ACQUIRED FIBRINOPENIA IN PREGNANCY

BY

ARTHUR P. BARRY, M.D., M.A.O., F.R.C.O.G.
Master, National Maternity Hospital, Dublin, C.5

FRANK GEOGHEGAN, M.D.
Pathologist, National Maternity Hospital, Dublin

AND

STEPHEN M. SHEA, M.B., B.Ch., M.Sc.
Assistant Lecturer in Pharmacology, Department of Biochemistry and Pharmacology, University College, Dublin

The occurrence of a blood coagulation defect in certain obstetrical emergencies is now well recognized. A considerable volume of literature has accumulated on this subject, especially in North America. More recently interest in the matter has been aroused here. There can be little doubt that failure to recognize this condition has accounted for some fraction of the maternal mortality attributed to haemorrhage occurring in circumstances where good transfusion facilities were available. It is generally agreed that an acquired fibrinopenia is responsible for the coagulation defect in the clinical phenomenon under discussion, but opinions differ regarding the mechanism by which this depletion of circulating fibrinogen is brought about.

This condition is most commonly seen in accidental haemorrhage, but it occurs also from time to time in association with amniotic fluid embolism, when it may lead to fatal post-partum haemorrhage. We have encountered it, as have others, following the delivery of a macerated stillborn foetus retained *in utero* for a considerable time in a rhesus-immunized mother, and very recently we have seen the condition occur in a case of missed abortion (eight weeks). In this case no abnormal haemagglutinin was detected in the mother, who was Group O, Rh (D) positive. It is interesting to speculate on the extent to which this phenomenon may be responsible for the apparently disproportionately severe haemorrhage sometimes encountered in evacuating the uterus in cases of missed abortion. Feeney (1954) has reported two cases of vulvo-vaginal haematoma in which laboratory tests indicated a deficiency of blood fibrinogen. We have recently been led to consider the possibility that lung injury associated with the inhalation of vomitus may be another exciting cause.

If one is conscious of this problem and of its importance to the obstetrician, severe depletion of blood fibrinogen can be recognized with comparative ease. In any intractable haemorrhage complicating pregnancy repeated determination of the coagulation time by the Lee and White method should be performed. This very simple procedure will detect extreme degrees of fibrinopenia. Even when the coagulation time lies within normal limits the "clot observation test" described by Weiner *et al.* (1950) may prove valuable. We have been interested in the rapid fibrinogen assay method devised by Schneider (1952), and we wish particularly to draw attention to a simple colorimetric method for the estimation of plasma fibrinogen recently described by Shea (1954). These two methods will detect degrees of fibrinogen deficiency not recognizable by the Lee and White technique. Both are well within the compass of the small clinical laboratory.

The following cases are illustrative of the occurrence of fibrinopenia in the various circumstances already referred to.

Case 1.—Coagulation Defect Associated with Concealed Accidental Haemorrhage

A 3-para aged 24. Previous obstetric history uneventful. Had antenatal care in present pregnancy from 24 weeks. Iron-deficiency anaemia detected. Responded well to treatment. Admitted at 36 weeks with history of bleeding before admission (about 250 ml.). General condition fair, shocked, restless, B.P. 110/70. Albuminuria +2. No oedema. In fairly strong labour. Uterus enlarged to size of full-term pregnancy. Tense but not tender. Head deeply engaged; foetal heart sounds absent. Diagnosis, concealed accidental haemorrhage.

Clotting-time (Lee and White) ascertained and self-retaining catheter placed in bladder to check urinary output. Membranes ruptured. Morphine, ¼ gr. (16 mg.). Blood taken for clotting-time did not coagulate. No improvement after 3 pints (1.7 litres) of blood. Renal splanchnic block. Fifty millilitres of ½% procaine with hyalase to each renal pedicle, as only a few drops of blood-stained urine had been passed in 2½ hours despite well-maintained blood pressure. Coagulation time at 8 p.m. was 90 minutes (Lee and White). Splanchnic block was followed immediately by free secretion of urine. No further anxiety occurred in relation to renal function. Some six hours after admission following transfusion of 5 pints (2.8 litres) of whole blood the uterus was still increasing in size. Schneider, very weak—1 in 50. Two pints (1.1 litres) double-strength plasma given rapidly, intravenously, and lower-segment section carried out under local analgesia. Immediately after infusion of double-strength plasma coagulation time was reduced to 3 minutes. Schneider test showed firm fibrin clot at 1 in 50 dilution with weak coagulum at 1 in 100. An extreme degree of Couvelaire uterus was found; there were about 4 to 5 pints (2.2 to 2.8 litres) of blood in the uterine cavity. After removal of blood and extraction of foetus, uterus contracted at once and no further bleeding occurred.

