strongly advocated (Rickham, 1952). Most paediatricians will agree that certain congenital abnormalities such as oesophageal atresias and genito-urinary malformations require the specialized surgical techniques available only at regional centres. Abdominal malformations of the alimentary tract, particularly obstructions of the small intestine, are probably the most urgent of the remedial congenital malformations. Early diagnosis and immediate pre-operative treatment are required. Available statistics suggest that after 96 hours the operative mortality even in the most capable hands is practically 100%. The delay and disturbance necessarily involved in transferring such cases from outlying hospitals to regional centres is unjustified. Rickham (1952) points out that a surgeon working in one hospital group is unlikely to see more than one or two such cases a year, and therefore unlikely to gather enough experience to deal correctly with the complicated surgical problems. On the other hand, the general surgeon, owing to the development of other surgical specialties, is a specialist in abdominal surgery, and neonatal abdominal surgery should rightly remain within his province.

Summary

Two cases of congenital obstruction of the small intestine in premature infants, with recovery after operation, are reported. The question whether congenital surgical abnormalities in the newborn should be treated locally or at regional centres is discussed. It is suggested that certain congenital abnormalities requiring specialized surgical technique should be transferred to regional centres, and that others, such as obstructive malformations of the small intestines, should be treated locally.

Our thanks are due to Dr. W. S. Dickson, Dr. W. Niven, and Miss K. M. Watson; to the junior medical staff; and to the nursing staff of the Huddersfield Royal Infirmary and the Princess Royal Maternity Home for their invaluable assistance.

REFERENCES

Duncan, P. A., Wearn, F. S., Jackson, H. F., and Waldron, W. S. (1943). *J. Amer. med. Ass.*, **123**, 764.
Gross, R. E. (1948). *Surgery*, **24**, 277.
Jarcho, J. (1937). *Surg. Gynec. Obstet.*, **65**, 593.
Ladd, W. E., and Gross, R. E. (1941). *Abdominal Surgery of Infancy and Childhood*. Saunders, Philadelphia.
Ministry of Health (1949). *Rep. Publ. Hlth Med.* Subject No. 94. London.
O'Neill, J. F., Anderson, K., Bradshaw, H. H., Lawson, R. B., and Hightower, Felda (1948). *Amer. J. Dis. Child.*, **75**, 214.
Rickham, P. P. (1952). *Lancet*, **1**, 332.
Stetten, De W. (1940). *Ann. Surg.*, **111**, 583.
Stevens, A. E. (1951). *Arch. Dis. Child.*, **26**, 166.
Wangensteen, O. H. (1942). *Intestinal Obstruction*. Thomas, Springfield, Ill.
Ward, C. S., jun., and Cooper, F. W., jun. (1943). *Ann. Surg.*, **117**, 718.

In 1911 Dr. M. David Eder read a paper on "A Case of Obsession and Hysteria Treated by the Freud Psychoanalytic Method" to the neurological section at the Annual Meeting of the B.M.A. It was the "first public contribution to clinical psycho-analysis" in Britain to be described publicly, and was later published in this *Journal* (1911, **2**, 750). Now, 42 years later, the case has been followed up—which in that respect probably makes it unique in the psychiatric literature, as Drs. Hunter and MacAlpine indicate in the *British Journal of Medical Psychology* (1953, **26**, 64). The patient first consulted Dr. Eder in 1910 because he was worried by a dull aching pain in the back of the neck which caused considerable depression. He was treated twice weekly for three months—the technique being based mainly on free associations and dream analysis. At the last session he was hypnotized, and Dr. Eder suggested to him that he was cured. At the age of 68 he still has some symptoms, mainly of intense pain and tension in the head, which he relieves with barbiturates. But on the whole, says the report, he seems to have made a satisfactory adaptation to life, and learned to live with his symptoms. An interesting point mentioned by these authors is that the patient, who was found to have a "mother complex" displaced on to his sister Ada, probably chose Dr. Eder because of the homophony of the names. But this, involving the concept of transference then little appreciated, went unnoticed by Dr. Eder.

