apparently caused by spasm or actual mechanical obstruction of the external iliac and femoral arteries when the limb was straightened on return to bed. The vessels had probably become shortened by prolonged flexion of the thigh during the period when the patient was bed-ridden, and the events indicate the necessity for gradual change in position after a limb has been held in an unusual attitude for a long time.

In the second case the nutrition of the limb never seemed to be in danger, even though not merely all the iliacs, but the epigastric anastomosis which forms the most obvious collateral channel, had been tied. The compensatory circulation must have been by blood entering the ligatured internal iliac through anastomoses with the lower lumbar arteries, the middle sacral, and the branches of the opposite internal iliac artery, and passing into the external iliac and femoral arteries through anastomoses between the ilio-lumbar and the deep circumflex iliac, the gluteal and the external circumflex, the obturator and internal circumflex, the sciatic and the superior perforating, and the internal pudic and the deep external pudic.

The most striking advance in surgery during the last four years is, without question, the progress that has been made in the use of whole blood. Improvements in operative technique have allowed us to do many things a great deal better than we used to do, sometimes with half the mortality. The sulphonamides and penicillin have increased the cure rate in venereal disease and allowed the early closure of war wounds in a high proportion of cases and with greater certainty than was formerly possible. But blood, used in the quantities and at the speed that we have been taught to use it, has introduced a new therapeutic principle, allowing us to save useful lives that have never been saved before. Without the provision and adequate administration of large quantities of blood a man with an injury to a large artery will certainly die; with it he can recover, and recover with perfect function. Loss of blood is not, like loss of any other tissue of the body, irreplaceable: bone and skin defects can be compensated by borrowing from other parts of the body, but the result is a good repair, not a normal restoration; blood, though it is the fuel of the corporal machine, is not an individual tissue, but one that can be replaced in any quality and quantity from a well-equipped filling station. Injury to an artery is not, like injury to any other structure, irreparable: for whereas muscles and nerves are unique, an artery is one of many alternative channels, the remainder of which will take over and supply the same areas with the same substance when one is gone.

Yet there seems to be a temperance campaign against blood, as if it were a fluid as disreputable and as liable to abuse as beer. We are constantly told that it is used too often and in too great quantities, never that it is used too seldom and too timidly. Articles without number are written about the dangers of blood, about Rh factors and reactions; none about the thousands of men who are alive to-day only because blood was ready for them as they came out of battle and given courageously. Post-traumatic anuria is discussed in every journal, the writers taking the line, "We can't prove that transfusion was responsible, but it looks mighty suspicious": the more rational interpretation—that "the patients who developed an anuria were men who had been in severe shock of sufficient degree to produce a relative renal ischaemia and that this ischaemia was maintained for sufficient time to cause a large amount of kidney damage,"* that is that the men developed anuria not because they were given too much blood but because they were given too little or it was given too late—though one widely held by forward surgeons, is apparently suppressed as running counter to the views of the haemophobes.

It is often said that few patients need more than three pints of blood; it would be truer to say that patients who need only three pints of blood do not need blood at all. A loss of two pints can be made up by fluid administered by mouth. A loss of three pints can be remedied reasonably well by transfusion of plasma. A loss of even four pints need not end fatally if the volume is restored fully and promptly by plasma, though with a haemorrhage of this extent some at any rate of the replacement should be by blood. But when not only is the blood loss considerable but further considerable loss is

expected, it is necessary to have large amounts of reliable blood ready for immediate administration. And this means a blood bank. To rely upon a group of donors, however ready they may be, is to court failure in cases where large amounts of blood could really save life. For no haemorrhage, however profuse, need be fatal if the rent from which it is pouring can be stopped. Blood loss, even from a vessel the size of the common iliac, can be stopped by packs and firm pressure; and though transfusion cannot possibly keep pace with the loss while bleeding is going on, the blood can be run in at the rate of a pint in two minutes by using both arms simultaneously, and the circulatory volume can be restored while the surgeon presses the pack in position, ready, at a signal from the transfusion officer, to remove it and make another attempt to control the bleeding hole more permanently.

Blood transfusion has undoubtedly got its dangers, but they are for the most part associated with the giving of blood to those who are gravely ill and who have been repeatedly transfused over a long period. Good blood prepared by a good transfusion service, and given by a good transfusion officer who can detect a doubtful bottle at sight and stop an incompatible transfusion at the first sign of reaction, seems to have no dangers in the type of massive post-traumatic haemorrhage in which it offers the only means of saving life.