Case 2

A 7-para. Non-booked. Admitted by flying squad from 60 miles. Severe combined accidental haemorrhage of six hours' duration. B.P. 150/90. Albumin +2. Foetal heart sounds absent. Transfusion (1 pint; 570 ml.) during journey in ambulance. On admission to hospital Lee and White test showed no coagulation. Transfusion continued, membranes punctured, pitocin, 3 minims (0.18 ml.). Delivery of stillborn infant 15 minutes later. Coagulation time now 4½ minutes, but Schneider titre only 1 in 10. Six hours later Schneider titre 1 in 50 (weak). After 24 hours 1 in 200 (good coagulum). Large ecchymoses appeared on both volar surfaces of forearms and on the lower abdomen during the first 72 hours of the puerperium.

Comment.—This case illustrates the sensitivity of the Schneider assay method for detecting degrees of fibrinopenia insufficient to disturb the Lee and White coagulation time. The figures quoted demonstrate the gradual replenishment of circulating fibrinogen from endogenous sources during the 24 hours following delivery.

Case 3.—Amniotic Embolism Associated with Fatal Post-Partum Haemorrhage

A 4-para. Booked case. History of previous manual removal. Admitted at term in labour. B.P. 170/90. Albumin a trace. Spontaneous delivery, living infant, 8 lb. (3.6 kg.) after 7½ hours' labour; second stage 15 minutes. Unusually strong contractions. Immediate post-partum haemorrhage with shock, slight cyanosis and short cough. Difficult manual removal of placenta, which was first-degree praevia

and was abnormally adherent over a small area. Haemorrhage continued despite usual oxytocics. Hot intrauterine douche and packing of uterus ineffective. Increasing shock. Blood transfusion (12 pints (6.8 litres) in all). In view of continuing haemorrhage and history of difficult manual removal, hysterectomy carried out. Operation very difficult, as oozing from entire field of operation could not be controlled. As the operation progressed the true nature of the condition was suspected (amniotic embolism with fibrinopenia). At this stage the laboratory staff reported that the blood samples sent for compatibility tests had failed to coagulate, and that serum for cross-matching had been secured only after centrifugation. Although pure human fibrinogen, 1.6 g., was given intravenously, haemorrhage could not be controlled, and the patient died five hours after operation.

Post-mortem Examination.—A large amount of free uncoagulated blood found in the peritoneal cavity. There was marked pulmonary oedema, but no macroscopic evidence of infarction. Histological examination confirmed the occurrence of amniotic embolus. Epithelial squames were seen in the lumina of the smaller vessels of the pulmonary circuit. No lanugo hairs were found.

Comment.—We believe that the diagnosis of pulmonary amniotic fluid embolus could have been made earlier in this case. The association of violent uterine contractions with the development of shock, cyanosis, and short cough were suggestive features. The post-partum haemorrhage following manual removal should then have been treated by blood transfusion combined with intravenous fibrinogen and the avoidance of active intervention, which served only to aggravate the bleeding. A grossly inadequate dose of fibrinogen was administered. As we have emphasized before (Barry and Geoghegan, 1954), it is quite impossible to correct gross fibrinopenia by even the most massive blood transfusions.

Case 4.—Coagulation Defect in Association with Retention of Macerated Foetus in an Rh-Immunized Mother

A 3-para aged 27. Booked case. Known case of Rh incompatibility. Husband homozygous CDe/CDe. *Previous obstetric history:* First baby, male, living. Second, induction of labour at 39 weeks ; infant survived 30 minutes ; severe haemolytic disease. Third spontaneous delivery at 32 weeks ; hydropic infant ; survived 30 minutes.

