred in the three cases. With the loss of whole blood the remaining circulating fluid should maintain its haemoglobin percentage and packed cell volume provided that there is no change in the water content. It is quite obvious that there has been a marked alteration in the water content and that fluid has entered the blood stream.

In the remainder of the cases it was impossible to obtain pre-shock values but with three exceptions these patients had become anaemic, some grossly so. The haemoglobin values in the 20 cases ranged from 45 per cent. to 78 per cent. The range of packed cell volumes was 18 to 37.5 per cent.

Immediately after transfusion the values of both haemoglobin and packed cell volume tend to increase (See Cases 2,3,33,48 and 51) but in some the values may be diminished despite the blood they have received (Cases 4 and 66). The picture is clarified if the values are studied on the day following transfusion (Day 2). Almost without exception there is a decline in values of both haemoglobin and packed cell volume. It would appear from this that the haemodilution process continues for some considerable

time after the onset of shock.

Discussion.

It has been established that a haemodilution occurs in cases of haemorrhagic shock. This may be due either to a passage of fluid from the tissues into the blood or to a "pooling" of concentrated blood in some area outside of the available circulation. If however, "pooling" does occur one would expect that, with recovery, this "pooled" concentrated blood would once more enter the circulation and a rise in haemoglobin and packed cell volume would thereby be brought about. It has been shown, however, that haemodilution continues for at least 24 hours following the shock phase and one must conclude that the original haemodilution is due to an inflow of fluid from the tissues.

As we have previously indicated there is a marked fall in blood sodium accompanied by a rise in potassium. The sodium, we have concluded, migrates into the tissues. If it were to remain in the tissue spaces one would expect that fluid would follow in order to maintain osmotic balance. This, however, does not occur and one must assume that the sodium

enters the cells in place of the potassium which has moved into the blood. Even so there must be some effect on osmosis particularly since the fall in sodium is greater than the increase of blood potassium. It may be that this is offset by the osmotic effect of the rapid mobilisation of sugar which we have shown to occur in these cases.

It is concluded that haemodilution occurs in haemorrhagic shock and continues for some considerable time thereafter. This haemodilution is due to a transfer of fluid from the tissues into the blood stream. At the same time there is a transfer of sodium from the blood stream into the cells. The consequent upset in osmotic balance will be partly compensated by the movement of potassium from the cells into the blood and to a greater extent, probably, by the hyperglycaemia.

THE RELATIONSHIP BETWEEN PRE-ECLAMPTIC TOXAEMIA AND SHOCK.

A clinical impression has been gained that a patient with pre-eclamptic toxaemia is more liable to develop shock and having developed shock is more liable to succumb than the non-pregnant patient. This may be due to the fact that such patients have a lowered resistance due to their illness or it may be that certain specific changes occur in the pre-eclamptic patient which pre-dispose to an earlier development of shock and a degree of shock more severe than in the non-toxaemic patient.

It is not feasible to establish whether the toxaemic patient is more liable to shock than the non-toxaemic. Obviously there must be a threshold stimulus level for the production of shock and this cannot be estimated in the patient. In addition the frequency with which shock occurs in toxaemic patients may merely be an indication that such patients are more likely to suffer a haemorrhagic catastrophe which will lead to shock. It appeared to us that the only method of comparing the toxaemic with the non-toxaemic patient in regard to the

liability to shock was to compute the mortality rate in the two groups.

Material

The figures for the 20 years period 1929-1948 in the reports of the Glasgow Royal Maternity and Women's Hospital were analysed. The patients were grouped into those judged to be suffering from pre-eclamptic toxaemia and those who were non-toxaemic. All cases of mixed and concealed accidental haemorrhage were included in the toxaemic group as Browne (1951) states that "There can no longer be any doubt that the chief aetiological factor (in these cases) is to be found in pre-eclamptic toxaemia."

Analysis

The figures for individual years are given in Table 28 and the total figures for the 20 year period are given in Table 29.

The incidence of fatal shock in non-toxaemic cases is 1 in 170.8 but in toxaemic cases fatal shock occurs in 1 in 99.7 cases.

Discussion

The patient with pre-eclamptic toxaemia who develops shock is much more likely to succumb than

Table 28.

	1929	1930	1931	1932	1933	1934	1935	1936	1937	1938
Total Deliveries	2446	2778	2900	3084	3198	3152	3229	3317	3287	3315
Deliveries in Non-Toxaemic	2087	2387	2595	2714	2700	2615	2592	2756	2686	2690
Pre-eclampsia	235	279	194	229	331	364	469	437	469	473
Eclampsia	93	59	54	66	78	73	67	49	43	61
Accidental Haemorrhage (Mixed & Concealed)	31	53	57	75	89	100	101	75	89	91
Total Toxaemic cases	359	391	305	370	498	537	637	561	601	625
Total Shock Deaths	28	35	19	18	24	23	27	15	20	19
Non-toxaemic shock deaths	21	28	17	12	13	15	17	13	11	14
Toxaemic Shock Deaths	7	7	2	6	11	8	10	2	9	5

	1939	1940	1941	1942	1943	1944	1945	1946	1947	1948
Total Deliveries	3140	3032	3024	3211	3361	3041	2772	3260	3365	3031
Deliveries in Non-Toxaemic	2384	2301	2218	2469	2346	2159	2007	2220	2474	2275
Pre-eclampsia	625	626	677	633	916	794	684	931	789	670
Eclampsia	38	46	60	45	57	47	37	57	56	28
Accidental Haemorrhage (Mixed and Concealed)	93	59	69	64	42	41	44	52	46	58
Total Toxaemic Cases	756	731	806	742	1015	882	765	1040	891	756
Total Shock Deaths	21	21	27	19	34	10	13	16	14	13
Non-toxaemic shock deaths	13	13	18	10	25	6	10	13	8	8
Toxaemic Shock Deaths	8	8	9	9	9	4	3	3	6	5

Table 29.

20 Years Totals

Non-toxaemic deliveries	-	48,675
Toxaemic deliveries	-	13,068
Non-toxaemic shock deaths	-	285
Toxaemic shock deaths	-	131.

the non-toxaemic patient.

This greater liability to a fatal outcome may be due to a lowered vitality in the toxaemic patient or it may be due to some specific changes occurring in the disease process which accentuate the changes occurring in shock.

A considerable volume of work has been performed in the investigation of the changes occurring in the blood constituents in pre-eclamptic toxaemia and these changes are now well recognised. In this section we will try to correlate the changes in the blood in pre-eclamptic toxaemia and in shock. The alterations in the blood in cases of shock have already been described under individual headings but here a composite picture will be given and any possible linkage demonstrated.

The nitrogenous constituents of the blood are

raised in pre-eclamptic toxaemia (Crawford, 1939; Best and Taylor, 1950). We have shown that in shock there is an increase in urea, uric acid and amino-acid nitrogen and furthermore the increase is greater in the patients with previous pre-eclamptic toxaemia. In both pre-eclampsia and in shock there is, then, a disturbance in nitrogen metabolism. When shock is superimposed on pre-existing pre-eclamptic toxaemia a greater disturbance is noted in nitrogen metabolism (Table 30). It is not possible to say whether this greater disturbance is due to a summation of the effects of pre-eclamptic toxaemia and shock on nitrogen metabolism or whether it is due to an accentuation of the effect of shock due to a previous sensitisation by the pre-eclampsia.

In our investigations into the carbohydrate metabolism in shock it was found that there was an increase in the sugar and pyruvic acid contents of the blood. In addition there was an apparent increase in the level of inorganic phosphate in the blood. When shock occurred in a patient with pre-eclamptic toxaemia a greater change in the

levels of pyruvic acid and phosphates was found than in non-toxaemic patients (Table 31).

Table 30

Showing the average values of nitrogenous constituents in toxaemic and non-toxaemic patients during shock.

	Urea	Uric Acid	Amino Acid Nitrogen
Toxaemic	35 mg.%	7.1 mg.%	6.81 mg.%
Non-toxaemic	28 "	5.55 "	6.19 "

Table 31

Showing the average values of pyruvic acid and inorganic phosphate in toxaemic and non-toxaemic patients during shock.

	Pyruvic Acid	Inorganic Phosphate
Toxaemic	3.0 mg.%	5.12 mg.%
Non-toxaemic	2.19 "	3.17 "

There is, then, a disturbance in carbohydrate metabolism in shock which is more marked if the patient had pre-eclamptic toxaemia. Pre-eclampsia is a relatively slow developing condition, and any disturbance in carbohydrate metabolism is more difficult to detect. Mukherjee and Govan (1950), however, in their investigations of the tissue fluid in oedema of pregnancy toxaemia reached some

interesting conclusions in this respect. They found that there was a retention of organic acids and inorganic phosphates in the tissue fluid and suggested that the increased concentration of organic acids and phosphates was related to an upset in tissue carbohydrate metabolism.

We have demonstrated that with the onset of shock there is a mobilisation of sugar in an attempt to satisfy some demand of the body for energy. We have also shown that there is apparently greater difficulty in metabolising this carbohydrate. In pre-eclampsia there is already present a difficulty in dealing with carbohydrate and with the onset of shock this must increase considerably the difficulties in supplying energy to the body.

Conflicting findings in the sodium levels in pre-eclamptic toxaemia have been reported by several workers (Breidert, 1939; Oberst and Plass, 1940; Parviainen, Soiva, and Ehrnrooth, 1950; Vara and Vehniäinen, 195; and Nordenstrahl, 1952). Some report a rise and some a fall in the sodium levels but there is agreement that the serum potassium levels in pre-eclamptic toxaemia remain

unchanged (Stander, 1927; Dieckmann, 1942 and Nordenstrahl, 1952). Nevertheless Nordenstrahl (1952) quotes several workers who have shown that there is retention of sodium and potassium in the body in pre-eclamptic toxaemia. Mukherjee and Govan (1950) showed that there is an increased concentration of electrolytes in the tissue fluid in pre-eclampsia. We have shown that a disturbance in the sodium and potassium contents of the blood occurs in shock although we can only conjecture at the site where the sodium is deposited.

A most interesting phenomenon occurs when shock is superimposed upon pre-existing pre-eclamptic toxaemia. There is a fall in the level of sodium and a rise in the level of potassium in the blood as in other cases of shock but the changes both in sodium and in potassium are delayed and prolonged. (Figs.7 and 8).

Several explanations may be advanced to explain this peculiar behaviour of the electrolytes in pre-eclamptic patients in shock, but the available evidence suggests that the following may occur. In pre-eclamptic toxaemia there is an

Figure 7.

To compare sodium levels in toxaemic and non-toxaemic patients.

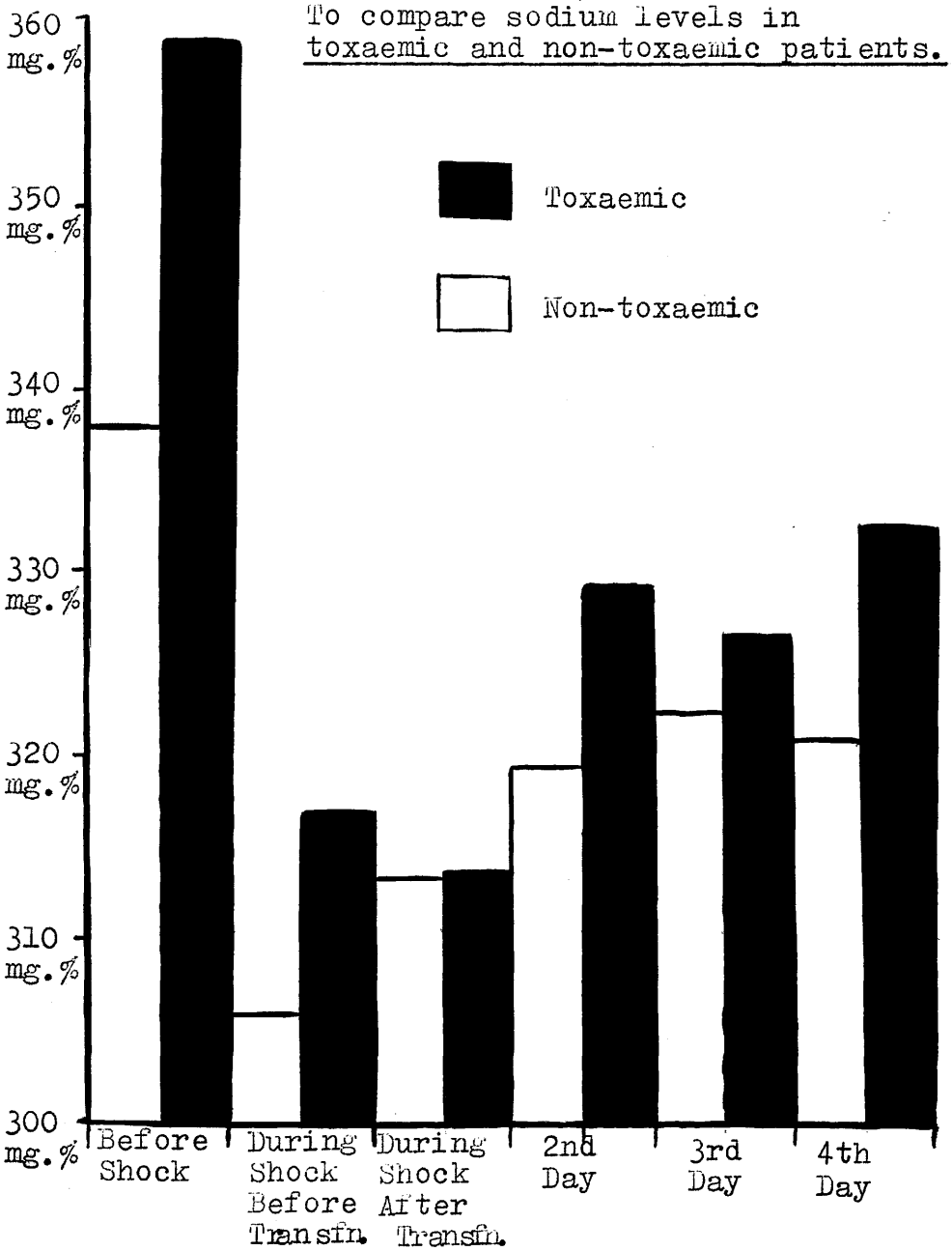
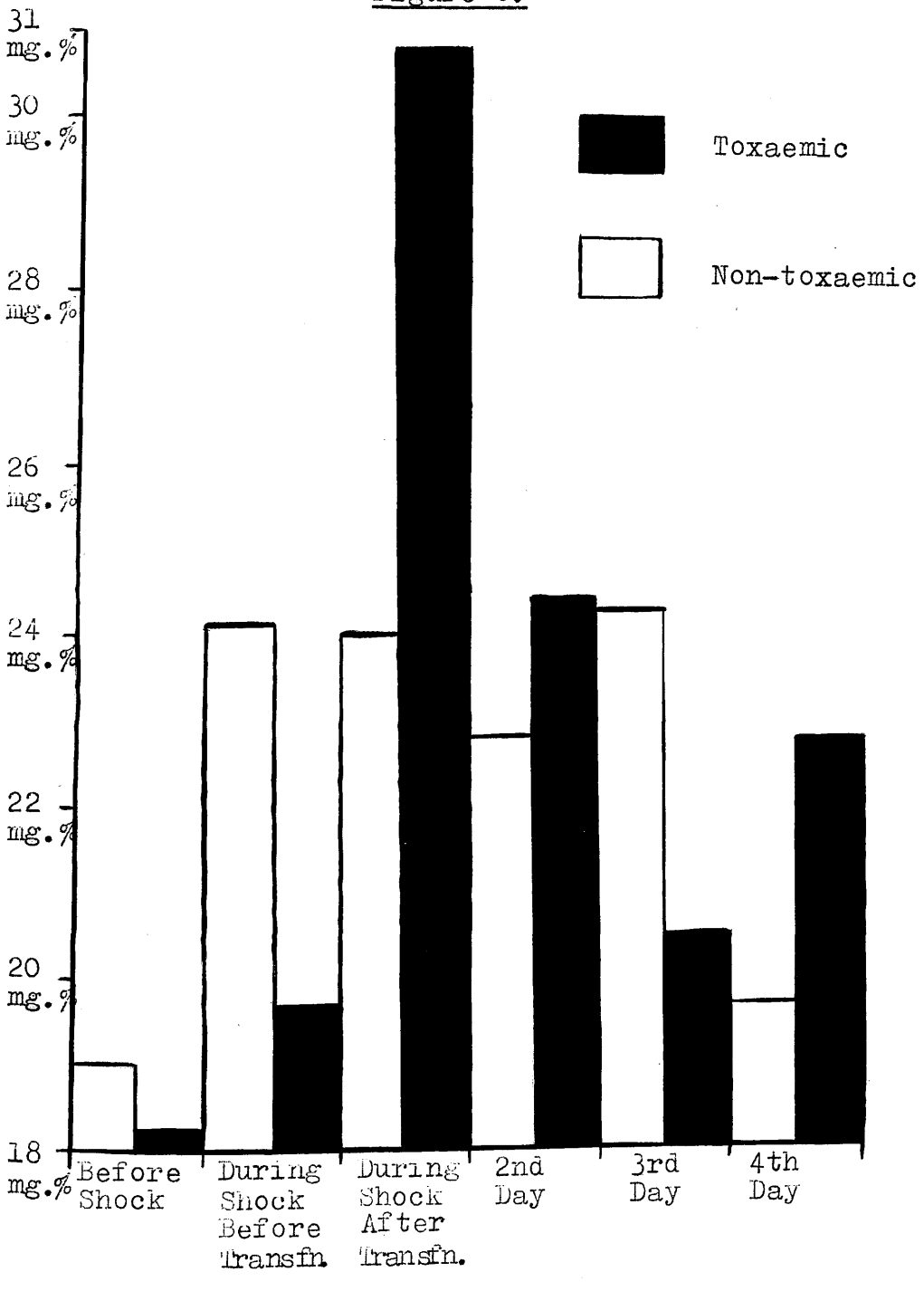


