hypotension, the effect of salt intake, the acquisition of tolerance, and numerous other factors will flounder between the dangerous and the ineffectual.

Summary

There is a close similarity in the hypotensive effects of penta- and hexa-methonium bromides, though formal tests show that hexamethonium bromide is usually slightly stronger in action. We have experienced no difficulty in interchanging these substances at approximately the same level of subcutaneous dosage.

Falls in blood pressure following penta- or hexa-methonium injections are influenced by posture, being greater as the patient approaches the vertical.

Under comparable conditions patients with the higher pressures tend to have the greater blood-pressure falls after hexamethonium bromide injections.

Following sufficiently large injections of these methonium halides, the casual blood pressure falls below the original level of the basal blood pressure, and may be well below this level even in the horizontal posture.

The effects of penta- and hexa-methonium injections on the pulse rate are not constant, but usually as the blood pressure falls the pulse rate increases. This statement applies to the blood-pressure changes induced by changes in posture.

Sensitivity tests to hexamethonium bromide have been carried out in 150 cases of high blood pressure, including 72 cases of fixed and 15 labile types of essential hypertension; 11 following sympathectomy; 11 patients with malignant hypertension; 21 with hypertension following pregnancy toxæmia; two with acute pregnancy toxæmia; 10 with impairment of renal function following surgical disorders of the kidney or nephritis; one case of hypertension associated with polycythaemia; and seven cases of miscellaneous aetiology. Poor response to penta- or hexa-methonium salts has so far been restricted to certain cases of renal damage; other cases with renal damage showed good blood-pressure falls. Fifty-three of the more severe cases were treated, and we have been able to maintain a substantial measure of control over the blood-pressure level.

On the basis of 150 test doses and treatment of 53 cases we would judge that, apart from some of the cases with impairment of renal function, almost all hypertensives can have their blood pressure controlled by these drugs. Among those with impaired renal function the four selected for treatment were readily brought under control without deterioration in their renal excretory capacity as judged by the T.N.P.N. estimations.

Repeated administration gives rise to considerable tolerance, such that 5 or 10 times the original dose may be required to produce the same effect. The acquisition of tolerance to hexamethonium bromide conveys an equivalent degree of tolerance to pentamethonium bromide, and vice versa.

Following repeated administration of penta- or hexa-methonium salts, patients who at the outset exhibit symptoms such as faintness on blood-pressure reduction usually become more tolerant of the lower blood-pressure levels.

The hypotensive actions of penta- and hexa-methonium salts are enhanced on a salt-poor diet (0.2 g. of sodium in 24 hours) to such a degree that dangerous reactions may occur if the effects of this potentiation are not allowed for in determining dosage.

Hypertensive headaches can be relieved in most patients.

The relief of signs and symptoms, when present, in cases treated over a period of months was prompt and striking. Particular reference has been made to the marked improvement of dyspnoea under treatment, and to the disappearance of papilloedema and retinal exudates. Pulmonary congestion disappeared, and there are indications of reduction in heart size and electrocardiographic improvement.

We desire to express our gratitude to Sister R. Wilson and Sister J. Woods; to Miss J. Rivers, Mrs. M. McLachlan, Miss A. Tunbridge, and Mr. C. Drake for technical help; to Miss M. Walsh and Miss M. Poppelwell for secretarial assistance; to Dr. W. R. Thrower, of May and Baker Ltd., who, knowing of our interest in other quaternary ammonium compounds, arranged for us to be supplied with penta- and hexa-methonium salts. Thanks are due to Dr. J. A. Kilpatrick for permission to quote in Table III work undertaken in collaboration with one of us. The expenses were defrayed in part by the Medical Research Council of New Zealand.

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BLOOD-GROUP FACTORS AND PHYSIOLOGICAL ICTERUS

BY

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Ever since the pioneering work of Yllpö (1913) and Hirsch (1913) it has been recognized that the icterus index of the serum of newborn infants is higher than the values considered normal for adults. Moreover, in most infants the icterus index rises during the first few days of life, not infrequently with resulting noticeable jaundice of the skin and mucous membranes. Most workers (Weech, 1947) consider that physiological jaundice is due to functional immaturity of the liver at birth. However, the course of the syndrome resembles so closely the course of erythroblastosis caused by mild sensitization to the Rh factor that the possibility has to be considered that physiological icterus may have a similar pathogenesis. For example, sensitization to the A and B agglutinogens has been shown (Halbrecht, 1944; Polayes and McNally, 1948; Wiener *et al.*, 1949) to be a not uncommon cause of a relatively benign form of icterus occurring in the newborn infant which has been designated as icterus praecox by Halbrecht (1944). Similarly it is possible that the benign syndrome of physiological icterus may be the result of some antigen-antibody reaction. Although

several studies have already been published on the blood-group factors in relation to physiological icterus (Lenart and Biro, 1929), a new study including the more recently discovered Rh-Hr blood types seemed in order, if only to exclude the A-B-O groups and Rh-Hr types as bearing a relation to the syndrome. In this paper we shall present studies on the icterus index, red-cell count, and haemoglobin concentration, as well as the A-B-O groups and Rh-Hr types, on 21 randomly selected newborn infants.