CUTANEOUS SCHISTOSOMIASIS INVOLVING S. HAEMATOBIIUM EGGS

BY

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Although the eggs in human schistosomiasis are deposited chiefly in the bladder and bowel, they are known to occur elsewhere, and may be found in organs drained by the systemic system. Deposits of the eggs of *Schistosoma haematobium* in the lungs, brain, spinal cord, heart, and kidneys are well recognized, and are mentioned in the textbooks. Deposits in the skin have, however, rarely been recorded in the literature, and are not referred to in the standard textbooks. Madden (1919) described deposits of eggs in the subcutaneous tissues, especially in the perineum, but also in the "bathing-drawers area" and rarely elsewhere, giving rise to fibrous nodules. He pointed out a resemblance to tuberculous subcutaneous nodules in the earlier stages, and continued as follows: "These nodules, or chain or irregular collection of nodules, are at first hard, then gradually enlarge and soften, and ultimately burst through the skin and discharge a thick dirty cheesy material and persist as a sinus, or as a fistula in more or less free communication with an adjacent organ or mucous surface." Girges (1934), in an account of the various sites affected in the case of *S. haematobium*, says: "Small, deep-seated, separate, multiple, elevated, dark-coloured deposits occur in the subcutaneous connective tissues in the perineum, penis, and scrotum, over the sacrum and coccyx, and particularly over the pubis, forming hard nodules closely resembling tuberculous glands. They may grow and become adherent to the skin, soften and open to the exterior, forming sinuses," which "are not as a rule connected to the neighbouring viscera." Garcia *et al.* (1940) described the case of a Filipino child with a chronic ulcer of the leg, sections of which showed the presence of *S. japonicum* eggs. The present paper describes two cases of schistosomiasis which developed a distinctive skin lesion, from which eggs of *S. haematobium* were recovered by aspiration, identical with those seen in the stools and urine in the course of investigating 130 European cases of schistosomiasis admitted to a West African general hospital in 1944. Two other cases are included because they had similar lesions, although ova were not recovered from the skin.

Case I

A British N.C.O. aged 21 had bathed in a freshwater lagoon in Southern Nigeria every day for five weeks from Jan. 23, 1944, in the course of training for jungle warfare. He frequently had to leave the water because of skin irritation, and had periods of itching during the nights after bathing. The itching affected his whole body, but was worst on the legs. He remained well until March 12, when he

* R. A. Phillips, Rockefeller Institute of Medical Research: personal communication.

developed cough, aching in the back of the neck, and nasal discharge which lasted for three days. On the fourth day he had a feeling of extreme weakness with diarrhoea, and his temperature rose to 101.2° F. On the fifth day he developed widespread urticaria and was admitted to hospital. The urticaria faded after three days, but an irregular pyrexia persisted for two weeks, during which the symptoms gradually subsided. The white cell count was 8,400 per c.mm., with an eosinophilia of 12%. Examinations of urine, faeces, and blood films were negative. After this illness he remained well except for the cough, which persisted, and occasional diarrhoea and abdominal discomfort. On May 3 the stool was found to be streaked with blood-stained mucus, in which eggs of *S. haematobium* were found. The white cell count was 9,000 per c.mm., with 19% eosinophils; the urine deposit was normal and contained no ova. The symptoms at this time were diarrhoea, abdominal pain, and cough which invariably troubled him at night.

FIG. 1.—Case I. Cluster of skin deposits.

Treatment with 40 c.cm. of stibophen, given by intramuscular injection over a period of 15 days, was started on May 6. On May 13 the patient drew attention to a skin lesion below the right nipple, which rather resembled and was at first thought to be herpes zoster. He had previously (May 1) noticed some spots on the scrotum, which cleared up within 10 days. The lesion below the right nipple had appeared about May 3 as a small group of pink spots which could be felt with the finger and gave a sensation of slight soreness but not pain. As fresh spots occurred in the same area they were first pink and later violet. When examined on May 13 the lesion (shown in Fig. 1, at a later stage) consisted of a crowded cluster of shotty papules of a violet colour and two outlying pink papules which had been the last to appear. Fresh clusters of papules developed during and after the stibophen course. In the latter part of the course each group contained fewer papules, many of which remained pink and small, and shrank and atrophied although some induration was detectable for several weeks. The lesions were confined to the lower chest and upper abdomen in front, and the lower part of the back and upper part of the buttock behind.

