action is a sound application of regional anaesthesia which is based upon the existing knowledge of the autonomic nerve supply of the genital tract.

Compared with orthodox methods of sedation, caudal analgesia can accelerate the course of a delayed first stage of labour and lessen the need for caesarean section or mutilating vaginal operations to expedite the course of labour. However skilfully these latter operations are performed, each imposes a greater maternal risk than caudal analgesia, the dangers of which have been unjustifiably exaggerated. A close collaboration between the anaesthetist and obstetrician is fully justified to substantiate the claims for its efficacy in these special circumstances.

It might reasonably be argued that the favourable outcome of labour in the caudal series arose from the omission of the morphine which was administered to the control series. The experiment was designed, however, to give an answer in terms of therapeutic expediency rather than exact physiological mechanisms, and its results in such terms are conclusive.

This paper is deliberately concerned with patients who have been in labour for more than two days, which is the accepted definition of prolonged labour; but experience has shown that in future practice the method should be given serious consideration before this time has elapsed, to avoid the increased hazard of uterine infection and placental failure, or the extra risks of a caesarean section performed late in labour, should this ultimately prove desirable.

The personal interest and support of Professors Harvey Evers and E. A. Pask are gratefully acknowledged, together with the generous co-operation of the obstetricians at Princess Mary Maternity Hospital, who made this study possible. I am also indebted to Professor S. D. M. Court and Dr. G. Knox, of the department of child health, for their help in planning this investigation, and the presentation of statistical data.

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According to the 1956 annual report of Manchester's medical officer of health, Dr. C. METCALFE BROWN, the outbreak of poliomyelitis in Manchester last year produced the largest total of cases, 321, ever recorded there. Of the eight fatal cases, seven were adults. Special tests showed that two other virus infections were present at the same time, one of these being Coxsackie virus, so that it is impossible to say with certainty how many non-paralytic cases of poliomyelitis were correctly notified. The paralytic cases numbered 93. In 20 households more than one case of the disease occurred: in three houses three non-paralytic cases in each house, in a further 12 houses two non-paralytic cases, and in the five remaining houses one paralytic and one non-paralytic case.

INFLUENCE OF HIGH-PROTEIN DIETS ON LIVER-FUNCTION TESTS IN KWASHIORKOR

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In a previous publication (Kinnear and Pretorius, 1956) liver function was evaluated in 107 consecutive cases of kwashiorkor. Of the tests used, albumin levels were found to be constantly low while bromsulphthalein retention was significantly high in 84% of cases tested. Thymol turbidity, thymol flocculation, serum colloidal gold, serum colloidal red, total serum bilirubin, and van den Bergh reactions were shown to have no diagnostic or prognostic value. It was also found that bromsulphthalein retention was significantly higher on admission in those patients who later died.

The composition of the diets and assessment of the clinical findings have been discussed elsewhere (Brock *et al.*, 1955; Pretorius *et al.*, 1956).

The Chart shows no significant statistical difference in the ability of the various diets in increasing the speed of production of albumin. Similarly, no statistically significant differences in the return to normal of the other liver-function tests could be demonstrated between the diets.

For these reasons it is proposed to treat all the cases as one group, and we report here the influence of a high-protein diet on serial liver-function tests in 107 consecutive cases of kwashiorkor. Albumin and globulin were estimated in a further 84 cases, while bromsulphthalein retention was estimated in 51 cases.

Liver-function tests were performed on cases of kwashiorkor on admission. They were repeated twice weekly for variable periods up to three weeks.

The methods used have already been discussed (Kinnear and Pretorius, 1956).

Results

Serum Albumin.—Table I shows the changes in concentration of serum albumin over varying periods of time. There is a steady upward trend, which in the cases of the Borden mixture seems to be better than the other diets (see Chart). However, the Borden cases would appear to be less severe cases of the disease, as their initial albumin values were about 2 g. per 100 ml. as compared with ± 1.5 g. per 100 ml. for the other diets. The different high-protein diets showed strikingly similar improvement of the serum albumin concentration in the groups studied.

Serum Globulin.—The value of 2.29 g. per 100 ml. on admission (Table II) is within the normal range for American children given by Kagan and Stern (1955). The steady increase in globulin values during treatment with high-protein diets confirms the findings of Trowell *et al.* (1954). No one diet gave better production of globulin than another. The prognostic value of total serum globulin is limited because of the many factors which influence its concentration in the plasma. Its extrahepatic origin makes its value as a liver-function test doubtful, but it undoubtedly plays a part in the mechanism of some of the flocculation tests of liver function.

