as in the case of L.K., and the cells, though small, were fully saturated with haemoglobin. Whereas in L.K. the microcytosis was mostly due to an excessive thinness of the red cells, in K.L. it could be related to a smaller diameter of the cells rather than to low M.C.T. As in L.K. so in K.L., the low mean corpuscular haemoglobin was compensated by a rise in the absolute number of cells. There was no suggestion of polycythaemia vera or a polycythaemia secondary to any condition other than the microcythaemia.

Although the group of Burmese so far examined is small, it is significant that the incidence of haemoglobin E should amount to 15%, and it may be expected that the Burmese resemble the Siamese in that respect.

NaNakorn *et al.* (1956) found the incidence of haemoglobin E to be 13.6% in 1,006 Siamese, but none was seen in 213 Chinese. Lie-Inju Luan Eng (1955) found an incidence of 3.6% in 500 Indonesians. Aksoy *et al.* (1955) found it to be 3.6% in 167 Veddas from Ceylon, but observed none in Sikh (Europoid-Mediterranean) and Nepalese (Mongoloid) Indian soldiers. Similarly, Lehmann and Sukumaran (unpublished) found no haemoglobin E in a series of aboriginal communities of the Nilgiri Hills in Southern India, among whom, however, the sickle-cell trait is present with considerable frequency. No haemoglobin E was found among 166 Australian aboriginals (Horsfall and Lehmann, 1956). On the other hand, one example was discovered among 131 Eti-Turks (Aksoy *et al.*, 1955); they are a small Arabic-speaking group in Southern Turkey among whom the gene for sickle-cell haemoglobin has been found with high frequency. No haemoglobin E was found in 110 pure Turks and in what amount to some thousands of examinations of bloods from all over Africa and Europe. The one exception is a patient with thalassaemia-haemoglobin E disease found among the "Cape Coloured" in South Africa (Budtz-Olsen and Brain, personal communication). Such an observation was not unexpected in view of the Malayan admixture which, under the Dutch, had contributed to the formation of the "Cape Coloured" group (Lehmann, 1955).

It is possible that haemoglobin E will be found to play a similar part in South-East Asia to that of sickle-cell haemoglobin in Africa. If this is so it will have similar implications to those already noted for that of haemoglobin S in anthropology, pathology, and population genetics.

We hope to extend the present investigation of the Burmese and to combine it with a determination of blood-group frequencies that is being carried on by Dr. A. E. Mourant and Miss E. W. Ikin, of the Blood Group Reference Laboratory, London.

Summary

Among 80 young Burmese, 12 were found with haemoglobin E. Ten were heterozygotes for adult haemoglobin and haemoglobin E (AE). Two were haemoglobin-E homozygotes (EE). They were considered fit and led active lives. On examination evidence was found of a mildly haemolytic condition. The red cells were much smaller than normal, and the resulting low mean corpuscular haemoglobin was compensated by an increase in the number of red cells to 7,400,000 and 8,440,000 per c.mm. respectively.

The distribution of haemoglobin E in Asia is discussed.

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MASSIVE BLOOD TRANSFUSION FOR TRAUMATIC POST-PARTUM HAEMORRHAGE

BY

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This case is worthy of record because of the large amount of blood that had to be transfused, and because the patient failed to respond satisfactorily until blood had been transfused by the intra-arterial route and operation performed.

Case Report

A 7-gravida aged 31 had had five full-term deliveries and one miscarriage. The last full-term delivery in 1952, at home, had been precipitate and the baby died. The miscarriage was in 1953. During the present pregnancy she had been very well but required much persuasion to come into hospital for confinement.

Labour started spontaneously on August 19, 1954. The first stage lasted ten minutes and the second stage five minutes. A living female infant weighing 7 lb. 4 oz. (3.3 kg.), was delivered at 7.25 a.m. A slight loss of blood accompanying delivery of the baby had been noted, but no significance had been attached to it. The placenta and membranes were expelled complete at 7.33 a.m., and there was then an immediate loss of 50 oz. (1.4 litres) of blood. Ergometrine, 0.25 mg., was given intravenously, and at the same time 0.25 mg. intramuscularly. The house-surgeon passed a speculum but no tear was noted. At 7.55 a.m. the pulse rate was 108 a minute and blood pressure 90/7. Dextrose (5%) intravenous transfusion was started whilst blood was being cross-matched, and at 8.45 a.m. (pulse rate now 125) blood transfusion was begun. The patient responded to this. By 9.15 a.m., and after 3 pints (1.7 litres) of blood, the pulse rate had fallen to 112 and the blood pressure was 80/60. The uterus was well contracted and there did not appear to have been further loss.