Present Pregnancy.—Admitted in labour at 37 weeks with heavy vaginal bleeding. No history of feeling foetal movement. Fundus at level of 26-weeks pregnancy. Abdomen soft. No tenderness. Clinically, missed abortion. Os dilated two fingerbreadths. Heavy bleeding accompanied vaginal examination. Small macerated foetus presenting by vertex. Bipolar version. Extraction with perforation of aftercoming head. Placenta removed by ovum forceps. Bleeding continuous and heavy during evacuation of uterus. Blood taken for Lee and White coagulation time did not clot. Transfusion begun (1 pint (570 ml.) Group O, Rh-negative) followed after 20 minutes by 1 pint (570 ml.) double-strength reconstituted plasma. Thirty minutes later Lee and White test showed weak coagulum at 8 minutes. One pint (570 ml.) blood with 10 units pitocin and 0.5 mg. ergometrine given. Blood loss diminished to slight trickle and arrested after a further pint (570 ml.) of double-strength plasma. Subsequent clinical course uneventful. The occurrence of a coagulation defect in these circumstances suggests that induction of labour should be considered immediately foetal death has occurred.

Case 5

This case is of interest because of the fact that a coagulation defect developed for no apparent reason.

A 2-para. Booked case. Admitted at term. Vertex R.O.A. Normal delivery, female living infant 6 lb. 15 oz. (3.1 kg.). Chloroform anaesthesia. There was troublesome vomiting. Normal third stage. Placenta and membranes complete. Intravenous ergometrine, 0.5 mg. Following expression of placenta there was continuous slight bleeding, though uterus was well contracted. Small perineal haematoma. Uterus and vagina explored (gas, oxygen, trichlorethylene anaesthesia). No significant trauma apparent. Uterus and vagina plugged. Bleeding continued through pack. Transfusion started. Blood taken for Lee and White clotting-time showed no coagulum at 30 minutes. Immediately a coagulation defect was diagnosed the pack was removed, being considered definitely harmful. Though uterus was well contracted a large amount of uncoagulated dark blood was expressed by pressure on the fundus. Bleeding continued. Whole blood (16 pints: 9.1 litres) given. Quadruple strength plasma (2 pints : 1.1 litres), and pure fibrinogen (1.4 g.) given. Bleeding gradually ceased. Coagulation time reduced to 4½ minutes. Schneider assay 24 hours after delivery 1 in 800 (a trace at 1 in 1,600). The puerperium was subsequently uneventful.

Comment.—There was no obvious reason why a coagulation defect should have developed in this patient. We have considered the possibility that inhalation of vomitus may have been of some significance—possible lung injury liberating thromboplastin.

Case 6.—Coagulation Defect in a Case of Missed Abortion in an Rh-positive Patient

A 1-para aged 24. Booked case. Full-term, normal delivery. Admitted for dilatation and curettage for missed abortion. Hogben test negative. Uterus had failed to enlarge beyond the size of 8-weeks pregnancy over a period of 5½ months. There was slight irregular bleeding for three weeks before admission. Routine dilatation and curettage with uterine plug at end of operation. Some three hours after operation undue haemorrhage was noted, seeping through the uterine plug. Ergometrine, 0.5 mg. (repeated), was without effect. It was assumed that evacuation had been incomplete. The patient now returned to the theatre, pack removed, and uterus re-explored. A small amount of debris removed and pack reinserted. Free haemorrhage continued. A coagulation defect suspected ; Lee and White test showed no coagulation. Schneider assay showed a titre of only 1 in 10, indicating a gross fibrinopenia. Patient was Group O, Rh (D) positive. Blood transfusion of 2½ pints (1.4 litres) over a period of three hours sufficient to arrest haemorrhage, though Schneider test performed at the completion of the second transfusion was positive only to a titre of 1 in 200 (weak). Same figure obtained 15 hours later.

Comment.—Experience with this patient suggests that delay in the evacuation of missed abortion is inadvisable.

Comment on Series

The foregoing cases have been selected in order to demonstrate the various circumstances in which intractable haemorrhage due to a defect of coagulation may be encountered in obstetrics. We (Barry and Geoghegan, 1954) have emphasized that when this condition is present any form of active interference serves only to increase blood loss. The pressing indication is the correction of the coagulation defect. In minor degrees this can be achieved by energetic transfusion of whole blood. In more severe degrees, although whole-blood transfusion is essential to restore blood volume, haemorrhage cannot be arrested unless pure fibrinogen, in dosage varying from 2 to 6 g., is given intravenously. The first report of the use of pure human fibrinogen in this connexion came from Moloney *et al.* (1949). When pure fibrinogen is not available we have found that triple- or quadruple-strength reconstituted plasma is equally effective. (One bottle of quadruple-strength reconstituted plasma may be expected to yield about 4.4 g. of fibrinogen.) It may be accepted that the overwhelming majority of transient blood coagulation defects complicating pregnancy and the puerperium are due to acquired fibrinopenia. A change in the traditional attitude of " watchful expectancy " in the management of missed abortion and dead foetus *in utero* may well be overdue.