The appearance of unrecognized skin lesions in a proved case of schistosomiasis, at about the time when eggs were first discovered in the faeces, suggested that they might be a manifestation of this disease. Accordingly tissue juice, sucked from the lesions by means of a small needle and syringe, was examined. On May 15 no eggs could be found. On May 21, after several attempts, scanty *S. haematobium* eggs were seen. By June 8 some of the violet indurated nodules on the right flank had developed a whitish apex resembling a small pustule. The contents, removed with a needle, were white and pasty, and contained large numbers of *S. haematobium* eggs, as many as five being seen in some low-power fields. Some were degenerate and opaque, but others seemed healthy and structurally perfect. After the stibophen course the stools remained normal and free of eggs for three weeks, but on June 14 blood and mucus reappeared, eggs were found, and sigmoidoscopy showed active disease in the rectum. Fresh skin lesions began to appear on the scrotum (Fig. 2) as clusters

of nodular pink papules which were soon surmounted by a white spot the size of a pinhead. On June 26 the contents of one of these spots were examined and two degenerate eggs of *S. haematobium* were seen, the shell and spine being intact, but the contents granular and structureless. By the middle of July there were numerous papules on the scrotum, perineum, and root of the penis, mostly arranged in groups. Eggs were obtained from these on numerous occasions. The papules were less regular in shape and more variable in size than those on the trunk; they were nodular and took on a distinctly violet colour. On the trunk two groups of lesions which had appeared during treatment and had atrophied without passing through the violet papular stage were still distinguishable as definite elevations at the sites of the original papules. The remainder had become rather softer but were still definitely nodular, with a shiny, pearly top and some wrinkling of the overlying skin. Constipation and abdominal pain became troublesome and pain on micturition developed for the first time. Eggs, with pus and red cells, now appeared in the urine as well as in the faeces. The liver edge was palpable on

FIG. 2.—Case I. Scrotal lesions.

inspiration, smooth, firm, and not tender. There was tenderness on palpation of the right and left iliac fossae. The white cell count was 11,000 per c.mm., with 9% of eosinophils. A second course of 40 c.cm. of stibophen was given, during which no further skin lesions appeared.

Case II

A British N.C.O. aged 28 had bathed almost every day for a month from Jan. 24, 1944, in the same lagoon as Case I. He itched all over the body after leaving the water, and towards the end of the month was troubled with an itchy and prickly rash which he described as like little pinheads, some watery, faint in the morning but red and irritating at night-time. He remained in normal health until March 3, when he was admitted to sick quarters with headache, shivering, and a temperature of 102.6° F. His temperature fell gradually to 100° F. during the first five days, with a daily fluctuation of less than one degree. In the next 10 days his temperature was 99 to 100° F. most evenings, and normal in the mornings. There was no further shivering after the onset, but headache continued, and on the fifth day he developed a dry cough and a rash on the front and back of the chest. He was transferred to hospital, with a tentative diagnosis of dengue, on the eighth day, by which time the rash was fading rapidly. The eosinophils rose in this illness from 1 to 34%, the total leucocyte count remaining between 5,000 and 7,000 per c.mm. Examination of stools, urine, and blood films was negative. After the temperature reached normal he felt quite well and was allowed to return to his unit. Weekly stool examinations were negative and the eosinophil count fell to 15%, but he began to have periodical looseness of the bowels and abdominal discomfort, and was readmitted to hospital on May 4. He now complained of itching of the penile urethra, and the abdominal pain was worse. The stools were formed, with strands of mucus on the surface which were found to contain eggs of *S. haematobium*. The urine deposit remained normal. The eosinophil count had risen to 39%.