Materials and Methods

The babies studied were all newborn infants delivered by the obstetrical service at the Jewish

Hospital, the majority being members of the negroid race. There were no "premature" babies in the group, all weighed over 2,500 g., and all had been delivered close to term. A sample of the baby's blood for typing was obtained from the umbilical cord at birth, and blood from the mother was usually obtained on the following day. On every day thereafter for the first five days of life a sample of the baby's blood was obtained from the femoral vein and mixed with oxalate as for the Wintrobe-Landsberg sedimentation test. The A-B-O and M-N type and the Rh-Hr type of every baby and its mother were determined in the usual manner. The icterus indices were determined on the oxalated plasma by the acetone method, and red counts

TABLE I.—Cases in which the A-B-O Groups and Rh Factor of Mother and Baby were Compatible

Case No.	Blood Types		Type of Test	Age of Baby (Days)				
	Mother	Baby		Cord Blood	1	2	3	4
1	OMNRh ₂ Rh ₀	OMNRh ₁ rh	I.I. Hb R.B.C.	8 — —	38 112 5.94	38 113 5.68	— 115 5.79	32 113 5.74
2	OMRh ₀	OMRh ₀	I.I. Hb R.B.C.	4 — —	8 107 5.45	8 111 5.59	8 — —	8 — —
3	A ₁ MNrh Anti-Rh absent	OMNrh	I.I. Hb R.B.C.	10 — —	16 100 4.69	16 103 4.72	— — —	— — —
4	ONRh ₀	OMNRh ₀	I.I. Hb R.B.C.	10 — —	16 115 5.70	— — —	16 117 5.86	— — —
5	OMNRh ₁ rh	OMNRh ₁ rh	I.I. Hb R.B.C.	6 — —	16 105 5.3	18 105 5.22	12 126 5.82	16 — —
6	ONRh ₀	OMRh ₀	I.I. Hb R.B.C.	10 — —	36 117 5.71	48 117 5.58	100 117 5.59	— — —
7	OMNRh ₀	OMNRh ₀	I.I. Hb R.B.C.	16 — —	48 128 5.34	— — —	— — —	— — —
8	A ₂ Nrh'rh Anti-Rh absent	ANrh'rh	I.I. Hb R.B.C.	20 — —	24 97 4.36	44 95 4.35	— — —	— — —
9	A ₂ MNRh ₁ rh	A ₂ MNRh ₁ rh	I.I. Hb R.B.C.	14 — —	32 115 5.93	40 110 5.72	48 110 5.74	46 — —
10	AMRh ₂ rh	AMNrh	I.I. Hb R.B.C.	— — —	20 95 4.92	24 97 5.63	21 — —	32 99 5.23

I.I. = icterus index; Hb = haemoglobin concentration; 100% = 14 g./100 ml.; R.B.C. = red cell count in millions per c.mm.

TABLE II.—Cases in which the Baby's A-B-O Group and/or Rh-Hr Type was Incompatible with that of the Mother

Case No.	Blood Type		Type of Test	Age of Baby (Days)				
	Mother	Baby		Cord Blood	1	2	3	4
11	BMRh ₂ Rh ₀	A ₁ MRh ₂ Rh ₀	I.I. Hb R.B.C.	6 — —	8 106 5.36	16 — —	14 — —	— — —
12	BMRh ₁ rh	BMRh ₁ Rh ₂	I.I. Hb R.B.C.	4 — —	— 110 5.94	8 108 5.40	8 110 5.47	— — —
13	OMrh Anti-Rh absent	OMNRh ₀	I.I. Hb R.B.C.	12 — —	20 110 5.51	44 112 5.31	44 107 5.34	48 106 5.34
14	ANrh Anti-Rh absent	BMNrh	I.I. Hb R.B.C.	8 — —	36 114 5.73	32 116 5.81	46 114 5.79	42 110 5.58
15	OMNRh ₁ rh	MNRh ₀	I.I. Hb R.B.C.	12 — —	16 92 4.14	12 93 4.16	— — —	— — —
16	A ₁ MRh ₁ rh	A ₁ MNRh ₂	I.I.	12	24	24	—	48
17	OMNRh ₁ rh	AMNRh ₀	I.I.	4	4	8	10	8
18	OMRh ₁ *Rh ₁	AMNRh ₁ *Rh ₁	I.I.	12	20	24	32	36
19	OMNRh ₀	OMNRh ₁ rh	I.I. Hb R.B.C.	8 — —	16 88 4.64	32 88 4.73	32 103 5.53	32 95 4.93
20	ONRh ₁ rh	ANRh ₁ rh	I.I. Hb R.B.C.	14 — —	32 106 5.62	40 104 5.43	48 103 5.42	— — —
21	ANRh ₂ rh	ABMNRh ₀	I.I. Hb R.B.C.	— — —	14 110 5.73	18 110 5.74	21 117 4.6	32 106 5.2

and haemoglobin determinations were carried out on the daily samples of the oxalated blood. Tests for Rh antibodies were made on the serum of all mothers found to be Rh-negative.