Figure 8.



To compare potassium levels in toxaemic and non-toxaemic patients.

increase of sodium in the tissue spaces. To maintain osmotic balance it is almost certain that the sodium content of the cells is also increased. This may in turn cause a diminution in the amount of cellular potassium. Presumptive evidence for this has been reported by Nordenstrahl (1952) who found that the potassium content of organs in patients dying of eclampsia is much reduced. With the occurrence of shock in a pre-eclamptic patient less potassium would be available for mobilisation and the movement of electrolytes would be considerably hindered. This process may be aggravated by the fact that the liver in pre-eclampsia contains less glycogen than normal and thus the hyperglycaemic reaction of shock would be less pronounced. It may be that this is the most important single factor and that, since there is interference with the hyperglycaemic reaction, the mobilisation of potassium does not occur with the same rapidity in the toxaemic patient.

As we have shown there is a withdrawal of fluid into the blood stream when haemorrhagic shock occurs. No definite explanation for this haemodilution could be advanced but it seems a necessary occurrence so

that the body can provide a more adequate circulation. It has been shown by several workers including Nordenstrahl (1952); Freis and Kenny (1948) and Berlin et al (1952), that there is an oligaemia in pre-eclamptic toxaemia and it is reasonable to assume that the fluid in these cases is transferred to the tissues causing oedema. The body and the cardiac action will become accommodated to the change in circulating volume but when shock occurs there will be a demand for an increased circulating volume which will be more difficult to attain than in the previously normal patient.

In cases of shock, then, there is a disturbance of both carbohydrate and nitrogen metabolism; an alteration in the electrolyte content of the blood; and a quite marked haemodilution. In pre-eclamptic toxaemia there is also a disturbance in carbohydrate and nitrogen metabolism and an alteration in the electrolytes of the body. In contrast to the haemodilution in cases of shock, however, there is an oligaemia in pre-eclamptic toxaemia. Although there is some interference with carbohydrate metabolism in shock it is quite obvious that the body makes

an effort to supply energy in this form and any further interference such as one finds in pre-eclampsia is bound to be to the disadvantage of the patient. The haemodilution of haemorrhagic shock has as one of its objects the restoration of the circulating volume. In addition it is necessary to keep in mind the normal hydraemia of pregnancy. Many normal pregnant patients can and do withstand the loss of almost a pint of blood without any untoward reaction. In the pre-eclamptic patient with oligaemia haemorrhage to the extent of one pint represents the loss of a considerable portion of her circulating volume and the inference to be drawn is obvious.

If any of these changes in carbohydrate or nitrogen metabolism, in electrolyte balance or in circulating blood volume are of primary importance in shock then the pre-existing alterations in these factors which are present in pre-eclampsia would in all probability accentuate the degree of shock. Even though these factors may not be of primary importance in the production of shock they are nevertheless intimately involved in the cyclical pattern of this condition. An aggravation of any of

the factors concerned in this cycle will tend to influence the whole pattern of events in shock.

In the pre-eclamptic patient there are already marked changes in metabolism, electrolytes and blood volume, all of them of a nature which tend to interfere with the normal body processes. It seems reasonable to assume that these changes will interfere with and probably exaggerate the changes caused by shock. This greater alteration in metabolism and electrolyte change along with the disturbance in circulating blood volume will no doubt increase the degree of shock in pre-eclamptic patients but this may not be the only reason for the greater liability of a fatal outcome to occur in the pre-eclamptic patient who suffers shock. It may be that the pathological changes known to occur in certain organs during the course of pre-eclamptic toxaemia are of prime importance in regard to the greater liability of these patients to succumb to the effects of shock. This will be discussed later.

Many points of similarity occur between pre-eclamptic toxaemia and shock. Some of the basic physiological processes occurring in the body,

particulary in regard to metabolism, are interfered with in both conditions. It does not seem surprising, therefore, that shock occurring in a patient with pre-eclamptic toxaemia is a much more serious condition and more liable to prove fatal than in the non-toxaemic patient.

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HEPATIC FUNCTION IN HAEMORRHAGIC SHOCK

In view of the marked changes in blood glucose, pyruvic and lactic acids, and the alteration in nitrogen values of the blood in shock it seemed reasonable to make a study of the main organ associated with the metabolism of these substances, namely the liver. In addition there are the pathological changes known to occur in the liver in toxaemia and it is possible that these play a part in the variations in the shock syndrome produced by that condition. Changes in the electrolyte concentration in the liver are known to occur in both shock (Darrow and Engel, 1945) and in eclampsia (Nordenstrahl, 1952) and it is possible that the explanation for these changes is to be found in the altered functional capacity of this organ.

The study of hepatic function was approached from two aspects. The concentration of certain substances in the blood which are altered when there is liver damage were estimated. These substances are amino-acid nitrogen, alkaline phosphatase and serum cholinesterase. The other method of study was the histological examination of sections of liver from

fatal cases of shock.

The biochemical tests of liver function will now be considered.

Biochemical Determinations to estimate Liver Function.

Amino-Acid Nitrogen

In the section on nitrogen metabolism (p.35) it has been shown that there is an initial rise in the amino acid nitrogen levels in haemorrhagic shock. After this initial phase, but while the patient is still in the "shock" state, the levels of amino acid tended to remain unchanged. As has already been indicated the initial rise in amino-acid nitrogen can be accounted for by increased protein catabolism. In the succeeding phase, however, when there is decreased protein catabolism, it would be reasonable to expect that the amino acid nitrogen levels would fall sharply if liver function were normal. This, however, does not occur and it is, therefore, concluded that there is some liver dysfunction at this stage.

Estimations of amino-acids and urea were made on successive days after shock and the results are shown in Tables 32 and 33 and also graphically (Figs.9 & 10).

Figure 9.

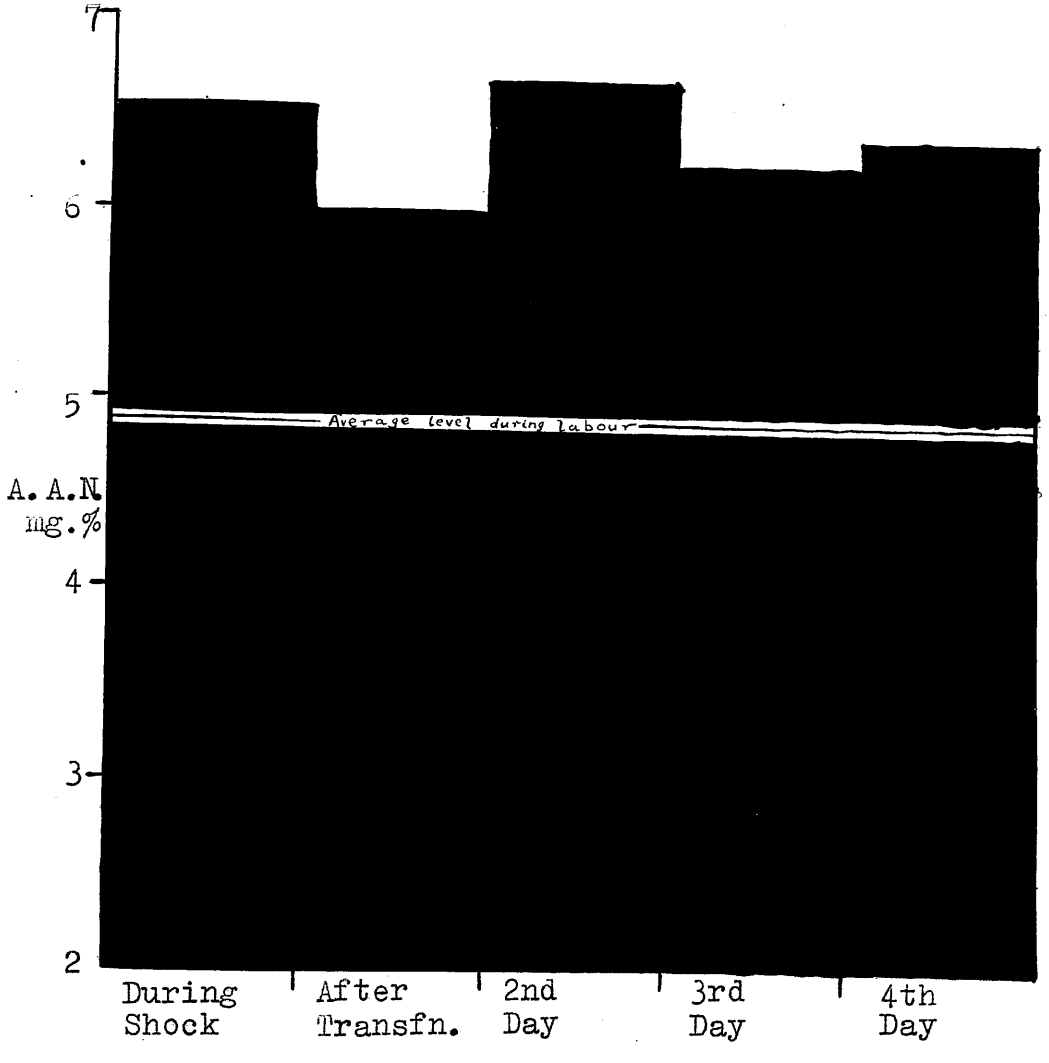

7
6
5
4
3
2
A. A. N
mg. %
Average level during labour
During Shock
After Transfn.
2nd Day
3rd Day
4th Day

Figure 10.

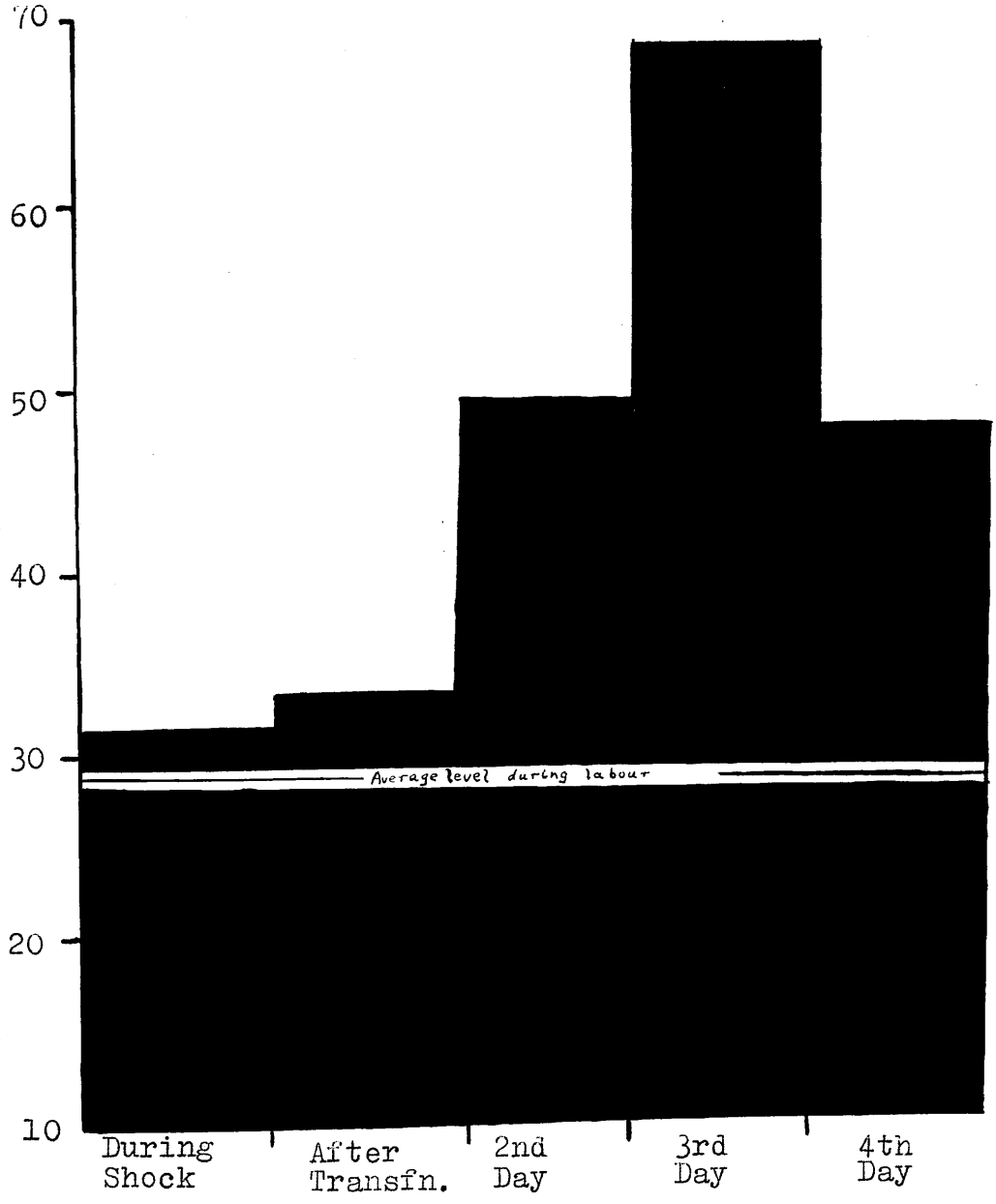

70
60
50
40
30
20
10
Average level during labour
During Shock
After Transfn.
2nd Day
3rd Day
4th Day

Table 32.

