can be seen from the Table, with tubocurarine and gallamine there was a significant decrease in the period of respiratory paralysis after sarin, whereas with succinylcholine there was a significant increase. This effect of sarin was temporary, the period of respiratory paralysis in general showing less change with a longer period of delay. Sarin had no appreciable effect on the respiratory paralysis following decamethonium iodide.

Cholinesterase Estimations.—The results obtained from the plasma cholinesterase estimations were so anomalous that no attempt was made to correlate them with the periods of respiratory paralysis. There was a wide variation between individual monkeys in their clinical response, as well as in the degree of blood cholinesterase reduction produced by sarin.

Discussion

The results of this investigation are in accordance with current theories of neuromuscular block (Paton, 1953). Tubocurarine and gallamine achieve their action by inhibiting acetylcholine at the neuromuscular junction, and this effect is antagonized by sarin. The duration of the block with succinylcholine is governed by the speed with which the drug is hydrolysed in the blood and at the end-plate; sarin, by preventing hydrolysis, prolongs the action. Since decamethonium iodide acts not by preventing the action of acetylcholine but by mimicking it, and is not destroyed by cholinesterase, anticholinesterases have no effect. The experiments showed that these changes were more marked when the relaxant was given soon after exposure to the anticholinesterase and diminished with the passage of time, presumably owing to the gradual regeneration of cholinesterase to effective physiological levels.

It is interesting to note the large dose of succinylcholine needed to produce respiratory paralysis in the monkey, approximately ten times the dose for man. There was much less species difference in the dosages of the other three drugs.

Conclusions

With the exception of decamethonium iodide, the duration of action of the relaxants commonly used in anaesthesia appears to be modified temporarily by the effects of anticholinesterase intoxication. With the extended use of these substances as insecticides the possibility of inadvertent poisoning must be considered (Barnes and Davies, 1951) if a relaxant has to be used. This may be of particular importance to Service medical officers and others who may be called upon, in the event of war, to anaesthetize casualties who have been exposed to sarin.

Summary

A description is given of a series of simple experiments designed to determine the effect of intoxication with sarin on the duration of muscular relaxation produced by tubocurarine, gallamine, succinylcholine, and decamethonium iodide.

The duration of the respiratory paralysis induced by tubocurarine and gallamine is decreased, that produced by succinylcholine is increased, and the effect of decamethonium iodide is unchanged following sarin.

The clinical implications of these results are discussed.

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FAMILIAL HYDRONEPHROSIS

BY

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The coincidence of more than one case of hydronephrosis in a family is rare enough to attract attention. The incidence of non-calculous hydronephrosis in the family here reported is remarkable, and in view of its bearing on the aetiology of non-calculous hydronephrosis in general this occurrence is worthy of record.

Details of Family.—The constitution of the family is shown in the accompanying diagram. All the members of the family other than the four patients here described are apparently healthy and no other congenital abnormalities are known. There was no consanguinity.

Genealogical tree of family, showing distribution of cases. Ages at time of writing in parentheses.

Case 1

An unmarried girl of 19 was first seen in April, 1951. Her only complaint was of embarrassment occasioned by a generalized and gradually progressive abdominal swelling, which she had first noticed three years previously. The rate of enlargement had been noticeably greater in the preceding three months. She had no other complaints, and, in particular, there was no history of pain or disturbance of micturition. There had been no previous illnesses.

Examination revealed abdominal enlargement almost to the size of a full-term pregnancy, and on palpation this appeared to be due to a cystic swelling, localized mainly in the lower abdomen and extending up over the whole of the right side of the abdomen.

Straight x-ray examination showed a complete absence of gas and bowel shadows in the right half of the abdomen, and the liver, renal, and psoas outlines were not visible. All the bowel shadows were displaced to the left, apparently by a large fluid-containing cyst which was thought to be probably ovarian.

Laparotomy on May 3 revealed the tumour to be a massive right-sided hydronephrosis which contained 11 pints (6.2 litres) of fluid. Practically nothing was left of the normal renal tissue. The tumour was removed. The ureter was not dilated. No cause for the hydronephrosis was discovered. Post-operative progress was satisfactory and the patient was discharged from hospital two weeks later, since when she has remained well.

Case 2

A female infant was delivered normally at full term in February, 1953. Her birth weight was 5 lb. 2 oz. (2.3 kg.).