On May 8 treatment with stibophen was started. On May 13 a group of pink papules was noticed in the left lumbar region. The

papules were about 3 mm. in diameter, and were palpable as small shotty nodules. On May 15 a second group appeared on the lower left chest in front. A small amount of milky fluid was obtained by aspirating one of the nodules and found to contain one perfect healthy-looking ovum of *S. haematobium*. Four further clusters and some scattered papules subsequently appeared on the left lumbar, sacral, and gluteal regions (Fig. 3). A course of 50 c.cm. of stibophen was given, after which the skin eruptions ceased. The skin lesions in this case were similar to those in Case I. Starting as firm nodules which projected above the surface as pink papules, they developed red areolae which became confluent. By June 6 the clustered papular lesions had taken on a dull-red colour. On June 16 the nodules had become soft and the overlying skin was atrophic, shiny, and somewhat wrinkled, and of a violet or purplish colour. No ova could be found by aspiration at this time. The patient remained well, and repeated stool examinations were negative for five weeks. The

FIG. 3.—Case II. Skin deposits. (The shadows are due to uneven developing of the negative.)

eosinophil count, however, remained high (38–39%), and early in July ova appeared for the first time in the urine, and shortly afterwards again in the stools, and a further course of treatment was started.

Case III

A British N.C.O. aged 27 had bathed in the same lagoon every day for four weeks from Feb. 4, 1944, and had a slight tingling sensation of the skin at the time of bathing. Toxaemic symptoms started on March 12, and nocturnal cough, diarrhoea, and abdominal pain persisted until admission to hospital on May 9. Ova of *S. mansoni* were found in strands of russet-coloured mucus on the surface of the stools. The urine deposit was normal and there was no eosinophilia. A course of 50 c.cm. of stibophen was given, after which the stools were free of ova and the patient was allowed to rejoin his unit, to remain under out-patient surveillance. He still had nocturnal cough, and when seen on June 16 there were two clusters of pink papules in the lumbar region which, he said, had been present for three days. Ova could not be found in the faeces, but there was now an eosinophilia of 11%. When seen again ten days later the spots were still present and *S. haematobium* ova were seen in the faeces. The urine contained pus and red cells, though repeated examinations failed to disclose ova. The patient was readmitted and given a second course of stibophen, after which the spots gradually atrophied. The lesions in this case lasted for over six weeks, and closely resembled those seen in Cases I and II, though ova were not found in them.

Case IV

A British N.C.O. aged 21 had bathed in the same lagoon every day for a month from Feb. 13, 1944. He had a prickling sensation after bathing, and noticed a rash like "prickly heat" on the limbs and trunk. He first felt ill about March 20 with headache and tiredness, followed by irritating cough and abdominal pain. On April 25 blood and slime were noticed in the stools and he was admitted to

hospital. *S. haematobium* ova were present in large numbers in the mucus, and there was an eosinophilia of 55%. A course of stibophen was given, the last injection on May 18, after which the stools were macroscopically normal and free of ova. The symptoms were relieved and he was discharged, to be kept under out-patient surveillance. Soon, however, cough, headache, and abdominal pain returned, and two weeks after the end of treatment he developed a group of spots to the right of the umbilicus. On June 21 he was readmitted, and *S. haematobium* ova were found in the stools and later in the urine. An unusual symptom, haemospermia, was reported, and the prostatic fluid was found to contain pus, red cells, and ova. Fresh skin lesions continued to appear on the lower chest up to and during the second course of treatment, after which the symptoms were relieved. Stools, urine, and prostatic smear showed no abnormality, sigmoidoscopy was negative, and no further skin lesions appeared. The lesions in this case persisted for two months, and were similar to those seen in the foregoing cases.

Discussion

The four cases described were heavily infected by repeated bathing over a period of a month or more. Each developed a definite toxaemic stage after an incubation period of several weeks; and local disease, indicated by the passage of eggs, about three months after the first bath. In each case the eggs appeared first in the faeces, and in three cases later also in the urine. Skin lesions appeared when local disease was established—in Cases I and II at about the time when eggs were first found in the faeces, and in Cases III and IV some two weeks after a course of treatment which was followed by the reappearance of eggs in the excreta.