During the morning slight blood loss was noted at intervals, and the blood was obviously clotting. The blood pressure remained at 80/60, and morphine, $\frac{1}{4}$ gr. (16 mg.), and methedrine, 10 mg., were given intravenously at 11.10 a.m.

One of us (G. G. L.) saw the patient for the first time at 12.45 p.m., when she was being transfused with her ninth pint of blood. Blood pressure was 50/nil and the pulse rate 100. The total loss had so far been estimated at 130 oz. (6½ pints, or 3.7 litres). Dr. T. R. Steen, consultant anaesthetist, anaesthetized her (atropine, 1/200 gr. (0.32 mg.) intravenously; nitrous oxide, oxygen, and ether) and G. G. L. explored the uterus manually. There were no placental fragments, no inversion, and no rupture. A left-sided cervical tear extending into the left fornix was found and sutured, and the uterus was packed. Bleeding appeared to be

controlled. G. G. L. remained with the patient thereafter, but instead of her condition improving it deteriorated.

By 2.15 p.m. she was having her sixteenth pint of blood into the left arm, and was also receiving oxygen by nasal mask for air-hunger. Despite rapid intravenous transfusion—1 pint (570 ml.) every five to ten minutes—her condition did not improve and noradrenaline infusion—2 mg. in a pint (570 ml.) of saline—was given into the right arm at the rate of 60 drops a minute. By 2.55 p.m., when 19 pints (10.8 litres) of blood had been transfused, it was appreciated that there was little or no response to this therapy and intra-arterial transfusion into the right femoral artery was begun by G. H. T. When the tubing of the giving set was disconnected from the needle to confirm that the artery had been satisfactorily entered, blood merely trickled from the needle hub, emphasizing the need for further and urgent replacement of blood volume.

The pack in the uterus was beginning to soak through, and on abdominal palpation it was appreciated that the uterus was being displaced towards the right side by a haematoma in the left broad ligament. By this time 2 pints (1.1 litres) of blood had been given into the femoral artery. During removal of the patient to the operating theatre the intra-arterial transfusion was disconnected.

At 3.45 p.m., when the pulse rate and blood pressure were still unrecordable, the patient was once again anaesthetized, by Dr. T. R. Steen (atropine, 1/200 gr. (0.32 mg.) intravenously; (induction) nitrous oxide, oxygen, and ether; (maintenance) oxygen and minimal ether, endotracheal) and the abdomen was opened. Total hysterectomy was performed. As soon as the uterus was out the haematoma evacuated, and while the clamps were still on the vessels intra-arterial transfusion was given into the left external iliac artery, as the patient was still failing to respond to intravenous transfusion. The artery was in intense spasm and the needle had to be guided to the lumen by feel.

Two pints (1.1 litres) of blood was transfused intra-arterially in seven minutes under a positive pressure of 211 mm. Hg, and for the first time for four hours the patient's blood pressure (brachial artery) became recordable at 100/80. After the transfusion of a further pint (570 ml.) of blood intra-arterially the patient's clinical condition had so improved that it was considered safe to continue with intravenous transfusion only. Technically, so far the intra-arterial transfusion had proved straightforward, but when the needle was removed from the external iliac artery haemorrhage from the point at which the needle had been inserted was worrying, but was controlled by clamping the vessel with a gauze-holding forceps. The uterine arteries and other pedicles were ligated, the vagina was closed, and before completing the peritonization the gauze-holding forceps were removed from the external iliac artery. The patient's condition was improving, and by 5.25 p.m. (after 32 pints (18.2 litres) of blood) her blood pressure was 100/?. The pulse rate was 100. At 5.40 p.m. the pulse rate was 120 and the blood pressure 100/?, and the 33rd pint of blood was run in slowly. Thereafter, the patient's condition steadily improved, and one further pint (570 ml.) of blood was started at 9.45 p.m., and given slowly, making a total transfusion of 34 pints (19.3 litres). Later the same evening she was vomiting and a Ryle tube was passed. Only small amounts of stomach contents were aspirated. The following morning (August 20) the patient's condition was remarkably good, pulse rate 88 and blood pressure 100/70. She was maintained on N/3 saline and dextrose and received a total of 7 pints (4,000 ml.) of water and 12 g. of salt in the first 24 hours. Morphine, 1/6 gr. (11 mg.), was given six-hourly. By August 22 all intravenous therapy was stopped, and the Ryle tube had been removed. The patient's subsequent progress was uneventful.