Results

The cases were divided into two categories depending on whether the A-B-O group and the Rh types were compatible or incompatible with those of the mother, and the results are summarized in Tables I and II. As will be seen, the average icterus index of the cord serum for the group with compatible blood types was 10.8 units, as compared with the average of 9.2 units for the group with incompatible blood types. In most babies of both groups the icterus index rose immediately after birth, and at the highest point in the compatible group the average icterus index was 36.8 units, in comparison with an average at the highest point of 30.9 for the incompatible group.

These results indicate that the high icterus index of the cord serum and the rise which occurs in the neonatal period are not ascribable to any incompatibility involving the A-B-O groups or Rh types. In accordance with the previous observations (Weech, 1947) the values of the blood counts and haemoglobin determinations remained constant from day to day, indicating that the rise in icterus index was not due to haemolysis.

Comment

Inadequacy of the excretory function of the liver has been shown to be one of the phenomena associated with physiological icterus. The cause for this malfunction has not been determined, though most workers in the field have ascribed it to "immaturity" (Weech, 1947). Because erythroblastosis foetalis is also attended by a marked diminution in the excretory capacity of the liver, Wiener (1951) has postulated a pathogenesis for physiological icterus on an analogous basis. Examination of women at term demonstrates the constant presence in their serum of auto-antibodies in tests carried out at ice-box temperature, especially when enzyme-treated test cells are used. Almost invariably the antibodies are of the univalent variety, so they are presumably capable of traversing the placental barrier and coating the foetal red blood cells. As in the case of mild Rh sensitization, the auto-antibodies derived from the maternal circulation are only occasionally demonstrable free in the cord serum, but the practically universal occurrence of hyperbilirubinaemia in the newborn infant could be explained by the universal occurrence of auto-antibodies in the maternal blood.

One of us (A. S. W.) has further postulated that, since the antibodies are of the cold variety, the cooling of the baby's skin that attends his birth brings about clumping of the coated red cells and acts as the trigger mechanism that sets off the explosion that is physiological icterus. The high incidence of icterus in premature infants, with their poor temperature control, may have a similar explanation, although here developmental immaturity also has great plausibility.

We have recently encountered a case in which an expectant mother was found on antenatal testing to possess cold antibodies in her serum with a titre approximately three times as high as the upper limit found in other mothers. The baby born to this mother developed mild jaundice and anaemia, the haemoglobin dropping to 65% by the time the baby was 3 weeks old.

No other cause for the anaemia could be demonstrated. As the titre of cold antibodies has been shown to be elevated in cases of atypical pneumonia and infectious mononucleosis, a search is being made for cases in which pregnant women had these ailments shortly before term.

Summary

Studies of the A-B-O groups and Rh-Hr types revealed no relationship between these blood factors and the occurrence of physiological icterus in the newborn infant. The average icterus index of the cord serum in babies with compatible and incompatible blood types did not differ, being 10.8 and 9.2 units respectively. At the peak of the hyperbilirubinaemia the values were 36.8 and 30.9 units respectively. There was no fall in red blood cell count or haemoglobin concentration accompanying the rise of icterus index. The possible relationship of auto-antibodies to the syndrome of physiological icterus is discussed.

We wish to express our appreciation to Mrs. Elaine Rieders and Miss Barbara Didio for the performance of the blood counts and the icterus index determinations.

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ANGIOCARDIOGRAPHY IN CONGENITAL HEART DISEASE

ANAESTHESIA AND TECHNIQUE

BY

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Kreutzer *et al.* (1950) state that "angiocardiology is simple and harmless so far as our experience shows." The results from a series of 172 cases of angiocardiology performed for congenital heart disease at Guy's Hospital make it impossible to agree with this statement.

Literature

Forssmann (1929) was the first to introduce a catheter into the heart (his own) and also to inject a dye (iodoxyl B.P., "uroselectan" 35-50%), but it was not until 1937 that the first *clear* view of the right side of the heart and pulmonary arteries in man was shown by Castellanos *et al.* (1938a). They were unable to show the left side of the heart and aorta, because of the poor contrast medium used. In the following year Robb and Steinberg (1939), using "diodrast" 70% (diodone; the diethanolamine salt of 3,5-diiodo-4-pyridone-N-acetic acid, containing 49.8% iodine), showed the left side of the heart and aorta as well. Their technique, or some modification of it, is the one most commonly used to-day. In these investigations general anaesthesia seems to have been used very infrequently.

Kreutzer and his colleagues carried out their investigations entirely on infants and children without any form of general anaesthesia. They used diodone 75% as the contrast medium in doses of 10 ml. for the