To show amino-acid nitrogen levels on successive days.

		Range	Average
36 cases	During Shock	3.3-10.3 mg.%	6.5mg.%
12 cases	After transfusion	3.68-9.75 "	5.98 "
20 cases	2nd day	3.5-10.35 "	6.71 "
14 cases	3rd day	3.5-9.36 "	6.23 "
10 cases	4th day	4.0-10.0 "	6.41 "

Table 33.

To show urea levels on successive days.

		Range	Average
35 cases	During Shock	16-53.3 mg.%	31.4 mg.%
25 cases	After transfusion	16-52.5 "	33.5 "
24 cases	2nd day	23-116 "	49.3 "
13 cases	3rd day	17-132 "	68.8 "
13 cases	4th day	25-116 "	48.1 "

From these results it can be seen that the amino acids remain high and at about the same level until at least the 4th day. The blood urea goes on rising until the 3rd day but on the 4th day falls quite markedly.

As shown in the section on nitrogen metabolism

the levels of amino acid nitrogen were higher in patients with pre-eclamptic toxaemia during shock.

Discussion

Amino-acid nitrogen is formed from the breakdown of protein. The further progress of the cycle of protein catabolism depends upon the breakdown of amino acids by the liver to form urea. When there is liver dysfunction this breakdown of amino acids to urea is hindered so that the amino acids accumulate in the blood. Evidence of this accumulation of amino acids in the blood has been shown in such cases of liver dysfunction as acute yellow atrophy, infective hepatitis and cirrhosis of the liver.

It is generally acknowledged, however, that a considerable degree of liver dysfunction must exist before an appreciable rise in amino acid nitrogen occurs. As we have shown there is a rise in amino-acid nitrogen in the blood during shock resulting from haemorrhage in obstetric cases. It is therefore concluded that liver dysfunction occurs in such cases.

Furthermore this liver dysfunction continues for several days after clinical recovery from shock. The

blood urea continues to rise until the 3rd day but as we have shown previously in the section on nitrogen metabolism this can mostly be accounted for by the renal dysfunction which is present in these cases although part of this urea formation will be due to breakdown of amino acids.

Although the amino acid nitrogen levels are above normal it is not suggested that complete failure of the liver is present but the lag in the return of amino acid nitrogen to normal levels indicates difficulty in dealing with these substances. Liver dysfunction appears to continue for some time after clinical recovery from shock.

As already stated in the first part of the thesis there appears to be a more marked breakdown of protein during shock in pre-eclamptic cases but this is due partly to the pre-existing increase in nitrogenous constituents noted in these patients (Crawford, 1939; Best and Taylor, 1950). The oligaemia will also tend to enhance these values.

Alkaline Phosphatase

The level of alkaline phosphatase in the blood is used as a measure of hepatic efficiency. It has

been found that an increase in this substance in the serum occurs in obstructive jaundice,(Roberts, 1933; Armstrong, King & Harris, 1934) and also in toxic and infective jaundice but not to such a marked degree. In view of these findings the level of alkaline phosphatase in the serum is used as a test of liver function although as shown by Herbert (1935) there may be no significant rise in some cases of jaundice.

Method

The method of King (1947) was employed using Folin-Ciocalteau phenol reagent and the readings were made in the photoelectric colorimeter.

Material

The alkaline phosphatase was estimated during the shock phase before treatment in 12 cases and after blood transfusion in 6 cases. The results are shown in Table 34.

The range during the shock phase before treatment was 6-15.5 units while the average was 10.5 units. The normal value for alkaline phosphatase is given as below 10 units (King and Armstrong, 1934). It is natural to expect that there will be considerable variations in the degree of liver dysfunction in shock

and this is reflected in the biochemical results. There is a slight rise in alkaline phosphatase in 9 of the 12 cases in the shock phase which indicates some degree of liver dysfunction. After transfusion the range was 5-14.3 units with an average of 10 units indicating that in many cases the liver has not yet regained its normal function.

Table 34.

Case No.	Condition	Before Transfn.	After Transfn.
62	Caes. Sect.	13.1 units	14.3 units
24	P.E.T.: P.P.H.	10 "	5 "
3	Caes. Sect.	15.5 "	10.0 "
73	P.E.T.: Dystocia	10.3 "	12.1 "
4	Caes. Sect.	12.5 "	12.7 "
44	P.P.H.	8 "	
46	Acc. Haem.	13 "	
58	P.P.H.	6 "	
38	Abortion	8 "	
40	Hydramnios: A.P.H.	10 "	
39	P.P.H.	10 "	
72	Ruptured uterus	10 "	

P.P.H. - Post-partum haemorrhage: Caes. Sect. - Caesarean Section with haemorrhage: P.E.T. - Pre-eclamptic toxaemia: A.P.H.- Ante-partum haemorrhage: Acc. Haem. - Accidental haemorrhage.

Discussion of Alkaline Phosphatase Levels in Shock

Alkaline phosphatase is an enzyme found particularly in bones but also in other tissues. Phosphatase is excreted by the liver; a marked rise in plasma phosphatase therefore occurs in obstructive jaundice and in jaundice due to liver damage, but not in the purely haemolytic type (Best and Taylor, 1950).

A rise in alkaline phosphatase is therefore indicative of liver dysfunction. Such a rise occurs in pregnant patients who suffer haemorrhage and become shocked and this is therefore taken as evidence of liver dysfunction in these cases. Unfortunately, there were insufficient cases to determine whether there was any significant difference between patients with pre-eclamptic toxaemia and non-toxaemic patients.

Pseudocholinesterase

The work of Mendel, Mundell, and Rudney (1943) has shown that at least two distinct enzymes occur in the blood; the true cholinesterase, which exists mainly on the membrane of the red cells and which hydrolyses acetylcholine most rapidly at low substrate concentrations and the pseudocholinesterase, which is almost entirely responsible for the serum activity

and which hydrolyses acetylcholine most rapidly in concentrations much higher than those normally encountered in the blood.

Here, we are concerned with the serum or pseudo-cholinesterase as it has been shown by Autopol et al (1938); McArdle (1940); Faker (1943); Kundel and Ward (1947); Wescoe et al (1947) and Alcalde (1950) that the level of this enzyme in the blood is lowered in cases of liver disease. The estimation of the level of pseudo-cholinesterase in the blood is therefore employed as a test of liver function.

Material

The pseudo-cholinesterase was estimated in 19 cases during the shock phase before any treatment was given; in 5 cases after transfusion; in 9 cases on the 2nd day; in 4 cases on the 3rd day; and in 6 cases on the 4th day.

Method

The method was that of Butt, Comfort, Dry and Osterberg (1941-42) titrating with N/100 NaOH. The value of pseudo-cholinesterase is measured as the equivalent of the volume in ccs. of N/100 NaOH required to keep the pH at 8.5.

The normal level of pseudo-cholinesterase in the blood in pregnant women is given as 1.27 ± 0.08 (Butt et al. 1941-42). Levine and Hoyt (1949) also found lowered values in pregnancy.

As the numbers of estimations of pseudo-cholinesterase in pregnancy are rather small a series of estimations were made in normal pregnant patients and also in patients in labour or who were recently delivered. This control series in parturient and post-partum cases was deemed advisable as the majority of the cases in the "shock" series came into this category.

Normal Pseudo-cholinesterase Values

The pseudo-cholinesterase levels were estimated in 24 normal patients, 12 during pregnancy and 12 in labour or post-partum. The range and average values are shown in Table 25.

Table 35

	During Pregnancy	In labour or Post-partum
Range	0.96 - 1.63	1.31 - 2.23
Average Values	1.27	1.76

Our findings during normal pregnancy agree with these of Butt et al (1941-42) but there is quite a considerable rise in the values in the serum of patients in labour or recently delivered.

Pseudo-cholinesterase values in Shock

The results are shown in Table 36.

Table 36

Results.

Case No.	Condition	Before Transfn.	After Transfn.	2nd Day	3rd Day	4th Day
28	Caes. Hysterectomy	1.23	1.19	1.16		1.0
7	P.P.H.	1.52			1.37	1.16
57	Ruptured Rudimentary Horn	1.88				
29	P.P.H.	1.85				
67	P.P.H.	1.18		1.08		
48	P.P.H.	1.45	1.48	1.71		1.41
51	P.P.H.	1.84	1.79	1.88		
9	Caes. Sect.	1.26		1.30	1.24	1.83
8	Abortion	1.61		1.32		
44	P.P.H.	1.82				1.36
46	Acc. Haem.	1.54				
58	P.P.H.	1.01				
71	P.P.H.	0.95			1.74	
59	Placenta Praevia	1.62	1.74	1.74		
74	P.P.H.	1.64				
38	Abortion	1.18				
40	Hydramnios: A.P.H.	0.84				
39	P.P.H.	1.62		1.33		1.16
45	Acc. Haem.	1.54	1.70	1.12	1.18	

Caes. Sect. - Caesarean Section:
P.P.H. - Post-partum haemorrhage: Acc. Haem. - Accidental haemorrhage: A.P.H. - Ante-partum haemorrhage.

When these values are compared with the values found during normal pregnancy there is apparently a rise in the amount of cholinesterase in the serum. The majority of patients in the shock series were in labour or post-partum and the values must therefore be compared with the normal values in labour or post-mortem. A comparison of the values during the phases of pregnancy, labour and shock are shown in Table 37.

Table 37

Showing pseudocholinesterase values in various phases.

	Range	Average Values
Pregnancy	0.96 - 1.63	1.27
Labour and post-partum	1.31 - 2.23	1.76
Shock	0.94 - 1.88	1.46
After Transfusion	1.19 - 2.28	1.56
2nd Day	1.08 - 1.88	1.40
3rd Day	1.18 - 1.74	1.38
4th Day	1.0 - 1.83	1.32

When these figures are compared it is found that there is actually a fall in the pseudo-cholinesterase values in the shock phase. The level rises slightly after blood transfusion but falls again on succeeding days.

Discussion

It has been shown experimentally by Brauer and Root (1946) and Sawyer and Everett (1947) that the liver is the main site of synthesis of cholinesterase. In any condition producing damage of the liver this synthesis will fail with a resultant fall in the level of pseudo-cholinesterase in the blood. As stated earlier such lowered values have been found by several workers in patients with liver disease.

Lowered values of pseudo-cholinesterase have been reported by Butt el al (1941-42) and Levine and Hoyt (1949) in pregnancy and our results in normal pregnant patients agree closely with the above workers. However, we have found that the levels of pseudo-cholinesterase are raised when such patients are in labour or are recently delivered. We do not propose to discuss the reasons for this rise as it is pertinent to the present problem only in so far as the values found in our series must be compared with these higher values as the majority of our cases were in labour or recently delivered.

In the series of patients in shock the values of pseudo-cholinesterase were found to be below the

average value for normal patients. Although there was a slight rise in the values after blood transfusion the levels remained below normal for some days after the occurrence of shock.

A lowered pseudo-cholinesterase activity in shock has been reported in non-pregnant patients by Augustinsson (1948) but so far as we are aware no comparable investigation has been carried out in pregnant patients who have suffered shock.

The results indicate that in shock there is liver dysfunction.

Discussion of biochemical tests of liver function in shock.

Hepatic function tests are not generally considered to be very reliable and gross changes are usually present when marked changes in the levels of amino acid nitrogen, alkaline phosphatase and pseudo-cholinesterase are found. Quite marked changes may occur in the liver without alteration in the levels of these substances. Any change in the level of these substances can therefore be taken as evidence of hepatic dysfunction.

These liver function tests are usually performed

in cases where there is organic disease of the liver such as hepatitis or cirrhosis. A like disturbance in liver dysfunction can, however, occur where there is functional disturbance of the liver without any gross disease process. In shock, it is such a functional disturbance that we visualise although, as will be shown later, massive necrosis may occur in certain cases.

In our series of shock cases the alterations in the levels of amino acid, nitrogen, alkaline phosphatase and cholinesterase were not very marked. Nevertheless, they do indicate a disturbance in hepatic function and this disturbance in hepatic function continues for some time after clinical recovery from shock.

To corroborate this evidence of liver dysfunction and to determine whether there was evidence of gross liver damage in shock a histological investigation of the liver was carried out. This will now be considered.

Histological study of the Liver in fatal cases of shock.

The results of liver function tests are notoriously unreliable and further evidence was sought to determine the effects of shock on the liver.

In recent years considerable evidence has been accumulating to show that the liver is of considerable importance in shock. It has been shown by Frank, Seligman and Fine (1946) by viviperfusion of the liver in shocked animals, that loss of liver integrity is a factor of considerable significance in the collapse of the organism in advanced haemorrhagic shock, and that the preservation of liver function is of crucial importance in recovery from that condition. They also concluded that anoxia of other organs or tissues is not important in the development of "irreversibility" in shock.

This work has been confirmed by Cohn and Parsons (1950). Chambers et al, 1944 and Shorr and his co-workers (1948, 1945 and 1951) have shown that the vasodepressor material (V.D.M.) which appears to play a major part in shock is formed in the liver under anaerobic condition in shock.

Hepatic lesions in shock have been mentioned by a few authors. Davidson and his colleagues (1946) describe changes varying from degeneration to necrosis affecting the central zones of lobules in fatal cases of medical shock. Bywaters (1946) in a detailed

analysis of cases of crush injury reports that a large proportion of cases show necrosis of the central or midzonal cells of the liver lobules which appears histologically to date from the time of injury. Moon (1936, 1938), however, although describing dilatation and congestion of capillaries and venules, makes no mention of necrosis. Similarly Sheehan (1939) has described in some detail the changes found in 97 cases of obstetric shock but makes no mention of changes in the liver.

Material

The material for this study was obtained from 63 fatal cases of obstetric shock.

Microscopic study of Liver

In a preliminary histological survey it was found that the cases could be divided into 5 groups according to the liver lesions found.

Group 1 - There were 13 cases in this group. In all the liver appeared to be normal and no pathological lesion could be detected.

Group 2 - This group, in which there were 5 cases, was characterized by the occurrence of small vacuoles in the cells of the central zones of the lobules. This

is illustrated in Figure 11. Unfortunately, with the material at our disposal, it was not possible to determine whether these vacuoles were in actual fact due to infiltration of fat, although their appearance strongly suggested this possibility. Rolleston and McNee (1929) have stated that fatty infiltration of the liver is normally present during pregnancy and lactation. Similarly Ingerslev and Teilum (1945), in liver biopsy studies on pregnant women have found fatty vacuolation in the central zones of the liver lobules. However, intra-cellular hydropic, non-fatty vacuoles have been described in the liver in anoxic states by Bywaters (1946), Kritzler (1944) and Pappenheimer and Hawthorne (1936).

Group 3 - Seventeen of the cases were included in this group. The most striking histological change in the liver was a marked deposit of brownish-yellow pigment granules in the cells of the central zones of the lobules. Most commonly this was the only change, but in some lobules the cell-columns in these zones were broken up and occasional cells were undergoing disintegration with karyolysis of the nuclei (Figure 12).