The day following operation (August 20) blood investigations were carried out as a check of the patient's clinical progress, with the following results: Hb, 14.4 g./100 ml. (97%); red cells, 4,960,000 per c.mm.; serum sodium, 133

mEq/l.; serum potassium, 2.6 mEq/l.; serum chlorides, 96 mEq/l.; serum protein, 12 mEq/l. A similar check, made 48 hours later, showed no significant change. Post-operative urinary excretion was satisfactory throughout.

Comment

One must regret that the slight trickle of blood during delivery of the child was ignored. This should have indicated trauma to the cervix and a tear. Although the house-surgeon passed a speculum and looked for a tear, more careful scrutiny under anaesthesia was called for.

In our opinion intra-arterial transfusion proved life-saving in this case. That it was not begun until 19 pints (10.8 litres) of blood had been transfused intravenously was due to the fact it was possible to give blood at a very rapid rate by the intravenous route and there were no signs suggesting right heart embarrassment. Intra-arterial transfusion was therefore delayed until it became clear that it was proving impossible to resuscitate the patient by intravenous transfusion. Following the transfusion of the first two bottles of blood intra-arterially (pints 20 and 21), the patient's blood pressure had improved enough to produce a small jet of blood to a height of about 1 cm. when the giving-apparatus was disconnected from the intra-arterial needle in the femoral artery. Transfusion via this route had to be disconnected because the needle became dislodged when the patient was being moved to the theatre. It was continued intravenously, however, and then recommenced intra-arterially via the external iliac artery as soon as the abdomen had been opened and the source of bleeding controlled.

So far as we are aware, no other patient in this country has required the urgent transfusion of 34 pints (19.3 litres) of blood before recovery. Reports have been published, however (Artz and Howard, 1954; Crosby and Howard, 1954), drawing attention to the survival of severely wounded battle casualties in Korea who had to receive similar massive transfusions. Artz and Howard concluded that, in their series, blood transfused by the intra-arterial route had no advantage over blood infused as rapidly by multiple intravenous routes. In our patient, however, no clinical response was obtained until blood was transfused intra-arterially, and we are of the opinion, therefore, that transfusion by this method is indicated, and may be life-saving, if despite rapid intravenous transfusion the patient is not responding. Intra-arterial transfusion is likewise indicated in a patient with severe haemorrhage to whom it proves impossible to transfuse blood at a rate of 1 pint (570 ml.) in not more than five minutes—for example, because of venous spasm.

Noradrenaline was resorted to in this case again because of the lack of clinical response to apparently adequate intravenous therapy. No improvement in the patient's condition could be attributed to its use, however, which is not surprising when the intense reactive spasm of the arterial system was found at operation. Upon reflection, we would now consider noradrenaline likely to be of value only if the patient's skin vessels are failing to show an adequate compensatory vasoconstriction.

It is noteworthy that, despite a period of severe hypotension lasting nearly three hours, when her blood pressure was unrecordable, the patient showed no subsequent evidence of renal or pituitary damage.

Bunker *et al.* (1955) have drawn attention to the possible danger of citrate intoxication following the transfusion of large volumes of stored blood. Krevans and Jackson (1955) have reported haemorrhagic disorders in patients receiving more than 10 litres of blood. No evidence of either such complication was apparent in this case. Subsequent experience with transfusion of large volumes of blood in several cases of accidental haemorrhage and afibrinogenaemia treated in this department have also failed to confirm the above dangers. Estimations of the blood volume in these cases have shown that more blood was necessary than was indicated by the clinical assessment of the patient (W. G. MacGregor and D. Tovey, 1955, personal communication).

Summary

A case is described of severe post-partum haemorrhage due to cervical laceration in a grand multipara.

The laceration extended into the lower uterine segment extraperitoneally without evidence of this when the hand explored the uterus.

The lesson is emphasized that a case of post-partum haemorrhage with a contracted uterus must be examined most carefully under general anaesthesia for high vaginal and cervical tears. Tearing of the cervix or vagina should be suspected when haemorrhage occurs round the head as it is delivered.