The characteristics of the lesions, though apparently modified as to the degree of local tissue reaction by antimony treatment, were sufficiently constant and striking to be easily recognizable, and distinct from the more familiar skin complaints. In each case they first appeared as deep, shotty pink papules 3 to 5 mm. in diameter, arranged singly or in clusters which appeared successively. There was sometimes transient local oedema with itching at first, which passed off in a few days, after which there were no symptoms, or merely a slight soreness. An area of erythema developed round each papule, and these areas became confluent within the clusters. The original papules remained distinct, and their nodular character was perceptible for six weeks or more. They changed to a dull red and then to a purplish or violet colour. Some groups and scattered papules which appeared during treatment failed to develop beyond the pink stage and slowly atrophied. The others enlarged somewhat and became softer, with wrinkling of the overlying skin. Finally a white spot appeared at the apex, the contents of which were white and pasty. The resemblance of the lesions at some stages to those seen in the bladder and bowel at endoscopy was striking.

The lesions described here correspond fairly well with the early stages of those described by Madden and by Girges—viz., small subcutaneous nodules, at first hard and later enlarging and becoming softer. Madden refers to the arrangement of the nodules in chains or irregular collections, and Girges mentions that they are elevated and dark in colour, and may discharge a cheesy material. The later stages of ulceration and sinus formation, as described by these authors, were not seen in the cases recorded here, which came under treatment at an early stage.

Madden gives the distribution on the body as: especially in the perineum, but also in the "bathing-drawers area," and rarely elsewhere. Girges includes the perineum, penis, scrotum, over the sacrum and coccyx, and particularly over the pubis. The scrotum, perineum, and root of the penis were heavily involved in one of the cases described above. Posteriorly, the majority of lesions were in the lower part of the back and upper part of the buttocks, though occasional ones were seen as high as the scapular angles. So far the agreement is quite close, but anteriorly the distribution was rather different, the area affected being higher—chiefly between the levels of the nipples and navel.

Paired *S. haematobium* worms may wander from their habitat in the pelvic plexuses of veins into the inferior vena cava, and Fairley (1919) found them in the inferior vena cava in necropsies on infected monkeys. From the iliac veins and vena cava they might ascend the scrotal, gluteal, and lumbar veins by their normal process of travelling against the blood stream. The lesions in the lower part of the chest and upper part of the abdomen are more difficult to account for: possible routes would be via the venous communications between the lumbar and

epigastric veins, or from the external iliacs via the inferior epigastric veins.

The nature of the nodules remained in doubt until eggs were obtained by puncture with a fine needle and withdrawal of a little tissue juice by suction with a syringe. The eggs were identical with those seen in a large number of examinations of stools and urine. Some were structurally perfect, while others, especially after treatment, showed no miracidial structure and had granular contents or were opaque. Tissue was obtained by biopsy from two of these cases, but when examined later the embedded material was found not to include any of the actual tissue from the nodules.

Compared with the skin affections due to cercarial penetration, and the urticaria of the toxæmic stage, cutaneous lesions arising during the stage of established local disease and associated with deposits of eggs have attracted little attention. The lesions described here were practically symptomless, and were noticed only because the white patients, being fastidious about skin complaints in the Tropics, drew attention to them. It seems quite likely, therefore, that this condition might fail to arouse the comment of native patients. Large outbreaks of schistosomiasis among Europeans are unusual, and with an incidence of only about 3% in, for the most part, heavily infected cases under observation in hospital, this complication would no doubt be of rare occurrence in normal practice.

Summary

In a series of 130 cases of schistosomiasis in Europeans, four cases were seen with a distinctive skin lesion. In two of these the lesions appeared at about the time when eggs were first discovered in the faeces. Tissue juice, aspirated from cutaneous nodules, was found to contain eggs of *S. haematobium*, identical with those seen in the urine and faeces. The skin lesions in the other two cases appeared about two weeks after unsuccessful treatment with stibophen, which was followed by the reappearance of eggs in the excreta. The lesions were similar, but eggs were not recovered from them.

The lesions and their distribution are compared with those previously recorded, and the way in which eggs may reach the skin is discussed.

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METHODS FOR DETERMINING PLASMA PROTEINS

VALUE IN A GROUP OF BOYS AGED 14 TO 15

BY

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We have determined the plasma proteins of a group of 45 normal schoolboys aged 14 to 15. Information as to the social condition and diet of the boys is given in a previous publication (Cook, Davidson, Keay, and McIntosh, 1944). As a considerable volume of plasma was obtained there was an opportunity of testing various methods of estimation. The standard method is the gravimetric estimation, in which the total proteins are isolated and weighed. To this method all others should be subservient. It should be stressed, however, that whether plasma "proteins" can be regarded as a distinct chemical species is a moot point. Particularly is this so in the mixed form in which they occur in the blood. In view of the importance of the determination of plasma proteins in clinical medicine and in nutrition surveys we present our results with

some practical details in the hope that they will be of value to other workers in this field.