Thymol Turbidity and Flocculation.—It has been shown that thymol turbidity and thymol flocculation tests have no diagnostic or prognostic value in kwashiorkor (Kinnear and Pretorius, 1956). We found that 21% of clinically cured cases showed thymol values which changed from negative to positive during the course of the disease, while 11% of clinically cured cases showed an elevated thymol turbidity test during

the whole period of treatment. The reason for the change from normal to positive is obscure, but lipids have been implicated in the mechanism of the thymol test (Recant *et al.*, 1945). Table III shows an initial low total serum lipid concentration which rises rapidly during the 3–14 days of treatment and then tends to fall again. The change-over point for the thymol tests from negative to positive generally fell

within the 2–15 days period, and it is tempting to postulate a relationship between the positivity of the thymol test and the elevated serum lipids. However, the protein-lipid interrelationships of the thymol test are not as simple as this, and the rise in total lipids was a general phenomenon and not confined to those cases which showed a change of thymol test from negative to positive. Also the globulins tended to rise with time, and the influence of gamma-globulin on the thymol and other flocculation tests is well known. Table IV shows that treatment with the high-protein diet had little effect on the thymol turbidity test. Thymol flocculation tests followed the pattern of the thymol turbidity tests.

Serum Colloidal Gold and Serum Colloidal Red Tests.—Only four cases showed abnormal gold and red tests on admission, and a further four cases developed positive gold and red tests during treatment. A high-protein diet did not cause these tests to revert to normal. All eight cases, however, showed inverted albumin/globulin ratios during the period of treatment.

Van den Bergh Reaction and Total Serum Bilirubin.—All cases on admission showed a negative direct van den Bergh reaction and all the serum bilirubin estimations were within the normal range. No deviations from this were noted during treatment with a high-protein diet.

Bromsulphthalein Retention.—Too few cases on the individual diets were subjected to the bromsulphthalein test to assess the effect of different high-protein diets on the test. All the results were therefore combined. All cases were normal at three days and the retention became less as treatment progressed (Table V). No differences could be found between the various diets. The fall of concentration of bromsulphthalein in blood is a function of several factors other than excretion into the bile. Extrahepatic removal (Cohn *et al.*, 1947, 1948), intrahepatic storage (Eberhard and Grafe, 1953; Shore and Zilversmit, 1954), and duodenal reabsorption (Lorber and Shay, 1950) may all play a part. Alteration of the circulatory dynamics of the liver seems to

Regression lines for serum albumin after treatment with various high-protein diets. S.A.D.M. = Dried skimmed milk without vitamin supplement. S.A.D.M. + V.S. = Dried skimmed milk with vitamin supplement. C₂ = Casein formula with vitamin supplement. C₃ = Casein formula without vitamin supplement.

TABLE I.—Changes in Serum Albumin Concentration on a High-protein Diet

	On Admission	$\frac{1}{2}$ Week	1 Week	1½ Weeks	2 Weeks	2½ Weeks	3 Weeks
No. of cases	191	174	165	149	140	74	55
Mean (g./100 ml.)	1.57	1.75	2.21	2.50	2.78	2.77	2.90
Standard deviation	0.457	0.474	0.578	0.557	0.545	0.337	0.270
Range (g./100 ml.)	0.66–2.44	0.71–3.30	0.92–3.55	1.19–4.20	1.25–4.82	1.0–3.9	1.5–4.0

TABLE II.—Changes in Serum Globulin on High-protein Diet

	On Admission	$\frac{1}{2}$ Week	1 Week	1½ Weeks	2 Weeks	2½ Weeks	3 Weeks
No. of cases	191	174	165	149	140	74	55
Mean (g./100 ml.)	2.29	2.52	2.82	2.99	3.10	3.27	3.04
Range	1.53–5.00	1.54–4.6	1.43–4.95	1.53–5.46	1.90–5.10	1.80–5.30	1.55–5.30
Standard deviation	0.587	0.601	0.624	0.709	0.627	0.532	0.455

TABLE III.—Changes in Total Serum Lipids on a High-protein Diet

	On Admission	$\frac{1}{2}$ Week	1 Week	2 Weeks	3 Weeks
No. of cases	35	28	28	22	11
Mean (mg./100 ml.)	271	456	560	531	403
Range	46–1,200	149–960	194–915	296–894	225–625