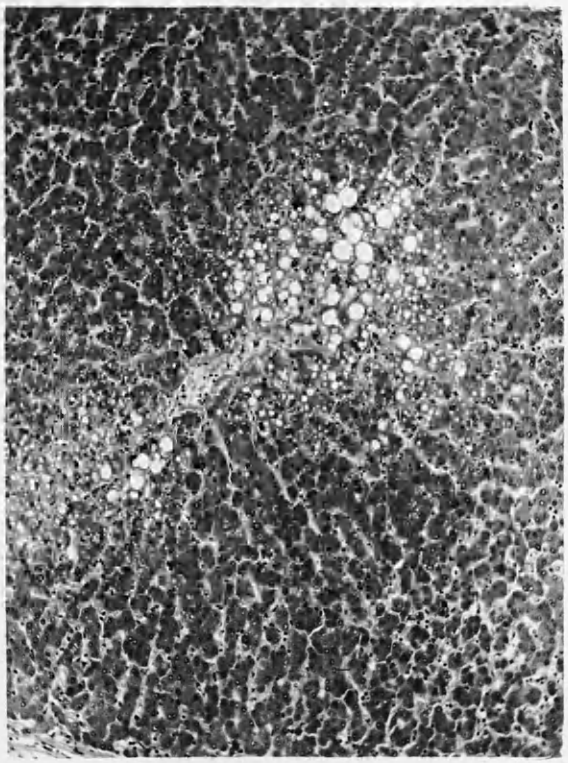


Figure 11.

Showing Group 2 type of liver lesion.

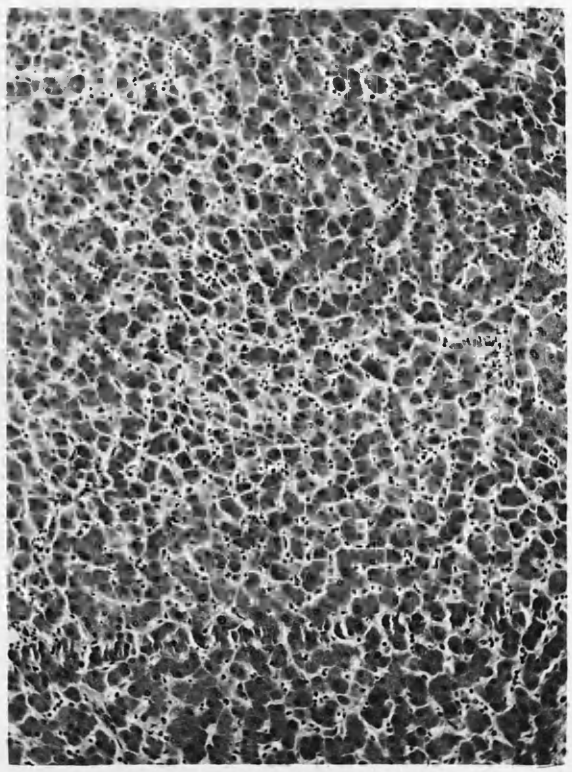


Figure 12.

Showing Group 3 type of liver lesion.

Group 4 - There were 16 cases in this group. In these cases there was a marked dilatation and congestion of the sinusoids of the central zones. The liver columns in this area were broken up and many of the cells were much narrower than usual. A variety of appearances were shown. In some instances the cells were merely narrow with dark nuclei and an accumulation of brown pigment granules in the cytoplasm. In others the cells were very eosinophilic with definite pyknosis of nuclei, while the surrounding cells showed a degree of fine vacuolation. Actual disintegration of a few cells was present.

Group 5 - The appearances in this group represented an advanced stage of those seen in Group 4. There were 12 cases and all showed well-marked necrosis which in almost all involved both central and mid-zones (Figure 13).

Incidence of Pre-eclamptic Toxaemia

One case in Group 2 had symptoms of pre-eclamptic toxaemia. In Group 3, 7 patients (41 per cent.) had pre-eclamptic toxaemia. Only 3 cases (18.75 per cent.) of Group 4 had pre-eclamptic toxaemia, while in Group 5 there were 5 cases (41.6

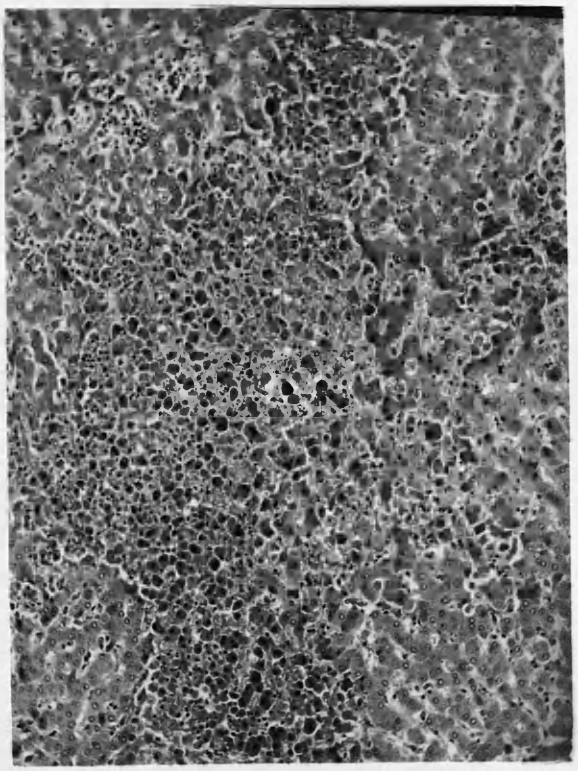


Figure 13.

Showing Group 5 type of liver lesion.

per cent. The majority of patients were healthy throughout pregnancy and there is no apparent relationship between toxaemia or other illness and the occurrence of hepatic necrosis in obstetric shock. More detailed analysis of the cases, however, has revealed the importance of toxaemia in this respect and this will be considered at length later.

Conditions causing shock.

Where there was more than one cause for the production of shock the cause which was considered most important has been given in Table 38.

Table 38.

	Group 1	Group 2	Group 3	Group 4	Group 5
Rupture of uterus	2	1	4	1	-
Retained placenta and post-partum haemorrhage	7	3	7	7	6
Dystocia	1	-	-	3	1
Inversion of uterus	1	-	-	-	-
Placenta praevia	1	-	-	2	1
Caesarean section	1	-	1	-	1
Caesarean section and hysterectomy	-	1	-	-	-
Accidental haemorrhage	-	-	5	3	4

It will be seen that haemorrhage in some form or other was the most common single cause and an even more significant feature in this analysis was

the occurrence of accidental haemorrhage in Groups 3, 4 and 5, and the absence in every case in Groups 1 and 2. This can be explained by the fact that accidental haemorrhage is almost always associated with pre-eclamptic toxaemia although this diagnosis could not be confirmed in all the cases in this series owing to a lack of ante-natal care.

Duration of Shock.

It is always difficult to assess accurately when a patient can be said to have recovered from the shock state and the assessment will obviously vary with the observer. Our scale is purely arbitrary and depends upon signs and symptoms of clinical improvement. The details are given in Table 39.

Table 39

Duration of shock in hours.

	0-2	2-4	4-8	8-16	16-32
Group 1	2	7	2	2	-
Group 2	2	2	-	1	-
Group 3	1	7	6	2	1
Group 4	-	1	4	6	5
Group 5	-	-	6	3	3

There is a rough correlation between the duration of shock and the incidence and severity of hepatic

lesions.

Survival Time.

The time of survival in the various groups is given in Table 40.

Table 40.

Hours	0-3	4-7	8-11	12-24	25-48	48+
Group 1	4	7	-	2	-	-
Group 2	3	1	1	-	-	-
Group 3	5	9	1	-	1	1
Group 4	1	4	3	4	4	-
Group 5	-	4	1	4	-	3

Several conclusions may be made from this survey. It can be seen that necrosis of the liver only develops after several hours. Secondly, cases which survived for a longer period and presumably therefore had a lesser degree of shock also showed necrosis of the liver, but the majority of cases with hepatic necrosis succumbed during the first 24 hours. It seems probable that the necrosis is related to events occurring within a relatively short space of time. On the basis of experimental work (Frank, Seligman and Fine, 1946), it is just possible too that some of those cases surviving longest might have survived altogether if the liver had remained intact. It is

evident also that the degree of shock is not sufficient to account for the necrosis in all cases.

Drugs

As most of the cases had associated blood loss oxytocics were frequently used. Ergometrine and extract of posterior pituitary were those employed either singly or in combination. (Table 41).

Table 41.

Group	1	2	3	4	5
Ergometrine	3	2	4	15	5
Posterior pituitary Extract	5	2	8	11	9

Strychnine was also given to one case in Group 5. Although, at first sight there is no relationship between either ergometrine or posterior pituitary extract and the occurrence of liver necrosis, a detailed scrutiny of the case histories showed that such a relationship might possibly exist. This will be discussed later.

No relationship could be established between the occurrence of the lesions and type of anaesthetic employed, amount of blood transfused or the severity of shock as judged by the blood pressure levels.

Biochemical Investigations.

Only 3 cases had a fairly complete biochemical investigation (Nos.61, 75 and 76). In these cases blood was withdrawn during the phase of shock before any form of treatment had been given.

Case 61 had a Group 3 type of liver lesion and in addition a patchy renal cortical necrosis. The urea value in this case was 43 mg.% while the amino-acid nitrogen was 3.5 mg.%. Case 64 had a Type 4 liver lesion, the urea value in this case being 25 mg.% and the amino-acid nitrogen value 4.83 mg.%. Case 75 had a Group 5 liver lesion and the urea was 46.5 mg.% while the amino-acid nitrogen was 6.36 mg.%.

The associated renal lesions in these cases produced a retention of urea and non-protein nitrogen, but the increase in amino-acids would tend to suggest some degree of liver failure. The normal amino acid nitrogen in pregnant women is given as 3.5 g. (Bonsnes, 1947). There is thus a definite increase in the amino acids in Cases 75 and 76, and the values are roughly proportional to the degree of hepatic damage in all 3 cases. Engel, Harrison and

Long (1944) have shown that the increase of blood amino acids during shock results from an increased breakdown of protein in the peripheral tissues, and that the acids accumulate in the blood either because they do not circulate through the liver at a sufficiently rapid rate or because, with continued anoxia, intrinsic damage to the hepatic parenchyma occurs and the liver is unable to dispose of them. They also found that anoxia of the rat liver for more than 45 minutes produced irreversible damage to this organ's ability to deal with amino acids.

Discussion

It is obvious that the etiology of these hepatic lesions in obstetric shock is not simple. The more marked degrees of liver damage were, in general, associated with prolonged shock but this was not so in all cases. Similarly, the degree of shock in these cases tended to be more severe but, again, no constant or direct relationship could be demonstrated. The lesions could not be attributed to any single factor and a combination of factors was therefore sought.

According to McMichael (1937), as the blood pressure falls the liver comes to depend more and

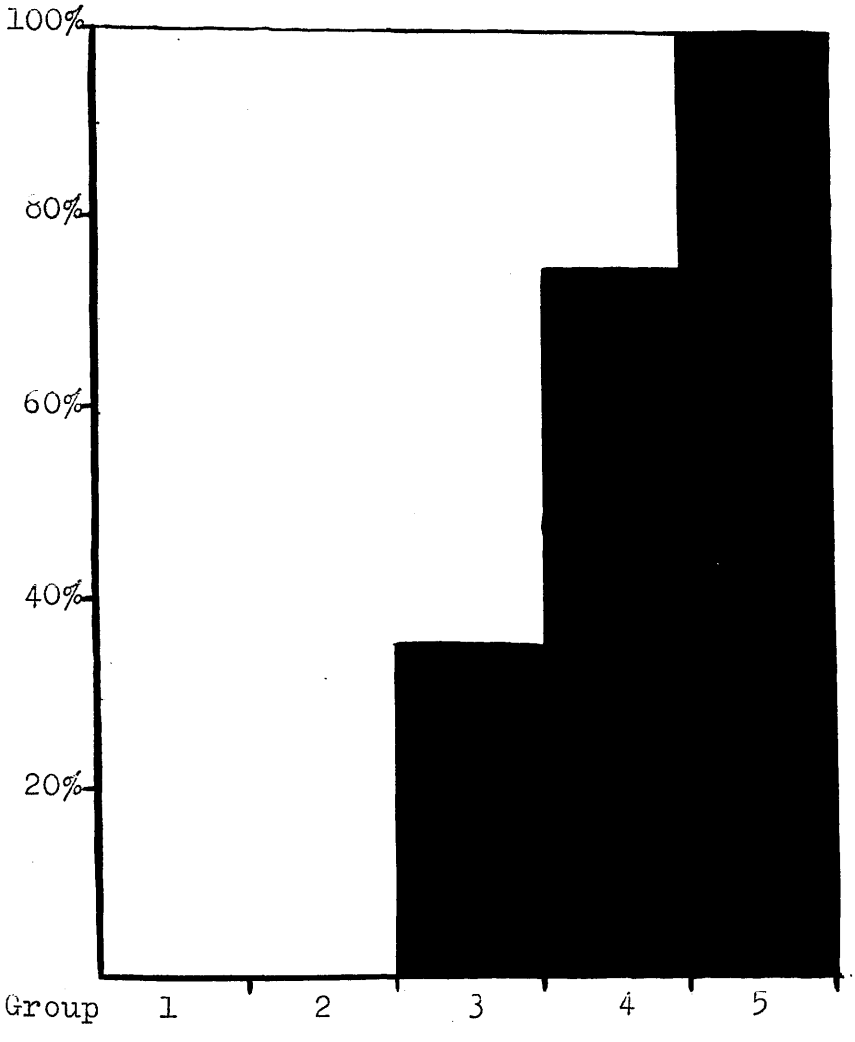
more upon its arterial supply, and Blalock and Mason (1936) found that constriction of the hepatic artery causes a marked diminution of the oxygen content of the hepatic venous outflow. Contrary to expectation they found that if constriction of the artery is maintained for some time the portal blood flow, after a temporary increase, returns to the pre-constriction level. The oxygen supply to the liver is therefore greatly diminished where vaso-constriction of the hepatic artery is prolonged. A similar state of affairs will follow upon marked diminution of the blood-pressure. Trueta et al (1947) have shown that the initial stages in the shock process are characterized by vaso-constriction, and, as is well-known, in the phase of fully-developed shock there is a vascular failure and the blood pressure falls. The effect on the liver will be more marked where shock is complicated by pre-existing vaso-constriction or where vaso-constriction is superadded to the fall in blood pressure. In our cases showing hepatic necrosis there was the association of severe shock with either pre-eclamptic toxaemia or the administration of posterior pituitary extract. For the purpose of this analysis an arbitrary

time of 5 hours was taken as indicative of prolonged shock. This time is convenient also since it has been shown that necrosis does not develop within the first 4 hours. This combination of prolonged shock and pre-eclamptic toxaemia or posterior pituitary extract occurred in 12 cases (100 per cent.) in group 5, 12 cases (75 per cent.) in Group 4, 6 cases (35.3 per cent.) in Group 3, and in none of the cases in Groups 1 and 2. This is shown graphically in Figure 14. Pre-eclamptic toxaemia is associated with marked vaso-constriction and posterior-pituitary extract is used because of its similar action on the vessels. Either of these superadded to shock will further reduce the blood supply to organs, and it seems reasonable to suggest that this was the mechanism producing hepatic necrosis in these cases.

The importance of these lesions is at least twofold. They are an indication that the liver may be severely damaged if shock is prolonged and according to Frank, Seligman and Fine (1946) this may be the deciding factor in producing irreversibility. This is merely another argument for early treatment of shock, especially by transfusions which will

Figure 14.

Illustrating relationship between prolonged shock and P.E.T. and pituitary extract.



· Percentage cases with combination of prolonged shock and pre-eclamptic toxaemia or posterior pituitary extract.

increase the blood supply to the liver. Also, any factor which may further diminish the blood supply to vital organs must be prevented or combated. Thus it would appear that the use of pituitrin is contra-indicated in the later stages of shock at least.