Rapid Laboratory Diagnosis of Acquired Fibrinopenia

We now propose to consider the practical laboratory methods for confirming the clinical diagnosis of fibrinopenia. When the scarcity of pure fibrinogen and the excessive cost of quadruple-strength plasma are considered it will be realized that the indiscriminate use of these preparations would not be viewed with equanimity by hospital managers.

Acute defibrination complicating pregnancy is easily recognized in those cases in which the coagulation time is strikingly prolonged. In the Lee and White test the blood does not clot. Unfortunately the coagulation time may remain within normal limits even when a degree of fibrinopenia exists which is of such magnitude that surgical intervention or any active manipulation may prove extremely hazardous for the patient. There is therefore a place for a rapid procedure which will confirm the clinical suspicion of the presence of less severe degrees of fibrinogen depletion. Weiner *et al.* (1950), as we have already pointed out, recommend observation of the coagulum formed in freshly drawn venous blood. Reduction of plasma fibrinogen below a critical level results in a failure of the clot to maintain itself, with dissolution of the coagulum. The normal range of plasma fibrinogen is about 220 to 400 mg. per 100 ml. Higher levels are attained in normal pregnancy as term is approached, reaching about 450 mg. per 100 ml. (range 300–600 mg. during labour). Still higher levels are attained in toxaemic subjects. It appears that when haemorrhage occurs in pregnancy in association with depleted plasma fibrinogen, haemostasis cannot be secured while the level remains below 200 mg. per 100 ml.

Schneider (1952) has described the following method for the rapid assay of plasma fibrinogen. The test does not claim to furnish more than a rough index of the fibrinogen level. In effect it consists of serial dilution of the patient's whole blood with observation of the highest titre in which a discernible fibrin coagulum is formed. The test may be carried out with or without the addition of thrombin. Feeling that the number of variables influencing the result of the test should be reduced when preformed thrombin is added, we have adopted the former method as a routine.

We have used the method extensively, and find it of value in the management of intractable haemorrhage in obstetrics.

Schneider Test

Materials.—Test-tubes, 3 by ½ in. (7.5 by 1.3 cm.), are arranged in a rack, a row of eight tubes being adequate for the performance of a single test.

Diluent.—Ringer's solution may be used, and is recommended in Schneider's original paper, but an alternative solution was also suggested which we have employed in our own laboratory. This consists of a mixture of nine parts of normal saline with one part of M/40 calcium chloride, a solution commonly available in the laboratory for use in one-stage "prothrombin" determinations.

Thrombin Solution.—The thrombin topical preparation of Parke, Davis & Co. is used. A stock solution of strength 200 units per ml. in 50% glycerol is stored in the refrigerator. This may be diluted to 100 units per ml. for use in the test. The stock solution is stable over a long period.

Procedure.—Place 3 ml. of the diluent in the second tube of the series, 4 ml. in the third tube, and 1 ml. in each succeeding tube. Withdraw 1 ml. of venous blood from the patient by means of a tuberculin syringe with suitable needle. The use of a tuberculin syringe offers the advantage that the syringe can be introduced directly into the tubes containing the diluent solution. Discharge 0.5 ml. of blood immediately into the first (dry) tube. The remaining 0.5 ml. is added to the 3 ml. of diluent in the second tube. After thorough mixing, 1 ml. of the mixture is withdrawn and added to the 4 ml. of diluent in the next tube. The process is repeated in the case of each succeeding tube, transferring a 1-ml. aliquot in each case. Assuming a haematocrit value of 35 vols.%, the dilutions of plasma represented by the several tubes in the series are 1, 10, 50, 100, 200, 400, 800, and 1,600.

To each tube 0.1 ml. of the thrombin solution (100 units per ml.) is then added. The tubes are shaken sufficiently to ensure adequate mixing. The tubes are then allowed to stand at room temperature.

Reading the Test.—Even when using added thrombin we have found it advisable to wait an hour before reporting on the highest titre in which a discernible fibrin coagulum is formed, but a result accurate enough for clinical guidance will be available after 15 minutes.