SUCCINYLMONOCHOLINE

BY

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Whittaker and Wijesundera (1951) reported that the product of succinylcholine (succinyldicholine SDC) hydrolysis by horse serum was succinylmonocholine (SMC). We decided to study this process, using human serum. While this work was in progress another communication by Whittaker and Wijesundera (1952) described work done with a highly concentrated horse pseudocholinesterase (33,000 units per ml.) confirming that, in the enzymatic breakdown of SDC, first SMC was formed, but that this was an intermediate which was subsequently hydrolysed to succinic acid and choline: SDC → SMC + choline; SMC → succinic acid + choline. We found the same with human serum, and when using similar concentrations (SDC 1.1, SMC 0.7 mg. active cation per ml.) could show that SDC was at first hydrolysed four to six times as fast as SMC, but that between 40 and 60% hydrolysis point the speed slowed and became identical with that of hydrolysis of pure SMC. Thus, using a highly concentrated human cholinesterase, we found that it contained for one unit SMC hydrolysis six for SDC. One unit equals 1 μl. CO_2/ml./min./37° C. obtained by the bicarbonate method according to McArdle (1940). At higher substrate concentrations the difference falls, and when they reach 15 times the values with which Whittaker and Wijesundera worked the ratio becomes less than 2 : 1 (see Table I).

TABLE I.—*μl. CO_2/min./ml. of Pseudo-cholinesterase (Human, 16,000 Units) Produced at 20% Hydrolysis Point of Succinyldicholine and Succinylmonocholine. Total Volume, 3 ml.; Enzyme Dilution, 1:60*

Substrate Concentration 10^{-3}M	Succinyldicholine SDC	Succinylmonocholine SMC
55	580	350
5·5	514	134

Whereas SMC resembles SDC in its response to pseudocholinesterase, as a substrate of the true cholinesterase of the red cells it occupies a position midway between acetylcholine and SDC. Table II shows that SMC, like acetylcholine and unlike SDC, is hydrolysed by true cholinesterase at low substrate concentrations. It resembles SDC in inhibiting acetylcholine hydrolysis by the true cholinesterase, but whereas SDC is still effective at very low concentrations (Evans *et al.*, 1952) SMC inhibits only at the high levels at which the acetylcholine itself becomes an inhibitor.

TABLE II.—*μl. CO_2/min./ml. of Packed, Washed, and Laked Human Red Cells, 37° C., Bicarbonate Buffer. Substances are Referred to as mg. Active Cation/ml. Total Volume, 3 ml.; Enzyme Dilution, 1:75*

	0·7 mg. Acetylcholine	0·9 mg. SMC
—	149 μl.	24 μl.
+7 mg. acetylcholine ..	71 ,,	71 ,,
+9 mg. SMC	69 ,,	21 ,,

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Effect on the Rabbit

SMC has been considered pharmacologically inactive by Bovet *et al.* (1951), but nevertheless they noted a "head-drop effect" with 10 mg. of SMC iodide per kg. of rabbit, compared with 0.2 mg. of SDC di-iodide per kg. As there was here a substance which had a pharmacological action and which could be destroyed by cholinesterases, we decided to investigate the effect on the rabbit in the first instance. The animals were females weighing between 2.5 and 3 kg. The dosages represent active cation of SMC injected intravenously in mg./kg. No effect could be seen below 0.8 mg.; 0.8 to 1.2 resulted in slight depolarizing twitches but no paralysis : 1.3 to 1.5 produced a transient head-drop ; from 1.5 to 4.5 there was paralysis of increasing duration—150 seconds at 2.5 and 570 seconds at 3.5. At this latter range the breathing was shallow, but there was no apnoea. A dosage above 4.5 could, and above 5 did, regularly cause respiratory paralysis. When given in doses above 7 mg.—that is, twice that producing 10 minutes' relaxation without apnoea—SMC caused a fall in blood pressure followed by a fall in heart rate. There seemed to be a hexamethonium-like effect on the peripheral blood vessels accompanied by "pooling" of blood in dependent parts of the body. It was followed by a depressant effect on the heart, which persisted after severing the vagus. Thus there is a wide range from the head-drop dose of 1.5 to the toxic dose of 7.5. SMC is much longer acting than SDC at similar pharmacological levels—doubtless because it is so much more slowly destroyed by pseudo-cholinesterase than SDC. An injection of 1 ml. of human pseudo-cholinesterase (16,000 units) terminated the effect of SMC as effectively as that of SDC. In fact, such treatment will allow a rabbit (female 2.5–3 kg.) to survive with impunity a threefold lethal dose of both SDC and SMC.

To find whether these results are applicable to man further work will have to be carried out on other mammals. One certainly would not like to embark on the injection of unusually large amounts of a choline derivative into man without ample reassurance. There exist for man a number of long-time relaxants which are readily controlled by neostigmine ; nevertheless a long-acting relaxant which could be counteracted by a harmless compound might be a useful addition to the equipment of the anaesthetist. Neostigmine tends to be given in emergencies and to patients who are already at hazard, and there is always a risk of a toxic effect. Be this as it may, at any rate so far as the rabbit is concerned there exists a cholinergic compound which resembles decamethonium in its prolonged curarizing action and succinylcholine in permitting this action to be terminated at will by the injection of pseudo-cholinesterase.