From our investigations into the biochemical and histological changes occurring in patients who have had shock due to haemorrhage it is concluded that damage occurs to the liver. Furthermore the damage is greater if there has been pre-existing pre-eclamptic toxaemia.

This damage to the liver may be merely coincidental and have no direct bearing on the clinical condition and possible fatal outcome in these shock cases but it seems likely to be otherwise. The importance of liver dysfunction in such cases now falls for discussion.

The role of liver dysfunction in shock.

Throughout the thesis reference has been made to the liver in the regulation of the various processes occurring in the body. A composite picture will now be presented of the various changes occurring in shock and their possible relationship to liver dysfunction.

In our studies we have been concerned mainly with the metabolic and electrolytic changes occurring in the blood when the patient is in a state of shock. These changes are so striking and the processes concerned are of such vital importance to the maintenance of normal function in the body that we feel that they are of primary importance in determining the degree of morbidity and possible mortality in patients with shock.

The factor or factors determining the alterations in metabolism and electrolyte balance will, therefore, require to be determined before the aetiology of shock can be known. In this section the relationship between liver dysfunction and the disturbances found in metabolism and electrolyte balance will be studied to try to determine whether liver dysfunction is the factor causing these alterations. In addition, in view of the apparently greater degree of shock sustained by patients with pre-eclamptic toxaemia, an attempt will be made to determine whether liver dysfunction plays any part in producing the more severe degrees of shock in these patients.

The liver in relation to metabolism in shock.

Nitrogen metabolism.

Nitrogen metabolism is at first increased in shock (Section 1) but in a later part of the shock phase there is a decrease in nitrogen metabolism. As we have previously noted the initial increase in nitrogen metabolism may be due to an "alarm reaction" as postulated by Selye (1950) in his "stress" theory which is related to activity of the suprarenal cortex.

In the succeeding phase of shock, however, nitrogen metabolism was found to be decreased; there was practically no rise in the level of blood urea even though the kidneys were inactive and at the same time the level of amino-acid nitrogen was maintained. This depression of nitrogen metabolism may be due to a reduced secretion of glucocorticoids from the suprarenal glands as postulated by Selye (1950) in his "stress theory" or it may be due to liver dysfunction. The possibility of a reduced secretion of glucocorticoids cannot be overlooked but this is purely a theoretical consideration. On the other hand it is known that liver dysfunction occurs

in these cases. Hepatic dysfunction will interfere with nitrogen metabolism as the liver is the main site of deamination although this process of breaking down of amino acids occurs to a lesser extent in the kidneys and other tissues. Interference with deamination due to liver dysfunction will cause a reduced formation of urea with a maintenance of blood amino acids such as was found in the patients with shock.

Although it may not be the only cause of reduced nitrogen metabolism in the later phase of shock, liver dysfunction would certainly seem to play an important role.

Carbohydrate metabolism.

As we have shown, there is a considerable disturbance of carbohydrate metabolism in shock. Although there is a marked rise in blood glucose levels the processes involved in carbohydrate metabolism are depressed.

The striking rise which occurs in blood glucose in shock requires consideration in regard to the activity of the liver, as the source of the glucose is the glycogen of the liver. Some of the glucose

is derived from muscle glycogen but this occurs indirectly through the liver as described in the Cori "cycle" (1927). Again, the glucose is in part derived from protein by the process of gluconeogenesis but here also the source is indirect as the liver once more acts as an intermediary.

The rise in blood glucose in shock can only be accounted for by a breakdown of liver glycogen.

Despite the large quantities of glucose produced in the blood in shock there is deficient utilisation of this glucose. There is a resultant accumulation of intermediate products of carbohydrate metabolism, such as pyruvic and lactic acids in the blood. In addition there is a reduced amount of inorganic phosphate in the blood.

Pyruvic and lactic acids, under normal circumstances, are partly catabolised and partly converted to glycogen in the liver. With an adequate supply of oxygen no lactic acid is formed, and of that produced anaerobically 1/5 is oxidised through pyruvic acid to carbon dioxide and water, and the remainder resynthesised to glycogen in the liver (Best and Taylor, 1950). When there is liver dysfunction

there will be a failure or a reduction in the amount of conversion of pyruvic and lactic acids to glycogen. This will cause a resultant increase in the amounts of pyruvic and lactic acids in the blood. Our results have shown just such an increase in the blood in shock and a comparable rise in lactic acid has been found by several workers (Riegel, 1927; Gesell et al, 1930; Gutmann et al., 1941; Swan, 1943; Cournand et al, 1943; and Beatty , 1945). Liver dysfunction may, therefore, be postulated as the cause of the increased amounts of pyruvic and lactic acids found in the blood of patients with shock.

Similarly the decrease in inorganic phosphates can be explained on the basis of hepatic dysfunction as the main site of the phosphorylation process is the liver.

Although it is doubtful whether liver dysfunction has any part to play in the rapid breakdown of liver glycogen to form blood glucose there is a distinct possibility that the deficiency in carbohydrate metabolism which occurs can be attributed to hepatic dysfunction.

The liver in relation to electrolytes in shock.

There is a quite marked fall in sodium and rise

in potassium in the blood of patients with shock. Several possible explanations for this have been advanced in the section on electrolytes. One explanation of the alteration in electrolytes is that sodium moves into while potassium passes out of damaged tissues. Liver damage may, therefore, be postulated as one factor concerned in the changes in electrolytes.

Liver function in relation to pre-eclamptic toxaemia and shock.

In a previous section we have shown that the degree of shock and likelihood of a fatal outcome are greater if the patient has had a pre-existing pre-eclamptic toxaemia. If liver dysfunction does play an important role in the production of the shock state then it would be reasonable to assume that a greater degree of liver damage occurs in these patients.

The existence of a state of hepatic dysfunction in pregnancy toxaemias has been suggested by Herold (1928); Hofbauer (1933); Botella-Llusia (1936); and Rowe et al (1936). Well marked changes are known to occur in the livers of patients dying of pre-eclamptic

toxaemia. In addition we found that the degree of liver damage sustained by pre-eclamptic patients who suffered shock was greater than non-toxaemic patients. The greater degree of shock evidenced by more marked changes in metabolism and electrolytes may, therefore, be partly explained by the greater degree of liver damage.

To summarise, then, we have established that hepatic dysfunction occurs in haemorrhagic shock. The changes noted in nitrogen and carbohydrate metabolism can, at least partly, be explained on the basis of liver damage. Electrolyte changes may be equally explained on this basis of hepatic dysfunction. The greater tendency of pre-eclamptic patients to suffer a more severe degree of shock may also be dependent upon the more marked damage to the liver sustained by these patients.

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SUMMARY AND CONCLUSIONS

In this summary we have recapitulated as briefly as possible the facts as we have found them in haemorrhagic shock of pregnancy. An attempt has been made to give a reasonable explanation for their occurrence and to provide a possible correlation between the various factors.

In the early phase of shock there is a rapid breakdown of protein and an outpouring of glucose into the blood stream. These two processes are probably related. The only feasible explanation for the hyperglycaemia is that the body demands a source of energy. The glycogen of the liver is mobilised and at the same time protein is broken down to replenish the store of hepatic carbohydrate. It is obvious, however, from a study of the intermediate products of carbohydrate metabolism and of blood inorganic phosphate that the further metabolism of carbohydrate is deranged. The subsequent phase of diminished protein breakdown is to be related to this fact. It is possible that with the accumulation of pyruvic and lactic acids some form of the Law of Mass Action is brought into play and this will

interfere with nitrogen catabolism.

It has been shown that there is a marked fall in blood sodium associated with a rise in potassium. The movement of sodium we feel is not a simple reaction due to any one factor. There is a pronounced acidosis in shock as witness the accumulation of pyruvic and lactic acids in the blood and also to some extent of chlorides. These acidic products are bound to be present in high concentration in the tissues particularly as the circulation is deficient. The migration of sodium is probably, in part at least, designed to ameliorate this tissue acidosis. There is however, no great movement of fluid into the tissues as one would expect if the sodium ions were accumulating in the tissue spaces. Our study of haematocrit readings shows that, on the contrary, haemodilution is a constant feature. It seems likely that much of the sodium enters directly into the tissue cells. This may be related to the movement of potassium from the cells into the blood. Increasing evidence has been found to indicate that potassium plays an important part in the metabolism of carbohydrate. In view of the results of our

investigation of carbohydrate metabolism it would be reasonable to interpret these changes in electrolytes as largely due to an active mobilisation of potassium in an attempt to maintain energy production by means of carbohydrate breakdown. At the same time it is possible that part of the change in the concentrations of these ions is due to their migration to and from damaged cells.

The occurrence of haemodilution in association with a migration of sodium to the tissues is surprising and not in accordance with current theories regarding body water regulation. It may be, however, that this movement of fluid in a direction contrary to the sodium ions is brought about by the osmotic effect of the increased blood glucose. Several workers have suggested that there may be a pooling of concentrated blood in certain parts of the vascular tree outside of the effective circulatory area during shock. This would lead to a marked rise in haemoglobin once the normal circulation was re-established. No such increase occurs in our cases and we are forced to conclude that this mechanism does not operate in haemorrhagic shock at least.

An investigation of liver function has shown that there is a considerable derangement of this organ in cases of haemorrhagic shock. To what extent this is responsible for the biochemical changes noted is not clear. Theoretically it is possible to explain many of the altered values on the basis of liver damage, particularly those related to the breakdown of carbohydrate and the later phase of diminished nitrogen metabolism. It is, however, difficult to imagine that liver dysfunction could be co-existent with the initial phase of hyperglycaemia and increased nitrogen metabolism. Nevertheless this upset in liver function is important and will have considerable prognostic influence. The degree of liver damage will vary according to circumstances but in some cases, as we have shown, it may be gross and lead to a considerable degree of necrosis. It is interesting to note that, according to Frank, Seligman and Fine (1948) and Cohn and Parsons (1950) the integrity of the liver is the factor which decides the reversibility of the shock syndrome. Apart from metabolic changes the liver may be responsible for some of the vascular changes by virtue of its VDM

production. It is likely that the interplay of hepatic VDM and renal VEM may decide the severity of the circulatory upset.

It will be seen from our results and the authorities we have quoted that the biochemical changes following haemorrhage in our patients resemble closely those reported in cases of traumatic shock. There is however a marked contrast in the blood volume changes in the two conditions. Haemorrhage is associated with haemodilution, traumatic shock with haemoconcentration. For this reason many authors (Cannon, 1923; Moon, 1938; Scudder, 1940) have made a differentiation between haemorrhage and shock. In our opinion, however, the alteration in blood volume in haemorrhagic shock is of secondary importance. In both traumatic and haemorrhagic shock the essential feature is anoxia; in the former it is of "stagnant" type whereas in the latter it is anaemic. It is felt that in either case tissue anoxia is the "trigger" which sets off the series of metabolic changes characterising the shock syndrome.

Thus far we have been able to show that, by and large, the same changes may be expected in traumatic

and haemorrhagic shock. It is known however that loss of blood in certain pregnant women leads to a more severe degree of shock than might be expected. A non-pregnant blood donor can lose as much as two pints without any marked effect. Such a loss in certain pregnant women would produce profound shock. This is particularly noticeable in patients suffering from pre-eclamptic toxaemia. We have been able to show that these patients are more liable to succumb following haemorrhage than normal pregnant women. A study of the biochemical changes showed that these cases had an apparently greater difficulty in metabolising glucose as indicated by the higher values for blood pyruvates. Other changes such as the movements of the electrolytes appeared to be hindered and delayed. This we have interpreted as being due to the pre-existing upset in carbohydrate metabolism and electrolyte balance. In addition these women suffer from oligaemia during the course of their toxaemia and this will interfere profoundly with the maintenance of the circulatory volume following haemorrhage. From a consideration of all these points and from a knowledge of the undoubted upset

of liver function in pre-eclamptic toxaemia it is not surprising that shock in toxaemic patients is associated with an increased mortality rate.

This greater susceptibility of the toxaemic patient to succumb from shock may well be related to the degree of liver damage sustained. In our histological investigations it was found that marked necrosis of the liver occurred only if there was a combination of prolonged shock and pre-eclamptic toxaemia or the administration of posterior pituitary extract. Pre-eclamptic toxaemia is associated with marked vaso-constriction and posterior pituitary extract is used because of its similar action on the vessels. Either of these superadded to shock will further reduce the blood supply to organs and it seems reasonable to suggest that this was the mechanism producing hepatic necrosis in these cases.

An incidental finding of interest was that in cases of accidental haemorrhage the rise in amino-acid nitrogen levels was no greater than in cases of post-partum haemorrhage. From this it is deduced that tissue destruction is not a major feature of accidental haemorrhage and, if it occurs, the products are not

absorbed to any significant degree.

Thus far we have described the changes in haemorrhagic shock in pregnancy and we have shown that they differ only slightly from those occurring in traumatic shock. The mechanism whereby they are brought about, however, is obscure and the evidence at our disposal will not allow us to make more than a tentative suggestion. We have indicated that some of the phenomena observed may be related to liver dysfunction but this cannot be a factor in the primary changes in the syndrome. The rapid liberation of glycogen and the increased nitrogen catabolism found in the initial phase are not compatible with any degree of hepatic derangement. They could however be associated with increased function of the adrenals, both medulla and cortex. The later phases of the syndrome nevertheless are probably related to upset in hepatic activity and this may play a large part in determining the severity and prognosis of the condition.

Throughout the thesis mention has been made of certain investigations which have been reported at length by the writer in papers published elsewhere.

A list of these references is appended below.

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PROTOCOL.

Case 1

Primigravida, aged 28. Spontaneous delivery. Placenta retained and post-partum haemorrhage. Placenta expelled 3 hours after delivery. One pint of plasma and 1 pint of blood transfused. Shock lasted for 4 hours and no urine was passed in the first 12 hours.

	Before Shock	During Shock (Before Transfn.)
Hb.	11.6 g. - 73%	9.5 g. - 60%
P.C.V.	35	28
Urea mg.%	38	46
Uric Acid mg.%	5.80	
Amino Acid Nitrogen mg.%	5.18	

Case 2

Para 2, aged 25. Dystocia; mid-forceps; slight post-partum haemorrhage. Shock lasted 8 hours. No urine passed in first 12 hours. Transfusion of 2 pints blood.

		During Shock	
	Before Shock	Before Transfn.	After Transfn.
Hb.	12.7g.-80%	10g.-63%	12g.-75%
P.C.V.	32	20	38
Urea mg.%	29.4	38.8	39.6
Uric Acid mg.%	-	5.55	-
Amino Acid Nitrogen mg.%	-	4.38	-

Case 3

Primigravida aged 27. Marginal placenta praevia. Classical Caesarean Section with excessive blood loss. Shock lasted 3 hours. No urine voided in first 12 hours. Transfusion 2 pints blood.

		During Shock		
	Before Shock	Before Transfn.	After Transfn.	4th Day
Hb.	7.5g.-50%	7.1g.-45%	7.5g.-47%	6.4g.-40%
P.C.V.	29	27	29	22
Urea mg.%	26	33.3	33.2	24
Uric Acid mg.%	3.2	4.1	4.0	3.3
Amino Acid Nitrogen mg.%	4.3	4.4	4.5	4.2
Sodium mg.%	341.5	290	327	345
Potassium mg.%	19.7	21.4	21.2	19.8
Chloride mg.%	658	652.3	649.4	585
Alkaline Phosphatase	10.4	15.5	10.0	10.3

Case 4

Para 3, aged 30. Repeat Caesarean Section. Shocked at end of operation. Shock lasted 3 hour and 4 ozs. of urine passed in 12 hours. Two pints blood transfused.