TABLE IV.—Changes in Thymol Turbidity on a High-protein Diet

	On Admission	$\frac{1}{2}$ Week	1 Week	1½ Weeks	2 Weeks	2½ Weeks	3 Weeks
No. of cases	107	97	90	83	81	53	40
Mean MacLagan units	5.1	6.1	6.2	6.2	6.3	6.9	6.4
Range	0–18	0–25	0–29	0–18	0–27	0–19	0–18
Standard deviation	4.15	4.12	4.63	3.77	4.67	4.54	3.70

TABLE V.—Influence of High-protein Diet on Bromsulphthalein Retention

	On Admission	$\frac{1}{2}$ Week	1 Week	2 Weeks	3 Weeks
No. of cases	51	35	40	31	21
Mean (%)	15.0	5.4	3.9	2.7	1.9
Range (%)	2.4–40.0	1.1–24.3	0–27.3	0–16.0	0–8.4
Standard deviation	9.25	7.29	4.98	3.68	1.91

affect bromsulphthalein abstraction, but the mechanism of abstraction is not simple, and, in fact, contradictory (Culbertson *et al.*, 1951; Bradley *et al.*, 1952; Heineman *et al.*, 1952). It appears, however, that the liver is capable of removing a definite proportion of the bromsulphthalein injected (Myers, 1949; Casselman and Rappaport, 1954), with the hepatic artery and the distribution of blood in the arterial bed holding key positions in the abstraction of bromsulphthalein from the blood (Andrews, 1955).

It has been suggested that the fat-laden liver cells of kwashiorkor compress the sinusoids, with resultant low abstraction of bromsulphthalein (Gillman and Gillman, 1951). Bromsulphthalein retention was normal within three days in 84% of cases, and coupled with this was the finding of elevated blood fats also at three days. It is tempting to postulate a liver source for the elevated blood fat. With the relief on tension in the liver cells and consequent decompression of sinusoids a better blood supply would give more efficient abstraction of bromsulphthalein from the blood. Evidence from liver biopsies tends to make the clearing of fat from the liver cells a slow process (Trowell *et al.*, 1954); however, there is often no correlation between structural changes in the liver and functional efficiency as judged by current liver-function tests.

Elucidation of the bromsulphthalein test is under investigation in this laboratory, using bromsulphthalein clearance as index (Kinnear and Pretorius, 1957).

Summary

Groups of kwashiorkor patients were treated with high-protein diets of different composition. The effect of these different diets on serial liver-function tests was assessed.

No difference in efficacy in returning liver-function tests to normal could be found between the various diets tested.

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ANTIHAEMOPHILIC GLOBULIN DEFICIENCY ASSOCIATED WITH A CAPILLARY DEFECT

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A report by Ingram (1956) of a case of multiple haemostatic defects in a female prompted us to record the following examples in a brother and two sisters. Our cases, although less prolific in abnormalities than Ingram's, are of interest in that they conform to a pattern described by others (see Table) of an increased bleeding-time and defective thromboplastin generation due to antihaemophilic globulin deficiency. We feel that these cases constitute a distinct entity which until now has been included in the omnibus terms "von Willebrand's disease" and "pseudohaemophilia." The low antihaemophilic globulin level emphasizes the need for differentiation.

Case 1

A youth aged 17 had a tendency to bleed excessively. This was discovered following circumcision when he was 3 months old. He has always bruised easily and has had spontaneous purpuric rashes. He bleeds readily from nose and gums. There is a history of joint haemorrhage in the knees and shoulders. Following swelling of the left knee aspiration of the joint produced blood only. Persistent haemorrhage following this necessitated transfusion. He had had two teeth extracted at 7 years of age and bled for seven weeks. Again he had to be transfused.

Laboratory Findings.—Red blood cells, 5,270,000 per c.mm.; haemoglobin, 96% (14.3 g. per 100 ml.); colour index, 0.91; white blood cells, 8,800 per c.mm. (polymorph neutrophils 72%, polymorph eosinophils 2%, lymphocytes 20%, monocytes 6%); platelets, 342,000 per c.mm.; serum proteins, 7.23 g. per 100 ml. (albumin 3.72 g.; globulin 3.51 g.); plasma fibrinogen, 0.2 g. per 100 ml. Blood group O, Rh positive, phenotype CCDee, which in all probability corresponds to the genotype CDe/CDe. Tourniquet test positive. Bleeding-time—Ivy's (Ivy *et al.*, 1941) method—22 minutes. No capillary abnormality was demonstrated. Clotting-time—Lee and White's (1913) method—at 37° C., 11 minutes. Prothrombin time (Quick's method, using human brain extract), 12 seconds (control, 12 seconds).