At birth she was noted to have a rather protuberant abdomen which contrasted markedly with the otherwise wasted appearance of the limbs, chest, and face. She was breast-fed from birth, but sucked poorly and initially vomited after her feeds, though after about three weeks this ceased. The abdominal distension increased, and appeared to be due to an ill-defined mass, dull to percussion, on the left side of the abdomen. By the end of the sixth week the infant's general condition was somewhat improved and she was feeding better, but the abdominal enlargement was still progressing. A pyelogram at this time revealed complete absence of excretion from the left kidney.

On May 1 the abdomen was explored through a left paramedian incision and the swelling was found to be due to a large left-sided hydronephrosis. The pelvis and calices were grossly dilated and the renal tissue was reduced to a mere shell. There was a well-marked uretero-pelvic junction and the ureter was not dilated. No cause for the hydronephrosis was found. Nephrectomy was performed.

The wound healed satisfactorily but the infant did not "pick up." Two weeks later she started vomiting, and gastric peristalsis was visible. This settled completely after a short course of "eumydrin," and her subsequent convalescence was uneventful, with a satisfactory weight gain. She was allowed home on June 18, since when, apart from two attacks of bronchitis, she has been well. She is, at the time of writing, a perfectly normal healthy-looking baby aged 1 year.

Case 3

This patient, a married woman of 23, was first seen in August, 1953, almost exactly a year after the delivery of a first child. She had been perfectly well during the pregnancy. Her presenting complaint was of a dull ache in the right loin which had started two weeks previously. In the preceding week she had felt generally ill, with occasional nausea and vomiting, had complained of headaches, and had sweated profusely. Micturition was frequent and somewhat painful, and she had to rise two or three times at night to pass water. There had been no previous illnesses.

Examination revealed a healthy-looking but febrile woman with herpes labialis. There was a tender cystic mass in the right flank which was thought clinically to be a hydronephrosis. The urine contained albumin and a deposit which microscopy confirmed as pus. Bacteriological examination produced a pure culture of *Bact. coli*. The infection settled quickly with alkalis and sulphonamides by mouth, and she was admitted to hospital one week later for further investigation.

At operation on September 18 the right kidney was removed through a right lumbar incision. It consisted of a thin shell of kidney tissue round a grossly distended pelvis. A large leash of blood vessels was observed at the uretero-pelvic junction. Post-operatively, recovery was uninterrupted and she has been perfectly well since.

Case 4

A married woman of 37, the mother of three children, aged 17, 15, and 3, was first seen in June, 1953. During her last pregnancy she had suffered from pre-eclampsia, but the obstetric history was otherwise normal. There had been no other illness. On June 26 she had noted a sudden onset of pain in the right loin during the afternoon. This was associated with vomiting. She felt generally unwell and had to go to bed. When first seen later that day she complained also of headache, pain on micturition, frequency, and sweats. There was marked right-sided renal tenderness but no palpable mass. The urine showed numerous pus cells in an uncentrifuged specimen. The blood pressure was 150/90. She had a course of alkalis and sulphonamides by mouth, and after a week felt perfectly well, was afebrile, and was again up and about. There was then no albumin or microscopical abnormality in the urine. She refused further investigation.

On September 11 she was again seen with a recurrence of pain in the right loin of one week's duration, less severe

but more persistent than that experienced previously. There were no febrile symptoms on this occasion and no disturbance of micturition. A cystic mass, clinically a hydronephrosis, was now palpable in the right flank. The urine showed a trace of albumin, a deposit of pus, and a growth of *Bact. coli* on culture.

Intravenous pyelography two weeks later revealed a somewhat enlarged right renal outline. Both kidneys excreted the dye. There was very well marked caliceal hydronephrosis on the right, but the pelvis and ureter contained no visible dye.

On October 16 a right lumbar nephrectomy was performed. There was gross caliceal and pelvic hydronephrosis. The ureter was of normal dimensions. The post-operative course was satisfactory and she was discharged from hospital three weeks later. Since then she has remained well.