		During Shock		
	Before Shock	Before Transfn.	After Transfn.	4th Day
Hb.		11.7g.-73%	11.3g.-71%	9.8g.-62%
P.C.V.		33.5	33.0	26
Urea mg.%	15	15.4	18.2	28
Sugar mg.%		181	141	
Sodium mg.%	335	300	293	320
Potassium mg.%	18.4	22.0	21.6	19.0
Chloride mg.%	648.7	684.5	649.3	

Case 5

Para 2, aged 32. Retained placenta with post-partum haemorrhage. Shock lasted for 3 hours and 8 ozs. of urine were passed in 24 hours. One pint of blood was transfused.

		During Shock		
	Before Shock	Before Transfn.	After Transfn.	3rd Day
Hb.	-	11.5g.-72%	9.9g.-62%	6.3g.-
P.C.V.	-	33	28	19.5
Urea mg.%	29.3	34.2	38.6	39
Uric Acid mg.%	-	4.1	4.2	3.85
Amino Acid Nitrogen mg.%	-	5.4	4.65	5.0
Sugar mg.%	-	140	138	94

Case 6

Primigravida, aged 24. Retained placenta with post-partum haemorrhage. Shock lasted for 3 hours and 6 ozs. of urine were passed in 9 hours. Blood transfusion 2 pints. Pseudo-cholinesterase during shock - 7.8.

Case 7

Para 3, aged 31. Post-partum haemorrhage. Shock lasted 12 hours. Ten ozs. of urine passed in 21 hours. Seven pints of blood and 1 pint Dextrose 10% transfused.

	Before Transfn.	3rd Day	4th Day	5th Day	6th Day
Hb.	12.8g.-80%	-	9.9g.-62%	11.0g.-69%	10.5g.-66%
P.C.V.	35	-	28.5	29	32.5
Urea mg.%	31	-	32	29	26
Amino Acid Nitrogen mg.%	5.3	-	-	6	6
Sugar mg.%	204	-	-	-	-
Pyruvates mg.%	1.88	-	0.56	1.24	0.64
Pseudo Cholinesterase	1.52	1.37	1.16	1.09	1.09

Case 8

Para 5, aged 34. Incomplete abortion with haemorrhage. Shock lasted for 10 hours and 6 ozs. of urine were passed in 17 hours. One pint of blood and one pint saline transfused.

	Before Transfn.	After Transfn.
Hb.	-	8.9g.-56%
P.C.V.	-	20
Urea mg.%	27	28
Sodium mg.%	327	321
Potassium mg.%	19.4	22.2
Pyruvates	0.68	1.94
Pseudo Cholinesterase	1.61	1.32

Case 9

Para 8, aged 34. Caesarean Section with excessive loss of blood. Shock lasted 5½ hours and output of urine was 12 ozs. in 24 hours. Four pints of blood transfused.

	Before Transfn.	2nd Day	3rd Day	4th Day
Hb.	10.5g.-66%	9.6g.-60%	8.8g.-55%	8.8g.-55%
P.C.V.	32.5	27.5	24.5	26.5
Urea mg.%	23	29	27	31
Amino Acid Nitrogen mg.%	4.7	4.0	5.3	9
Sodium mg.%	306	312	312	327
Potassium mg.%	24.4	27.3	31.1	-
Pyruvates mg.%	1.44	1.24	1.04	1.80
Inorganic Phosphates mg.%	2.4	-	2.4	-
Pseudo-Cholinesterase	1.26	1.30	1.24	1.83

Case 10

Para 5, aged 28. Retained placenta with post-partum haemorrhage. Shock lasted for 7½ hours and no urine was passed in 12 hours. Blood transfusion 3 pints.

	Before Transfn.	After Transfn.	2nd Day
Hb.	10.3g.-65%	13.0g.-82%	9.1g.-57%
P.C.V.	31	37	28
Urea mg.%	16	16	29
Uric Acid mg.%	11	12.1	9.5
Amino Acid Nitrogen mg.%	8.7	8.1	8
Potassium mg.%	24.4	26.7	28.0
Pyruvates mg.%	1.42	-	1.33

Case 11

Primigravida aged 22. Mixed accidental haemorrhage. Retroplacental clot 1-6/16 lbs. Shock lasted for 5½ hours and no urine was passed in first 12 hours. One pint plasma and 2 pints blood transfused.

	Before Transfn.	5th Day
Hb.	8.8g.-55%	5.6g.-35%
P.C.V.	24	16.5
Urea mg.%	24.9	24.0
Uric Acid mg.%	2.4	3.45
Amino Acid Nitrogen	7.3	4.56

Case 12

Primigravida, aged 24. B.P. 150/90 mm.Hg. and oedema for one month. Forceps delivery and post-partum haemorrhage. Shock lasted 4 hours and output of urine first 12 hours was 3 ozs. One pint plasma and one pint blood transfused.

		During Shock		
	Before Shock	Before Transfn.	After Transfn.	4th Day
Hb.	-	8.1g.-51%	8.4g.-53%	5.7g.-35%
P.C.V.	-	26	26	16.5
Urea mg.%	25.6	40	40.5	23.5
Sugar mg.%	-	126.5	-	-
Sodium mg.%	350	310	306	345
Potassium mg.%	18.0	21.2	20.8	23.5
Chloride	605.2	667	626	-

Case 13

Para 4, aged 27. B.P. 204/150 mm.Hg., oedema and albuminuria. Post-partum haemorrhage. Shock lasted for 1 hour and 6 ozs.of urine were passed in 12 hours. One pint of blood and one pint 5% saline transfused.

	Before Transfn.	After Transfn.	4th Day
Hb.	8.5g.-53%	8.2g.-52%	7.0g.-44%
P.C.V.	30	30	21
Urea mg.%	32.5	37.6	36
Uric Acid mg.%	4.2	4.2	3.8
Amino Acid Nitrogen mg.%	4.8	4.55	4.0

Case 14

Para 4, aged 35. Retained placenta with post-partum haemorrhage. Shock lasted for 5 hours and urinary output was 2 ozs. in 12 hours. Two pints of blood and 1 pint 5% glucose saline transfused.

	Before Transfn.	After Transfn.	2nd Day
Hb.	8 g.-50%	7.3g.-46%	8.4g.-53%
P.C.V.	23.5	22	26
Urea mg.%	25	35.5	25

Case 15

Primigravida, aged 28. Post-partum haemorrhage. Shock lasted for 2 hours and anuria occurred for first 12 hours. One pint plasma and one pint blood transfused.

	Before Transfn.	After Transfn.
Hb.	10.9g.-68%	11.1g.-70%
P.C.V.	32.5	31
Urea mg.%	28	31
Uric Acid mg.%	4.1	4.1
Amino Acid Nitrogen mg.%	7.8	5.0

Case 16

Para 2, aged 29. Post-partum haemorrhage. Shock lasted for 7 hours. Two ozs. urine obtained in first 12 hours. Two pints blood and 1 pint plasma transfused.

	Before Transfn.	After Transfn.	7th Day
Hb.	11.0g.-69%	10.9g.-68%	8.9g.-56%
P.C.V.	26	26	22
Urea mg.%	31.7	33.0	30.0
Uric Acid mg.%	4.3	3.8	3.65
Amino Acid Nitrogen mg.%	4.3	4.8	5.0

Case 17

Primigravida aged 24. Retained placenta with post-partum haemorrhage. Shock lasted for 4 hours. No urine passed in 12 hours. One pint plasma and 2 pints blood transfused.

	Before Transfn.	After Transfn.	2nd Day	3rd Day
Hb.	12g.-75%	11.5g.-72%	11.6g.-73%	11.6g.-73%
P.C.V.	26	24	26.5	21.5
Urea mg.%	17	25	23	17
Uric Acid mg.%	3.2	3.2	3.2	3.2
Amino Acid Nitrogen mg.%	5.7	3.15	5.7	4.5
Sodium mg.%	350	335	335	335
Potassium mg.%	21	22	18	20
Chloride mg.%	500	525	525	530

Case 18

Para 5, aged 34. Post-partum haemorrhage. Shock lasted for 4 hours. No urine obtained in first 12 hours. Three pints of blood and one pint plasma transfused.

	Before Transfn.	After Transfn.	2nd Day	4th Day
Hb.	10.2g.-64%	8.2g.-52%	6.1g.-38%	5.2g.-32%
P.C.V.	34	30	22.5	17
Urea mg.%	40	29	30.5	30.0
Uric Acid mg.%	8.9	3.7	5.5	4.45
Amino Acid Nitrogen mg.%	10.0	4.9	4.8	4.8

Case 19

Para 4, aged 27. Hydramnios due to anencephaly. Artificial rupture of membranes with ante-partum haemorrhage, shock lasted for 2 hours. No urine passed in 12 hours. One pint plasma transfused.

	Before Transfn.	After Transfn.	3rd Day
Hb.	8.5g.-53%	7.8g.-49%	5.7g.-34%
P.C.V.	28.5	25.5	19
Urea mg.%	37.8	30	25.0
Uric Acid mg.%	4.2	4.25	3.25
Amino Acid Nitrogen mg.%	4.2	4.4	4.34

Case 20

Para 11, aged 44. Mixed accidental haemorrhage with 7 ozs. retroplacental clot. Shock lasted for 18 hours. Oliguria lasted for 3 days. Four pints of blood and 1 pint plasma transfused.

	Before Transfn.	2nd Day	3rd Day
Hb.	10.5g.-66%	8.5g.-53%	-
P.C.V.	30	25	-
Urea mg.%	42.0	91.5	132.0
Uric Acid mg.%	3.9	8.6	9.0
Amino Acid Nitrogen mg.%	7.5	8.0	8.5
Chloride mg.%	525	520	470

Case 21

Para 8, aged 37. Mixed accidental haemorrhage with 1½ lbs. retroplacental clot. Shock lasted for 18 hours and oliguria persisted for 2½ days. One pint of plasma and 5 pints of blood transfused.

	Before Transfn.	After Transfn.	2nd Day	3rd Day	4th Day
Hb.	7.5g.-47%	-	-	8.0g.-50%	-
P.C.V.	19	-	-	22	-
Urea mg.%	40.5	80	80	88	63.0
Uric Acid mg.%	6.6	-	11.6	14.2	13.5
Amino Acid Nitrogen mg.%	6.35	-	6.65	6	5.8
Sodium mg.%	348	-	377	-	-
Potassium mg.%	13.3	-	18	-	-
Chloride mg.%	524	585	570	575	-

Case 22

Primigravida aged 30. Mixed accidental haemorrhage with 18 ozs. retroplacental clot. Duration of shock was 5 hours and there was anoxia for 16 hours. Half pint plasma and 2 pints blood transfused.

	Before Transfn.	After Transfn.	2nd Day	3rd Day
Hb.	11.5g.-72%	11.2g.-70%	9.6g.-60%	9.1g.-57%
P.C.V.	28	31.5	22.5	25
Urea mg.%	31	36	40	32
Uric Acid mg.%	6.25	8.5	8.5	7.2
Amino Acid Nitrogen mg.%	6	5.8	6.9	6.26
Inorganic Phosphates mg.%	3.1	5	5.7	

Case 23

Para 7, aged 30. Concealed accidental haemorrhage with retroplacental clot of 2-5/16 lbs. Shock lasted for 20 hours and oliguria persisted for 2 days. Blood transfusion of 1½ pints given.

	Before Transfn.	2nd Day	3rd Day
Hb.	8.0g.-50%	5.4g.-34%	4.3g.-27%
P.C.V.	21	16	13.5
Urea mg.%	31.5	44	50
Uric Acid mg.%	7.3	10.3	-
Amino Acid Nitrogen mg.%	6.5	6.2	-
Sodium mg.%	300	311	-
Chloride mg.%	580	580	-

Case 24

Para 4, aged 27. Hypertension (140/90 mm.Hg.), oedema, albuminuria, headache and visual disturbances during pregnancy. Hydrops foetalis with large placenta. Post-partum haemorrhage occurred. Duration of shock was 12 hours. Oliguria persisted for 4 days. Jaundice appeared on the day following shock. Patient gradually improved and was discharged from hospital. She died one month later in her own home. No post-mortem performed.

	Before Transfn.	After Transfn.	2nd Day	3rd Day	4th Day
Hb.	9.7g.-61%	9.9g.-63%	8.4g.-53%	6.6g.-41%	6.9g.-43%
P.C.V.	26	25	22	17	15
Urea mg.%	24	52.5	116	67	80
Amino Acid Nitrogen mg.%	7.4	9.5	7.78	9.36	8.5
Sugar mg.%	212	-	-	-	-
Sodium mg.%	392	315	347	347	347
Potassium mg.%	28	52	42	-	32
Chloride mg.%	585	535	555	545	545
Alkaline Phosphatase mg.%	10	5	-	-	-

Case 25

Primigravida aged 21. Mixed accidental haemorrhage with 22 ozs. retroplacental clot. Shock lasted for 5 hours and there was anuria for the first 24 hours. No transfusion was given.

	Before Transfn.	3rd Day
Hb.	11.3g. - 71%	8.5g.-53%
P.C.V.	31.5	24
Urea mg.%	31	24.5
Sodium mg.%	321	327
Potassium mg.%	17.6	19.4
Pyruvates mg.%	2.59	1.50

Case 26

Para 5, aged 41. Mixed accidental haemorrhage, with 19 ozs. retroplacental clot. Hypertension (200/120 mm.Hg.), oedema and albuminuria during pregnancy. Shock lasted for 24 hours and oliguria persisted for 4 days. Three pints of blood transfused.

	Before Transfn.	2nd Day	3rd Day	4th Day
Hb.	12.4g.-78%	10.6g.-67%	8.3g.-52%	-
P.C.V.	28	26	20	-
Urea mg.%	43	54	49.5	-
Uric Acid mg.%	6.0	16	-	16
Amino Acid Nitrogen mg.%	6.6	10.35	6.9	-
Sodium mg.%	327	333	327	306
Pyruvates mg.%	2.14	3.77	-	1.70

Case 27

Primigravida aged 20. Hypertension (195/145 mm. Hg.), oedema, and albuminuria during pregnancy. Mixed accidental haemorrhage with retroplacental clot of 14 ozs. Shock lasted for 12 hours and there was oliguria for 2 days. One pint of blood transfused.

	Before Transfn.	2nd Day	3rd Day	4th Day
Hb.	8.4g.-53%	5.5g.-34%	7.1g.-45%	-
P.C.V.	18	14	17	-
Urea mg.%	42	55	72	54
Uric Acid mg.%	7.75	-	-	-
Amino Acid Nitrogen mg.%	5.85	-	-	-
Chlorides mg.%	590	-	-	-

Case 28

Para 5, aged 38. Caesarean Section followed by hysterectomy because of placenta accreta. Duration of shock was 24 hours and oliguria persisted for 4 days. Six pints of blood transfused.

	Before Shock	Before Transfn.	After Transfn.	2nd Day	4th Day	6th Day
Hb.	-	-	10.3g.- 65%	10.3g- 65%	-	7.5g.- 47%
P.C.V.	-	-	28	27	-	19.5
Urea mg.%	24	-	45	65	-	50
Chloride mg.%	-	-	546	567	-	530
Pyruvates mg.%	-	1.16	4.6	-	3.93	3.85
Cholinesterase mg.%	-	1.23	1.19	1.16	1.0	-

Case 29

Para 2, aged 37. Retained placenta with post-partum haemorrhage. Shock lasted for 6 hours and 3 ozs. of urine were passed in the first 24 hours. Four pints of blood were transfused.