The Function of Pseudo-cholinesterase

It has hitherto not been possible to allot to the pseudo-cholinesterase a function in life, particularly as, unlike true cholinesterase, it can be removed by specific inhibitors in man and animals *in vivo* without notable ill effect. The most important study on the distribution of pseudo-cholinesterase was that carried out by Ord and Thompson (1952) on brain and nerves of man and animals ; they demonstrated by the interplay of specific substrates and inhibitors that the pseudo-enzyme is largely in the white matter of the central and peripheral nervous system in close association with the true cholinesterase of the grey substance. There are now at least four compounds which "poison" the true cholinesterase and are destroyed by the pseudo-cholinesterase : acetylcholine and SMC in high concentrations, SDC and suxethonium at high and low concentrations. Except for acetylcholine, the compounds tested have been synthesized *in vitro*, but it is obvious that similar substances must arise in the intermediary metabolism of the body. It may therefore not be unreasonable to suggest that a function of pseudo-cholinesterase is that of protecting true cholinesterase from non-specific inhibitors.

Summary

Succinylmonocholine inhibits true cholinesterase of man and is broken down by the pseudo-cholinesterase. In rabbits at concentrations of 3.5 mg. of active cation per kg. of body weight it produces muscular relaxation of 10 minutes' duration without apnoea ; its effect can be terminated at will by the injection of pseudo-cholinesterase. Prior injection of pseudo-cholinesterase will protect rabbits against toxic doses.

It is suggested that a function of pseudo-cholinesterase is that of protecting true cholinesterase against non-specific inhibitors.

We thank Professor D. Bovet and Messrs. May and Baker Ltd. for gifts of succinylmonocholine. We are indebted to Professor K. J. Franklin, who kindly gave us the hospitality of his laboratory for the kymographic recording of blood pressure changes; to Dr. G. Boissard, for assistance in this part of the work ; and to Drs. F. T. Evans and P. W. S. Gray for helpful discussions. Dr. E. B. McLean kindly provided us with a concentrated pseudo-cholinesterase solution produced by a further fractionation of Cohn's fraction IV–6–1 with ammonium sulphate. We are grateful to the Medical Research Council for an expenses grant, and for a maintenance grant to one of us (E. S.).

REFERENCES

Bovet, D., Bovet-Nitti, F., Guarino, S., Longo, V. G., and Fusco, R. (1951). *Arch. int. Pharmacodyn.*, **88**, 1.
Evans, F. T., Gray, P. W. S., Lehmann, H., and Silk, E. (1952). *Lancet*, **1**, 1229.
McArdle, B. (1940). *Quart. J. Med.*, n.s. **9**, 107.
Ord, M. G., and Thompson, R. H. S. (1952). *Biochem. J.*, **51**, 245.
Whittaker, V. P., and Wijesundera, S. (1951). Ibid., **49**, xlv.
—— —— (1952). Ibid., **52**, 475.

Medical Memorandum

Stevens-Johnson Syndrome

A further case of this rare disease is reported in the hope that the photographs will be of help to others who have not encountered it. Involvement of the nails is a feature that has not been mentioned in previous cases.

CASE REPORT

A boy aged 5 years 3 months had been in good health since the removal of his tonsils and adenoids two months previously on account of frequent attacks of tonsillitis. The only other illnesses were measles at 3, whooping-cough at 5, and several large epistaxes. The family history was not relevant. On September 7, 1949, a slight discharge from both eyes was noticed, and his appetite became poor. This discharge increased rapidly and the lids became oedematous. The next day his lips began to swell, a rash appeared, and he was febrile. He was admitted on September 9. The clinical picture is shown in the photographs, taken the next day. The features of the case were :

Bilateral angular conjunctivitis, with a profuse purulent discharge and much irritation, which made him rub the oedematous lids. There was no corneal ulceration.

Haemorrhagic crusting of the lips, strikingly confined to the red margins, extending neither to the mucous membrane inside the lips nor to the relative normal surrounding skin, producing by contrast the appearance of circumoral pallor (Fig. 1).

The Rash.—The distribution was general but more pronounced on the face, extensor surface of the forearms, palms (but not the soles), and nail margins. On the face the cheeks were the most affected, with fewer lesions round the mouth, on the forehead, and (not shown) behind the pinnae. The penis was involved no more than the trunk, and there was no urethritis. The configuration was pleomorphic, the discrete lesions varying from 2 to 5 cm. in diameter and tending to be circular or oval. The lesions

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