Methods

Collection of Blood and Preparation of Plasma.—Since other blood constituents such as vitamin A and ascorbic acid were to be determined it was necessary to withdraw 40 ml. of blood from each boy. As an anticoagulant potassium oxalate was used. Into a tube prepared to contain 20 ml. of blood 1.5 ml. of 6% (w/v) solution of potassium oxalate was placed. The tubes were put on a metal tray and the solution evaporated to dryness (leaving a deposit of oxalate crystals) by gentle application of heat from a Bunsen burner. Overheating, which converts oxalate into carbonate, must be avoided (Harrison, 1937). The syringe used for withdrawing blood was previously flushed out several times with sterile saline. The small amount of saline left might be regarded as a diluent of the blood, but experiments on haemoglobin determinations using a completely dry and a saline-moistened syringe show that at most a dilution altering the results by 1% is obtained. The boys were seated during the puncture of the vein, a rubber tourniquet being loosely applied round the middle of the upper arm. As soon as the vein was entered the tourniquet was slackened. It was sometimes found necessary to apply slight pressure during the withdrawal of the sample. The oxalated tube was gently rotated during the addition of the blood. In no case was there any coagulation. Haemolysis to a slight degree occurred with three samples. Within three hours the blood was centrifuged for 20 minutes at 2,500 r.p.m. and the plasma pipetted off.

The micro-Kjeldahl determinations and gravimetric estimations were carried out within 24 hours of collection. In the case of the specific gravity method the plasma had been stored for two months at -4°C .

Micro-Kjeldahl Method.—As this method, though often used, is open to a number of fallacies, we propose to describe our procedure in detail.

(i) **Total Nitrogen.**—The method advocated by Peters and van Slyke (1932) is to dilute 1 ml. of the plasma to 10 ml. with 0.9% (w/v) NaCl and then to digest 1 ml. aliquots of the diluted plasma. This procedure, in our opinion, involves unnecessary manipulation and may introduce errors. The procedure adopted was to pipette from a standardized pipette 0.1 ml. of undiluted plasma into the digestion flask and wash it in with 1 ml. of saline. Comparison of this procedure with the dilution method gave substantially the same results. Each sample of plasma was set up in duplicate. To the digestion flask were added 0.5 g. of digestion mixture described by Chibnall, Rees, and Williams (1943) and 2 ml. of conc. A.R. H_2SO_4 . In view of the findings of these writers that low N values may be obtained for proteins if the heating is not continued for a number of hours after clearing, as a normal procedure all digestions were carried on four hours after clearing, which normally took place in about half an hour. It may be added that preliminary experiments showed no difference in the results between 2, 4, 8, and 16 hours' heating. "Blank" digestion flasks containing saline, acid, and digestion mixture were set up for each 6 determinations. The liberation of the ammonia was carried out in a Parnas-Wagner type of apparatus. The NH_3 was determined by back-titration of N/100 HCl.

As a check on the apparatus and standard solutions frequent controls, using known amounts of NH_3 as a solution of ammonium sulphate, were carried out. Recoveries of 98 to 102% of theory were always obtained.

The "blank" determinations were approximately 3% of the experimental value. It would appear that this blank is largely due to carriage over of alkali from the distillation flask, as it is little altered if the digestion mixture is omitted from the flask, and becomes negligible if distilled water is substituted for the soda. As a normal procedure a constant measure of 15 ml. of 40% (w/v) NaOH was added to the flask. This stabilized the blank at a maximum value of 0.028 mg. N. All our results are corrected for the blank determination. Any results that did not agree to within 2% were repeated.

(ii) **Plasma N.P.N.**—This was determined on the Folin-Wu filtrate (see Peters and van Slyke, 1932) in 11 samples of plasma.

Gravimetric Method.—The method used was that of Guil-laumin, Wahl, and Laurencin (1929). This procedure involves considerable manipulation and is very laborious. In the series only two of the determinations were carried out in duplicate. Two ml. of plasma was used for each determination. A point that must be strongly emphasized in the gravimetric method is care in drying the coagulated protein to constant weight. This often takes a considerable time.