	During Shock. Before Transfn.
Hb.	11.4g. - 71%
P.C.V.	38.5
Urea mg.%	30
Amino Acid Nitrogen mg.%	2.4
Sodium mg.%	306
Potassium mg.%	35.5
Pyruvates mg.%	2.42
Pseudo-Cholinesterase	1.85

Case 30

Primigravida, aged 23. Post-partum haemorrhage. Shock lasted for 5 hours and no urine was passed in first 12 hours. Blood transfusion 2 pints.

	Before Transfn.	After Transfn.	3rd Day
Hb.	8.8g.-55%	7.3g.-46%	6.9g.-43%
P.C.V.	28.5	25.5	20.5
Urea mg.%	29.5	32	25.0
Uric Acid mg.%	3.0	4.2	3.28
Amino Acid Nitrogen mg.%	6.4	6.2	4.0

Case 31

Para 3, aged 23. Mixed accidental haemorrhage with 6 ozs. retroplacental clot. Shock lasted for 18 hours and no urine was passed in 20 hours. No transfusion was given.

	Before Transfn.	After Transfn.	2nd Day
Hb.	9.3g.-58%	9.0g.-57%	8.7g.-55%
P.C.V.	25	30	24
Urea mg.%	44.8	43.5	40.8
Uric Acid mg.%	4.52	4.15	5.15
Amino Acid Nitrogen mg.%	5.09	3.23	5.20

Case 32

Para 6, aged 36. Oedema, headaches and visual disturbances during pregnancy. Mixed accidental haemorrhage with 10½ ozs. retroplacental clot. Shock lasted for 8 hours and 2 ozs. of urine were passed in 24 hours. One pint blood was transfused.

	Before Transfn.	2nd Day	6th Day
Hb.	7.1g.-45%	8g.-50%	7.5g.-47%
P.C.V.	16	22	18
Urea mg.%	30	36	32.5
Uric Acid mg.%	7.07	6.7	-
Amino Acid Nitrogen mg.%	10.05	7.6	7.6
Sodium mg.%	373	410	410
Chloride mg.%	595	585	595

Case 33

Para 2, aged 29. Retained placenta and post-partum haemorrhage. Shock lasted for 4 hours and 2 ozs. of urine were obtained in 24 hours. Blood transfusion of 3 pints.

	Before Transfn.	After Transfn.	2nd Day
Hb.	9.9g.-62%	11.5g.-72%	8.9g.-56%
P.C.V.	31	34	27
Urea mg.%	31	31	29.5
Uric Acid mg.%	3.2	4.4	3.9
Amino Acid Nitrogen mg.%	4.9	6	5.6
Sodium mg.%	342	321	321
Potassium mg.%	19.5	-	19.5

Case 34

Primigravida, aged 22. Mixed accidental haemorrhage with 10 ozs. retroplacental clot. Shock lasted for 8 hours and oliguria lasted for 3 days.

Case 35

Para 2, aged 38. Hypertension (156/100 mm.Hg.), albuminuria, and oedema during pregnancy. Dystocia and forceps delivery. Shock lasted for 6 hours and anuria was present for 12 hours. One pint of blood and one pint plasma transfused.

	During Shock Before Transfn.	4th Day
Hb.	12g. - 75%	8.8g.-55%
P.C.V.	36	26
Urea mg.%	20	16.5
Uric Acid mg.%	8.0	7.0
Amino Acid Nitrogen mg.%	4.55	5.6
Sodium mg.%	300	306
Potassium mg.%	17	16
Chloride mg.%	613	613
Pyruvates mg.%	2.16	0.98

Case 36

Para 3, aged 27. Post-partum haemorrhage. Shock lasted for 4 hours and no urine was passed in 12 hours. Three pints of blood transfused.

	During Shock Before Transfn.
Urea mg.%	39
Amino Acid Nitrogen mg.%	7
Sodium mg.%	309
Chloride mg.%	639

Case 37

Para 2, aged 27. Post-partum haemorrhage. Shock lasted for 5 hours and no urine was obtained in 12 hours. One pint blood transfused.

	During Shock Before Transfn.
Hb.	-
P.C.V.	32.5
Urea mg.%	27
Uric Acid mg.%	3.7
Amino Acid Nitrogen mg.%	4
Sodium mg.%	321
Potassium mg.%	23
Chloride mg.%	631
Pyruvates mg.%	2.22

Case 38

Primigravida, aged 21. Abortion after 12 weeks gestation. Shock lasted for 7 hours and 4 ozs.of urine were passed in 12 hours. Two pints blood transfused.

	Before Transfn.
Hb.	11g. - 69%
P.C.V.	29.5
Pseudo-Cholinesterase	1.18
Alkaline Phosphatase	8.0

Case 39

Para 2, aged 24. Post-partum haemorrhage. Shock lasted for 8 hours and 2 ozs.of urine were passed in 12 hours. Two pints blood transfused.

	Before Transfn.	2nd Day	4th Day
Hb.	10.4g.-65%	10.2g.-64%	-
P.C.V.	37	30.5	-
Inorganic Phosphates mg.%	3.6	4.4	2.9
Pseudo-Cholinesterase	1.62	1.33	1.16
Alkaline Phosphatase	10	10	6

Case 40

Para 5, aged 30. Hydrops foetalis with hydramnios. Ante-partum haemorrhage occurred. Shock lasted for 4 hours and 9 ozs. of urine were passed after 12 hours. Two pints blood transfused.

	During Shock Before transfn.
Hb.	9.4 g. - 59%
Chloride mg.%	600
Pseudo-cholinesterase	0.94
Alkaline Phosphatase	10

Case 41

Primigravida, aged 20. Retained placenta with post-partum haemorrhage. Shock lasted for 3 hours. No urine passed in 7 hours. Blood transfusion of 1 pint.

	Before Transfn.	2nd Day	3rd Day	4th Day	5th Day
Hb.	9.6g.-60%	8.8g.-55%	-	-	-
P.C.V.	27	25	-	-	-
Urea mg.%	37	39.5	-	-	-
Uric Acid mg.%	7.0	5.6	-	-	-
Amino Acid Nitrogen mg.%	7.4	6.47	-	-	-
Sodium mg.%	330	333	-	-	-
Potassium mg.%	22	24	-	-	-
Pyruvic Acid mg.%	-	1.58	2.14	1.80	1.90

Case 42

Para 5, aged 41. Mixed accidental haemorrhage with 22 ozs. retroplacental clot. Shock lasted for 20 hours and 5½ ozs. urine were passed in first 24 hours. Two pints blood transfused.

	Before Transfn.	2nd Day	3rd Day	4th Day
Hb.	9.4g.-59%	7.0g.-44%	7.5g.-47%	7.6g.-50%
P.C.V.	24	-	19	-
Urea mg.%	38	62.5	31	37.5
Uric Acid mg.%	4.9	-	7.4	-
Amino Acid Nitrogen mg.%	5.9	-	6.47	-
Sodium mg.%	321	-	333	-
Potassium mg.%	16.2	-	18.4	-
Pyruvic Acid mg.%	3.60	-	3.68	-

Case 43

Para 5, aged 40. Concealed accidental haemorrhage with 18 ozs. retroplacental clot. Shock lasted for 7 hours and there was anuria for 24 hours. Two pints blood transfused.

	During Shock Before Transfn.	2nd Day	4th Day
Hb.	9.1g. - 57%	7.8g.- 49%	8.8g.- 55%
P.C.V.	27	23.5	23
Urea mg.%	53.3	89	43
Uric Acid mg.%	14.7	18.3	8.3
Amino Acid Nitrogen mg.%	10.3	9.0	7.6
Sodium mg.%	325	330	330
Potassium mg.%	20	28	25
Pyruvic Acid mg.%	2.22	-	1.87

Case 44

Para 3, aged 29. Retained placenta and post-partum haemorrhage. Shock lasted for 2 hours and 9 ozs. of urine were passed in 12 hours. Five pints blood transfused.

	During Shock Before Transfn.
Hb.	10.4 g. - 65%
P.C.V.	28.5
Sugar Mg.%	198
Chloride mg.%	620
Inorganic Phosphates mg.%	2.8
Pyruvates mg.%	1.38
Pseudo-cholinesterase	1.82
Alkaline Phosphatase	8

Case 45

Para 6, aged 29. Mixed accidental haemorrhage with 28 ozs. retroplacental clot. Shock lasted for 7 hours and there was oliguria for 2 days. Four pints blood transfused.

	During Shock			
	Before Transfn.	After Transfn.	2nd Day	3rd Day
Hb.	9.4g.-59%	9.7g.-61%	7.0g.-44%	6.7g.-42%
P.C.V.	26.5	28.5	19.0	18.0
Urea mg.%	28.8	40.0	47.0	51.1
Amino Acid Nitrogen mg.%	12.4	14.6	14.6	13.7
Sodium mg.%	306	312	306	300
Potassium mg.%	33.4	-	36.6	22.2
Inorganic Phosphates mg.%	3.5	4.1	4.4	3.0
Pyruvic Acid mg.%	1.09	0.72	1.36	0.90
Psuedo-Cholinesterase	1.59	1.74	1.12	1.18

Case 46

Para 4, aged 28. Concealed accidental haemorrhage with 44 ozs. retroplacental clot. Shock lasted for 18 hours and 1 oz. urine was passed in 24 hours.

	During Shock Before transfn.
Hb.	7.8g. - 49%
P.C.V.	22.5
Chloride mg.%	547
Inorganic Phosphate mg.%	8
Pseudo-Cholinesterase	1.54
Alkaline Phosphatase	13

Case 47

Para 7, aged 44. Mixed accidental haemorrhage with 20 ozs. retroplacental clot. Shock lasted for 10 hours and there was anuria for 24 hours. No blood transfusion given.

	During Shock Before Transfn.
Hb.	8.6g. - 54%
P.C.V.	27.5
Urea mg.%	36
Sodium mg.%	300
Potassium mg.%	17.7
Pyruvic Acid mg.%	7.11
Inorganic Phosphates mg.%	3
Pseudo-Cholinesterase	1.17

Case 48

Para 6, aged 29. Retained placenta with post-partum haemorrhage. Shock lasted for 20 hours and 5 ozs.urine were passed in 24 hours. Three pints blood transfused.

	During Shock			
	Before Transfn.	After Transfn.	3rd Day	4th Day
Hb.	8.8g.-55%	-	-	8.0g.-50%
P .C.V.	27.5	-	-	24.5
Urea mg.%	37	32	28	26
Sodium mg.%	300	-	321	300
Potassium mg.%	-	40	22	24
Pyruvic Acid mg.%	2.92	1.24	3.28	1.38
Inorganic Phosphate mg.%	-	2.7	-	2.7
Pseudo-Cholinesterase	1.45	1.71	1.41	1.72

Case 49

Para 9, aged 36. Concealed accidental haemorrhage with retro-placental clot of 10½ ozs. Shock lasted 11 hours and oliguria persisted for 2 days. Blood transfusion 1 pint.

	During Shock Before Transfn.	2nd Day	3rd Day	4th Day	6th Day
Hb.	9.6g. - 60%	7.2g.- 45%	6.6g.- 41%	8.3g.- 52%	8.8g.- 55%
P.C.V.	29.5	25	20	25	30.5
Urea mg.%	27	48	71	67	69
Uric Acid mg.%	12.4	16.3	21.7	21.7	14.4
Amino Acid Nitrogen mg.%	6	7.65	6.2	7.24	7.65
Sodium mg.%	284	324	327	320	320
Potassium mg.%	17.5	20.4	22.2	24.8	20
Chloride mg.%	635	617	612	601	612

Case 50

Para 5, aged 26. Concealed accidental haemorrhage with 7 ozs. retroplacental clot. Shock lasted for 7 hours and oliguria persisted for 2 days. One pint 10% glucose saline transfused.

	During Shock Before Transfn.	2nd Day
Hb.	10.5g. - 66%	9.6g.-60%
P.C.V.	32	27
Urea mg.%	32	41
Uric Acid mg.%	1.14	6.3
Amino Acid Nitrogen mg.%	6.3	7.5
Sugar mg.%	144	-
Pyruvates mg.%	3.58	-
Sodium mg.%	319	326
Potassium mg.%	18.4	14.5

Case 51

Para 5, aged 39. Post-partum haemorrhage. Shock lasted for 9 hours and 10 ozs. of urine were obtained in 24 hours. Four pints blood transfused.

	During Shock		
	Before Transfn.	After Transfn.	2nd Day
Hb.	-	8g.-50%	7.2g.-45%
P.C.V.	-	24	21
Urea mg.%	37	32	32
Sodium mg.%	306	306	315
Potassium mg.%	27	16.6	13.3
Pyruvates mg.%	0.68	1.32	1.18
Pseudo-Cholinesterase	1.84	1.37	1.88

Case 52

Primigravida aged 24. Mixed accidental haemorrhage with 8 ozs. retroplacental clot. Shock lasted 12 hours and 6 ozs. urine were passed in 24 hours. Two pints blood transfused.

	During Shock Before Transfn.	2nd Day
Hb.	9.9g. - 62%	8.9g.-56%
P.C.V.	28.6	28.5
Urea mg.%	22	23
Amino Acid Nitrogen mg.%	3.3	4.4
Sodium mg.%	327	306
Potassium mg.%	23.0	24.4
Pyruvates mg.%	2.46	0.96
Inorganic Phosphates mg.%	-	2.5
Pseudo-Cholinesterase	-	0.92

Case 53

Primigravida, aged 26. Mixed accidental haemorrhage with 30 ozs. retroplacental clot. Shock lasted for 5 hours and 3 ozs. of urine were passed in 24 hours. One pint Dextran (plasma substitute) transfused.

	During Shock Before Transfn.	2nd Day
Hb.	11.2g. -70%	11.0g.-69%
P.C.V.	25	23
Urea mg.%	28	32
Uric Acid mg.%	8	8
Amino Acid Nitrogen mg.%	8.7	6.5
Sodium mg.%	319	327
Potassium mg.%	10.3	17
Chloride mg.%	560	570

Case 54

Para 10, aged 40. Caesarean Section with excessive blood loss. Shock lasted 5 hours and 12 ozs. urine were passed in 24 hours. Three pints blood transfused.

	During Shock Before Transfn.	2nd Day
Hb.	10.7 g. -67%	-
P.C.V.	31	-
Urea mg.%	27.5	25.0
Amino Acid Nitrogen mg.%	4.7	5.8

Case 55

Primigravida, aged 23. Incomplete abortion. Two pints blood transfused. Shock lasted 3 hours and 3 ozs. urine obtained in 12 hours.

	During Shock Before Transfn.
P.C.V.	19
Urea mg.%	28
Uric Acid mg.%	5.7
Amino Acid Nitrogen mg.%	6
Sugar mg.%	230
Pyruvic Acid mg.%	1.52
Sodium mg.%	329
Potassium mg.%	20
Chloride mg.%	730

Case 56

Para 4, aged 33. Incomplete abortion. Shock lasted 7 hours and there was anuria for 12 hours. Three pints blood transfused.

	During Shock Before Transfn.	3rd Day
Hb.	7.2 g. - 45%	-
P.C.V.	19	-
Urea mg.%	32	-
Pyruvic Acid mg.%	1.8	1.08
Inorganic Phosphorus mg.%	2.6	-

Case 57

Primigravida, aged 27. Rupture of a rudimentary uterine horn after 20 weeks gestation. Shock lasted for 9 hours and oliguria persisted for 2 days. Three pints blood transfused.