We have not encountered any normal pregnant patient with a Schneider titre lower than 1 in 200, and it is suggested that failure to form a well-defined coagulum in a titre of 1 in 100 or in any lower dilution may be accepted as a pointer towards the necessity for replenishment of the patient's reserve of plasma fibrinogen.

Since the objection has been raised that the Schneider assay does not bear a true relation to plasma fibrinogen level we compared the results obtained by the Schneider method with the actual plasma fibrinogen level in a short series of normal and abnormal cases (18 patients). The results are stated in Table I.

TABLE I.—*Range of Plasma Fibrinogen (Shea's Method) in Relation to Schneider Titre*

Schneider titres (No. of observations in brackets)	1:100 (3)	1:200 (5)	1:400 (8)	1:800 (2)
Plasma fibrinogen (mg./100 ml.)	62–100	120–225	150–300	200–300

The comparative figures in three cases in which fibrinopenia was suspected are of interest (Table II). The titre 50–100 implies good coagulum formation at a dilution of 1 in 50 with very weak coagulum at 1 in 100.

TABLE II.—*Comparative Schneider Titre and Plasma Fibrinogen Level*

Clinical State	Schneider Titre (Pre-transfusion)	Plasma Fibrinogen (Same Sample)
Abruptio placentae	50–100	100 mg./100 ml.
,, ...	50–100	90 ,,
Missed abortion	50–100	62 ,,

The two cases in Table III illustrate the behaviour of the Schneider titre over a period of 24 hours after admission to hospital with intractable bleeding due to abruptio placentae.

TABLE III.—*Serial Schneider Assays in Two Cases of Intractable Accidental Haemorrhage*

Hours after Admission:	0	4	8	20	24
Case A	100	100	100–200	200–400	—
,, B	10	—	50	—	200

Rapid Fibrinogen Estimation

The need for a simple and rapid method for the estimation of plasma fibrinogen has become acute. The most convenient methods depend on colorimetric estimation, using a phenol reagent or a biuret reagent, but few are both rapid and easy to use. Of the methods using a phenol reagent, one of the most practical is that described by Quick (1951). One of us has introduced a biuret method which can be carried out rapidly and conveniently in any small laboratory (Shea, 1954). While for analytical accuracy 90 minutes are required with this method for the estimation, a 90% recovery of fibrinogen can be secured in about 10 minutes, and the fibrinogen estimated in a further 30 minutes. In emergency, accuracy of this order is more than sufficient as a guide to

clinical treatment. The following is an account of the practical details of this biuret method for fibrinogen estimation :

Reagent:

Sodium potassium tartrate ..	9 g.
$CuSO_4.5H_2O$	3 g.
Potassium iodide	5 g.
0.1 N NaOH	to 1 litre
Distilled water	to 1.9 litres

Thrombin Solution:

P.D. & Co. thrombin topical in 50% glycerol-saline.

Procedure.—Take blood in the Heller–Paul (Wintrobe) oxalate mixture. If possible secure 3 ml. of plasma. Add 20 units of thrombin per ml. of plasma. Clotting should occur within about 5 seconds, and rapidly even at 5° C. Provided that the plasma clots within 60 seconds, upwards of 97% of the fibrinogen will be precipitated in one hour, even if clotting occurs and is allowed to continue at a temperature as low as 5° C. After one hour at 5° C. or 37° C. the clot is spilled out on to a filter paper or a paper towel (preferable) and the plasma expressed in three or more stages. The clot is washed in distilled water, and the fluid again expressed. The clot is then transferred to a boiling-tube containing 0.5 ml. N NaOH, and dissolved by heating in a boiling-water bath for two to three minutes. Then 9.5 ml. of the biuret reagent is added and the colour developed by heating in a water-bath at 30–32° C. for 30 minutes. A reagent blank is prepared by the addition of 9.5 ml. of the reagent to 0.5 ml. N NaOH with similar incubation at 30° C. for 30 minutes. The optical density of the test is read against the reagent blank in a photo-electric colorimeter at 555 μ, each tube being at about 30° C. The instrument is calibrated by duplicate estimations by the Kjeldahl method. The reagent described gives a colour which follows Beer's law.