After stitching a cervical laceration and packing the uterus the patient's condition should improve when blood is transfused. If it does not, broad-ligament haematoma should be suspected and hysterectomy carried out without waiting for resuscitation of the patient—resuscitation which will not occur until haemorrhage has been arrested.

Intra-arterial transfusion of blood can induce a quick response during operation when the bleeding-points have been secured.

This patient required transfusion of 34 pints (19.3 litres) of blood and two operative procedures before recovery was assured.

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VALUE OF PROPANTHELINE BROMIDE IN TREATMENT OF ENURESIS

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There is no simple statement which adequately covers the phenomena of enuresis, whether one is speaking of causation, of mechanisms, or even purely of description. Most people now regard enuresis as a sign of immaturity or as evidence of regression to an immature form of behaviour under the stress of insecurity. The mechanism is much more complex than merely that of lack of continence of the bladder. Intermittent diuresis is apparent in most cases and probably present in all, and this is itself reminiscent of the lack of concentrating power of the infant kidney. The social disability of the symptom in the later years of childhood or in adult life is severe. Winnicott (1953) emphasized the need for "symptom tolerance" in paediatrics, by which he meant a refusal to become enthusiastic in the treatment of symptoms in disregard of the total situation of the sick child. He took as his text the life history of a child in whom enuresis appeared as one symptom of a necessary emotional regression, and showed how inadequately treated such a child would be if, presenting to the doctor through his parents' anxiety on account of the bed-wetting, treatment should be directed solely to the cure of this symptom.

Such limited understanding of enuresis in the life of a child accounts for the fact that not one of the many remedies employed has more than limited success. But

with understanding by doctors, parents, and teachers of the significance of the symptom, and a willingness to make a serious and continuing effort to restore the child's confidence, the symptom itself disappears. Short cuts in the treatment of enuresis are therefore only justifiable if a serious attempt has been made to secure this confidence. Any remedy which is harmless has a place in treatment if its employment is understood to be no more than an adjuvant, a lifting of the secondary burden of discomfort and feeling of social inadequacy, and possibly an encouragement to an understanding mother or guardian. Conditioning apparatus with which rather remarkable success can be obtained (at least in older children) falls into this category, and so do several drugs which it has been customary to use.

The mode of action of such drugs is not clear. Amphetamine, for example, which has some action on the peripheral autonomic nervous system, has a much more profound central action, and its effects in enuretic children are comparable to those which follow its use in psychiatry. Drugs with an atropine-like action have been used in the treatment of enuresis for a century; their mode of action also is central, not a simple peripheral one. Toxicity—that is, undesirable effects not contributing to the anti-enuretic action—limits the use of the naturally occurring drugs of this group, but there are now synthetic analogues which are relatively free from some of these unpleasant effects and which could therefore be tried as adjuvants in the treatment of enuresis, with some prospect of success.

Present Investigation

Propantheline bromide ("pro-banthine") is such a drug. It has been used fairly widely in conditions where it was believed that overaction of the parasympathetic was playing a part in symptom production. In order to see whether any anti-enuretic effect could be obtained, a controlled trial of the drug, used in a dosage which was known to be free of "toxic" symptoms, was undertaken. Eighty-two children took part in the trial, and these were allocated as they presented themselves to one of two groups alternately. Group A, the treatment group, were given propantheline, 15 mg. daily for the first four days, 30 mg. for the next four days, and 45 mg. for six days; group B, the control group, were given as placebo the excipient, without the propantheline, made and packed in exactly the same form by the manufacturer. The identity of the drug and the placebo was not disclosed to anyone taking part in the trial, either patients or staff, until all the results were collected. Eight children in group A and nine in group B failed to complete the trial, leaving 33 in group A and 32 in group B. In both groups, parents and guardians were asked to record wet beds and dry beds for a total period of eight weeks—for two weeks before the tablets were given, for two weeks during the taking of the drug, and for four weeks after it was discontinued. No child under 5 or over 15 was included. The age constitution of the two groups is shown in Table I.

TABLE I.—Age Incidence

Age in Years:	5-7	8-10	11-15	Total
Group A	8	14	11	33
" B	10	14	8	32
Total	18	28	19	65

No child was included who was recorded to have had less than two wet nights during the 14 days of preliminary observation. Of the 65 children completing the test, 29 were "deprived"—that is, separated from their families and living in children's homes; there were 15 of such children in group A and 14 in group B.