	During Shock Before Transfn.
Hb.	11.4g. - 71%
P.C.V.	25%
Urea mg.%	24
Amino Acid Nitrogen mg.%	6
Sodium mg.%	300
Potassium mg.%	18.8
Pyruvic Acid mg.%	3.60
Inorganic Phosphates mg.%	4.3
Pseudo-cholinesterase	1.88

Case 58

Para 2, aged 25. Retained placenta with post-partum haemorrhage. Shock lasted 2 hours and anuria was present for 12 hours. One pint blood transfused.

	During Shock Before Transfusion
Chloride mg.%	620
Inorganic Phosphates mg.%	2.9
Pseudo-Cholinesterase	1.01
Alkaline Phosphatase	6

Case 59

Para 4, aged 34. Placenta praevia. Shock lasted for 8 hours and 8 ozs. of urine were obtained in the first 12 hours. Four pints blood transfused.

	During Shock		
	Before Transfn.	After Transfn.	2nd Day
Hb.	11.5g.-72%	10.5g.-66%	8.9g.-56%
P.C.V.	31	28.5	25
Urea mg.%	16	19	25
Sodium mg.%	300	315	307
Pyruvic Acid mg.%	0.82	1.62	0.86
Pseudo-Cholinesterase	1.62	1.74	1.74

Case 60

Para 3, aged 30. Retained placenta with post-partum haemorrhage. Shock lasted 6 hours and there was anuria for 24 hours. Two pints blood transfused.

	During Shock	
	Before Transfn.	After Transfn.
Hb.	9.4g. - 59%	7.8g. - 49%
P.C.V.	22	19
Urea mg.%	23.5	28

Case 61

Para 15, aged 41. Mixed accidental haemorrhage with 18 ozs. retroplacental clot. Shock lasted for 24 hours and there was oliguria until death on the 5th day. The patient had a group 3 type of liver lesion and a patchy renal cortical necrosis.

	During Shock Before Transfn.	2nd Day	3rd Day	4th Day	5th Day	6th Day
Hb.	5.6g. - 35%	3.4g - 22%	4.3g - 27%	4.4g - 27%	4.2g - 26%	4.0g - 25%
P.C.V.	14.0	9.0	11.5	10.5	14.0	12.0
Urea mg.%	43	48.7	68.0	106.0	125.5	156.0
Non-Protein Nitrogen mg.%	29.4	54.2	67.3	61.7	60.77	88.76
Creatinine	0.96	1.26	1.48	1.78	1.77	2.2
Uric Acid mg.%	6.0	10.45	10.75	14.6	15.8	20.1
Amino Acid Nitrogen mg.%	3.5	3.4	3.33	3.4	7.37	4.24

Case 62

Primigravida, aged 37. Caesarean Section with excessive blood loss. One pint blood transfused.

	During Shock	
	Before Transfn.	After Transfn.
Hb.	9g. - 57%	9.4g. - 59%
P.C.V.	28	27.5
Urea mg.%	23.1	25.2
Alkaline Phosphatase mg.%	13.1	14.3

Case 63

Primigravida, aged 25. Post-partum haemorrhage. Shock lasted for 3 hours. Two pints blood transfused.

	Before Transfn.	2nd Day
Hb.	10.3g. - 65%	-
P.C.V.	29.1	-
Urea mg.%	13	21
Uric Acid mg.%	6.5	7.2
Amino Acid Nitrogen mg.%	8.45	10.4
Sodium mg.%	326	319
Potassium mg.%	11	17
Chloride mg.%	525	555

Case 64

Para 3, aged 24. Post-partum haemorrhage. Shock lasted for 6 hours. Two pints blood transfused.

	Before Transfn.	After Transfn.	4th Day
Hb.	10.3g. - 65%	9.5g.-60%	7.5g.-47%
P.C.V.	28	24	20
Urea mg.%	32	29	25.2
Uric Acid mg.%	4.15	4.10	3.55
Amino Acid Nitrogen mg.%	4.24	4.74	5.40

Case 65

Para 7, aged 33. Retained placenta with post-partum haemorrhage. Two pints of blood and 2 pints glucose saline 5% transfused.

	Before Transfn.	After Transfn.	4th Day
Hb.	8.2g.-52%	9.9g.-62%	11g.-75%
P.C.V.	26	29	28
Urea mg.%	36.2	36.8	28.5

Case 66

Para 9, aged 36. Placenta praevia. Delivered by Caesarean Section. One pint blood transfused. Shock lasted 12 hours.

	Before Transfn.	After Transfn.
Hb.	8.6g.-54%	6.4g.-40%
P.C.V.	24	19
Urea mg.%	40.5	48.5

Case 67

Para 2, aged 22. Retained placenta with post-partum haemorrhage. One pint blood transfused. Shock lasted 3 hours.

	Before Transfn.	2nd Day
Hb.	11.7g. - 78%	9.6g.-60%
P.C.V.	37.5	27.5
Urea mg.%	18	30
Amino Acid Nitrogen mg.%	4	4
Sodium mg.%	300	-
Pyruvic Acid mg.%	6.08	6.88
Pseudo-Cholinesterase	1.18	1.08

Case 68

Para 7, aged 37. Mixed accidental haemorrhage with 12 ozs. retroplacental clot. Blood transfusion 1 pint.

	During Shock
P.C.V.	25
Urea mg.%	20
Uric Acid mg.%	6.3
Amino Acid Nitrogen mg.%	10.3
Sodium mg.%	312
Pyruvic Acid mg.%	2.24

Case 69

Primigravida, aged 31. Hypertension (150/100 mm.Hg.), oedema and albuminuria during pregnancy. Caesarean Section performed with excessive blood loss.

	During Shock
Hb.	12.8g. - 80%
P.C.V.	39
Urea mg.%	46
Uric Acid mg.%	9.2
Amino Acid Nitrogen mg.%	7.2
Sodium mg.%	315
Pseudocholinesterase	7.2

Case 70

Para 9, aged 40. Hypertension (160/100 mm.Hg.) during pregnancy. Rupture of uterus. Shock lasted 16 hours and oliguria persisted for 4 days. Five pints blood transfused.

	During Shock Before Transfn.	2nd Day
Hb.	11.5g. - 72%	12.8g.-80%
P.C.V.	22	39
Sugar mg.%	167	-
Urea mg.%	24	27
Pyruvic Acid mg.%	3.96	0.96

Case 71

Para 2, aged 24. Post-partum haemorrhage. Two pints blood transfused.

	During Shock		
	Before Transfn.	After Transfn.	3rd Day
Pyruvic Acid mg.%	0.76	1.40	1.13
Pseudo-Cholinesterase	0.95	-	1.74

Case 72

Para 2, aged 32. Previous Caesarean Section. Ruptured uterus. Laparotomy performed. Two pints blood and 1 pint saline transfused. Shock lasted 12 hours.

	Before Transfn.	After Transfn.	2nd Day
Sodium mg.%	282	345	303
Potassium mg.%	30	32	32
Chloride mg.%	585	623	-
Inorganic Phosphates mg.%	3.6	3.5	3.8
Alkaline Phosphatase	10	6	6

Case 73

Primigravida, aged 27. Hypertension (165/110 mm.Hg.), oedema and albuminuria during pregnancy. Brow presentation. Manual correction and forceps delivery. One pint plasma transfused.

		During Shock		
	Before Shock	Before Transfn.	After Transfn.	4th Day
Hb.	8.6g.-54%	12g.-75%	10g.-63%	9.7g.-61%
P.C.V.	33.5	41	34	24.5
Urea mg.%	27.6	45	48.6	31.2
Sodium mg.%	368	325	320	350
Potassium mg%	18.5	24.3	21.4	21.0
Chloride mg%	678.6	652.3	666.9	614
Alkaline Phosphatase	9.9	10.3	12.1	10.0

Case 74

Para 3, aged 27. Post-partum haemorrhage. One pint blood transfused.

	During Shock Before Transfn.
Hb.	14.7g. - 92%
P.C.V.	46.5
Sodium mg.%	325
Pyruvates mg.%	0.71
Pseudo-cholinesterase	1.64

Case 75

Para 7, aged 34. Mixed accidental haemorrhage with 32 ozs. retroplacental clot. Patient remained shocked until death 8½ hours later. There was a Type 5 liver lesion and early renal cortical necrosis at post mortem.

	During Shock Before Transfn.
Hb.	9.3g. - 58%
P.C.V.	20
Urea mg.%	46.5
Uric Acid mg.%	8.45
Amino Acid Nitrogen mg.%	6.36
Non-protein nitrogen mg.%	29.1
Creatinine mg.%	1.0

Case 76

Para 11, aged 30. Central placenta praevia. Caesarean Section performed. Remained shocked until death 11¾ hours after operation. Two pints blood transfused. At post-mortem a Type 4 liver lesion was found.

	During Shock Before Transfn.
Hb.	7.9g. - 50%
P.C.V.	31.5
Urea mg.%	25.0
Uric Acid mg.%	6.40
Amino Acid nitrogen mg.%	4.83
Plasma Protein	5.7
Non-protein nitrogen mg.%	25.7
Creatinine mg.%	1.25

Group 1 - Normal Liver.

Case No.	Age	Condition	Toxaemia	Shock Hours	Blood Transfn.	Anaesthetic	Drugs
77	21	P.P.H.	-	3	-	-	Pit.
78	27	Inversion of Uterus	-	4	-	-	-
79	28	P.P.H.	-	14	+	$CHCl_3$	Erg.
80	29	Ruptured Uterus	-	1	-	-	-
81	34	Caes. Sect.	-	5	+	$N_2O_1O_2$,E	-
82	26	P.P.H.	-	2½	-	-	-
83	23	P.P.H.	-	4	+	$CHCl_3$	Erg.
84	28	Placenta Praevia	-	1	-	-	-
85	25	P.P.H.	-	4	+	-	Pit.
86	32	P.P.H.	-	4	-	-	Pit.
87	27	Ruptured Uterus	-	6	+	$N_2O_1O_2$,E	-
88	35	P.P.H.	-	12	+	$N_2O_1O_2$,E	Erg.
89	30	P.P.H.	-	4	+	$CHCl_3$	Pit.

P.P.H. - Post-partum haemorrhage: Caes. Sect. - Caesarean Section with haemorrhage: Pit. - Pituitrin: Erg. - Ergometrine.

Group 2 - Liver showing vacuolar degeneration.

Case No.	Age	Condition	Toxaemia	Shock Hours	Blood Transfn.	Anaesthetic	Drugs
90	34	Ruptured Uterus	-	3	+	$CHCl_3$	Pit.
91	41	P.P.H.	+	1	+	$CHCl_3$	Erg.
92	28	P.P.H.	-	2	+	$CHCl_3$	Pit.
93	41	P.P.H.	-	10	+	$CHCl_3$	Erg.
94	37	Caesarean Hysterectomy	-	4	+	$CHCl_3$	-

P.P.H. - Post-partum haemorrhage.

Pit. - Pituitrin: Erg. - Ergometrine.

Group 3 - Liver with degeneration.

Case No.	Age	Condition	Toxaemia	Shock Hours	Blood Transfn.	Anaesthetic	Drugs
95	28	Acc.Haem.	+	4	+	-	-
96	32	P.P.H.	-	5	+	-	Erg.Pit.
97	38	Acc.Haem.	+	6	-	-	Pit.
98	41	Acc.Haem.	+	5	+	-	Erg.Pit.
99	27	Acc.Haem.	+	10	+	-	-
100	43	P.P.H.	-	$6\frac{1}{2}$	+	-	-
101	43	Rupt.Ut.	+	$\frac{1}{2}$	-	$N_2O_1O_2$,E	Pit.
102	41	Rupt.Ut.	-	3	-	-	Pit.
103	31	P.P.H.	-	4	+	-	-
104	38	Caes.Sect.	+	$3\frac{3}{4}$	+	$CHCl_3$	-
105	32	P.P.H.	-	3	+	-	Pit.
106	31	P.P.H.	-	$6\frac{1}{2}$	+	-	Erg.
107	44	Rupt.Ut.	-	3	-	-	Pit.
108	40	Rupt.Ut.	+	$23\frac{1}{2}$	+	$CHCl_3$	-
109	32	P.P.H.	-	$5\frac{1}{2}$	+	-	-
110	37	P.P.H.	-	4	+	-	-
61	41	Acc.Haem.	+	24	+	$CHCl_3$	Pit.Erg.

Acc.Haem. - Accidental haemorrhage: P.P.H. - Post-partum haemorrhage: Rupt.Ut. - Ruptured uterus. Caes.Sect. - Caesarean Section with haemorrhage: Erg. - Ergometrine: Pit. - Pituitrin.

Group 4 - Early liver necrosis.

Case No.	Age	Condition	Toxaemia	Shock Hours	Blood Transfn.	Anaesthetic	Drugs
111	24	Acc.Haem.	+	21	+	Cyclopropane	Erg.
112	22	Dystocia	+	11	+	$N_2O_1O_2$, Trilene	Erg.
113	21	P.P.H.	+	30	+	-	Pit.Erg.
114	32	P.P.H.	-	5	+	-	Pit.Erg.
115	26	Dystocia	-	7	-	$N_2O_1O_2$,E	Pit.Erg.
116	40	P.P.H.	-	$5\frac{1}{2}$	+	-	Pit.
117	29	P.P.H.	-	$5\frac{1}{4}$	+	-	Pit.Erg.
118	30	P.P.H.	-	30	+	$CHCl_3$	Pit.Erg.
119	30	P.P.H.	-	$10\frac{1}{2}$	+	-	Pit.Erg.
120	26	Caes.Sect.	-	$13\frac{1}{2}$	+	$CHCl_3$	Pit.Erg.
121	41	P.P.H.	-	$11\frac{1}{2}$	-	$CHCl_3$	Erg.
122	39	Rupt.Ut.	-	26	+	-	Pit.Erg.
123	35	Acc.Haem.	-	10	+	-	Pit.Erg.
124	32	P.P.H.	-	3	-	$N_2O_1O_2$,E	Pit.Erg.
125	22	P.P.H.	-	30	+	$N_2O_1O_2$,E	Erg.
76	38	Caes.Sect.	-	$11\frac{3}{4}$	+	$N_2O_1O_2$,E	Erg.

Acc.Haem. - Accidental haemorrhage: P.P.H. - Post-partum haemorrhage: Caes.Sect. - Caesarean Section with haemorrhage: Rupt.Ut. - Ruptured uterus.

Pit. - Pituitrin: Erg. - Ergometrine.

Group 5 - Marked liver necrosis.

Case No.	Age	Condition	Toxaemia	Shock Hours	Blood Transfn.	Anaesthetic	Drugs
126	38	Acc.Haem.	+	23	-	Cytopropane	Erg.
127	34	P.P.H.	-	7½	+	Pentothal	Pit.
128	23	P.P.H.	-	19	+	$N_2O_1O_2$, Trilene	Pit.
129	37	P.P.H.	-	7¼	+	-	Pit.
130	28	P.P.H.	-	5	-	-	Pit.
131	37	P.P.H.	+	6	-	$CHCl_3$	Pit.Erg.
132	27	Caes.Sect.	-	7	-	Ether	Pit.
133	27	Caes.Sect.	-	20	-	$CHCl_3$	Pit.Erg.
75	34	Acc.Haem.	+	8½	+	Ether	-
134	22	Acc.Haem.	+	5	+	-	Erg.
135	37	Acc.Haem.	+	12	+	-	Pit.
136	36	P.P.H.	-	13	+	-	Pit.

Acc.Haem. - Accidental haemorrhage: P.P.H. - Post-partum haemorrhage: Caes.Sect. - Caesarean Section with haemorrhage:

Pit. - Pituitrin:

Erg. - Ergometrine.