Summary

Two methods of confirming the clinical diagnosis of acquired fibrinopenia in pregnancy are described. Patients who show a Schneider titre of 1 in 100 or less (plasma fibrinogen probably below 120 mg.) should be regarded as potential victims of a haemorrhagic diathesis. If haemorrhage occurs it cannot be checked without restoring the blood fibrinogen. Even if there is no manifest haemorrhage, disastrous bleeding may be provoked by active intervention. Since stored blood for transfusion will have a fibrinogen content of 200 mg. per 100 ml. or less, it may not be possible to raise the blood fibrinogen to a safe level by transfusion of whole blood. If pure fibrinogen is not available a rapid restoration of clotting power may be achieved by the intravenous injection of triple- or quadruple-strength plasma (1 pint (570 ml.) of quadruple-strength plasma yields about 4.4 g. of fibrinogen).

REFERENCES

Barry, A. P., and Geoghegan, F. (1954). *Irish J. med. Sci.*, 189.
Feeney, J. K. (1954). *J. Irish med. Ass.*, **35**, 310.
Moloney, W. C., Egan, W. J., and Gorman, A. J. (1949). *New Engl. J. Med.*, **240**, 596.
Quick, C. J. (1951). *Physiology and Pathology of Haemostasis*, pp. 156-158. Kimpton, London.
Schneider, C. L. (1952). *Amer. J. Obstet. Gynec.*, **64**, 141.
Shea, S. M. (1954). *Irish J. med. Sci.*, 36-37.
Weiner, A. E., Reid, D. E., and Roby, C. C. (1950). *Amer. J. Obstet. Gynec.*, **60**, 1015.

The British Red Cross Society's report for the year 1954 has just been published. It contains information about the various activities undertaken by the British Red Cross Society, such as first-aid and ambulance work, nursing, blood transfusion, welfare, and the administration of auxiliary hospitals, homes, and settlements. Some of the homes for old people established by the Society are for permanent residents, while others receive short-stay guests. The report states that the demand for the latter type of accommodation is increasing.

BLOOD COAGULATION FAILURE IN OBSTETRICS

EFFECTS OF DEXTRAN AND PLASMA

BY

JAMES S. SCOTT, M.B., M.R.C.O.G.

(From the Department of Obstetrics and Gynaecology, University of Liverpool)

In the course of a study of coagulation failure associated with hypofibrinogenaemia in obstetrics (to be reported in detail elsewhere), a review was carried out of maternal deaths, and of cases of accidental ante-partum haemorrhage, among 85,000 deliveries in the practice of certain hospitals in Birmingham, Liverpool, and London between 1937 and 1955. Eight cases of coagulation failure were discovered, seven of them serious and four being fatal. In five the condition complicated accidental ante-partum haemorrhage. One of the most interesting findings of the inquiry was that only one of the cases occurred prior to 1951, the remainder being encountered during the period 1951–5. This is in keeping with the fact that, although coagulation failure in association with accidental haemorrhage was described as early as 1901 (De Lee), very few instances were recorded until the present decade, while the last few years have seen a spate of case reports and articles on the subject in medical journals throughout the world.

There seems little doubt that the recent increase in the incidence and clinical importance of this problem is real and not apparent, and consideration of the available evidence suggests that the most likely explanation for it is the introduction and widespread use of artificial macro-molecular substitutes for blood and plasma. In this country the most popular preparation of this kind is dextran,* and it is remarkable that it is only since it was widely adopted about five years ago that cases of afibrinogenaemia have been relatively common. Moreover, in six of the seven cases mentioned above which occurred during the 1951–5 period, dextran was transfused in comparatively large amounts—the average amount per case was a little more than 3½ pints (2 litres)—and most of it was given before there was evidence of the blood failing to clot. In the seventh case, failure of the blood to coagulate was a transient phenomenon which disappeared quickly, without causing serious anxiety, when 2 pints (1.1 litres) of whole blood was transfused. Moreover, in one of the above cases serial haematological studies revealed a striking deterioration in the quality of the clot formation within a period of 15 minutes during which 1 pint (570 ml.) of dextran was administered. In another of our patients 5 pints (2.8 litres) of dextran was given as part of the treatment of atonic post-partum haemorrhage, and this appeared to precipitate coagulation failure, which had not been present previously. The clotting function in this case was not properly restored until 12 hours later, by which time 6 pints (3.4 litres) of blood had been transfused.

These observations receive support from the published accounts of other cases. McKay *et al.* (1955) described a case in which coagulation failure developed rapidly after

*Dextran is a complex polysaccharide of large and variable molecular size. Commercial preparations vary, but in the one used in most of these cases 63% of the molecules fell within the weight range of 130,000–250,000. It was administered as a 6% solution in normal saline.