Discussion

The occurrence of four cases of non-calculous hydronephrosis in two generations of one family would appear to rule out coincidence as an explanation. All the patients were females. In one generation three out of four sisters were affected. I have not been able to examine the other, apparently healthy, members of this family to see if any present a symptomless hydronephrosis, but obviously such a possibility exists, since the cases here reported came under observation only because of the large size of the tumour or because of the accident of infection. Thus in Case 1 the hydronephrotic sac had reached enormous proportions, containing 11 pints (6.2 litres) of fluid; in Case 2 abdominal enlargement due to the hydronephrosis was already present at birth; and Cases 3 and 4 presented with the signs and symptoms of a urinary infection.

In speaking of the aetiology of hydronephrosis Winsbury-White (1951) states: "Heredity can claim some cases." A search of the literature, however, reveals few reported cases of familial hydronephrosis. Blackwood (1896) quotes Virchow as having described the case of a woman who gave birth to three premature children, each with hydronephrosis. The cases in the family reported by Mackay (1944) differ from those here described in that they were associated with megaloureter. The history in this family was remarkable. Of seven siblings, five had congenital kidney lesions, three having megaloureters (in one bilateral) and two having congenital sarcomata of the kidney. The paternal grandfather had had a calculous pyonephrosis and may therefore have had a congenital hydronephrosis. Aaron and Robbins (1948) reported the cases of two brothers, aged 12 and 16, with hydronephrosis. In both "aberrant lower pole vessels were definitely established as the cause of hydronephrosis."

The pathogenesis of the hydronephrosis in the cases reported here is obscure. In only two is there any suggestion of a definite cause—in Case 3, which presented following pregnancy and in which aberrant vessels were reported at operation, and in Case 4, in which the patient had had three pregnancies, the last three years previously. There was no history of pyelitis of pregnancy in either of these women. Unless the remarkable familial incidence is ascribed to coincidence alone, the underlying causal factor must be presumed to have been the same in each case. Neither the aberrant vessels, present in one case only, nor pregnancy, which had occurred in only two, could therefore be of primary aetiological significance. This supports the belief of Winsbury-White (1925) that the vascular factor is of merely secondary significance in the aetiology of hydronephrosis. He contends that obstruction of the ureter by a blood vessel occurs simply as an additional factor when the renal pelvis, dilating from some other cause, reaches a sufficient degree of distension, though it may add a very severe mechanical obstruction to the primary cause of the dilatation, whatever that happens to be.

If we disregard, then, the aberrant vessels reported at operation in Case 3, we are left with the problem of the cause of the hydronephrosis in all four cases. In each the

ureter was apparently normal; the pelvis and calices alone were dilated; the uretero-pelvic junction was well marked; and yet no cause of ureteric obstruction was found.

Jewett (1940), after careful study, showed that normally there is no absolute uretero-pelvic junction, the pelvis blending into the ureter in a funnel-shaped prolongation. He believed that when such a junction exists, as it did in the cases described here, stenosis should be considered, particularly if there is pyelectasis. The fact that he considered this stenosis often congenital, since there were no acquired factors to explain it, would make such a mechanism an exceedingly attractive explanation for the present series of familial cases. However, no evidence of stenosis was found. *Faute de mieux*, we must therefore fall back on such a conception as inadequacy of the ureter as an efficient urinary duct which has been posited as a causal factor in hydronephrosis; or we must postulate a functional defect in the neuromuscular mechanism of the renal pelvis, as the familial and inherited primary aetiological factor, though there is no positive evidence for either supposition. Consideration of the familial nature of these cases does, however, serve to show that, contrary to general opinion, a pelvic and caliceal hydronephrosis of this type can occur as a congenital condition without evidence of ureteric obstruction.

Summary

Four cases of non-calculous hydronephrosis occurring in two generations of a family are described. The literature is reviewed. The aetiology of the condition is discussed.

I am indebted to Mr. R. J. Rutherford, who was responsible for the surgical care of Case 1; to Mr. M. C. Pinkerton, who was similarly responsible for Cases 2, 3, and 4; and to Dr. C. H. Kitchen, who carried out the radiological examinations.

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UNUSUAL CASE OF JUVENILE G.P.I.

BY

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AND

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Juvenile general paralysis is commonly thought to manifest itself as a gradual dementing process similar to that seen in the adult disease, but with the differences in symptomatic conduct and behaviour disorder that the onset in childhood or the school years would produce. Thus intellectual deterioration may appear as a failure to ascend the normal educational ladder or as an unexpected loss of already acquired learning. Grandiose delusions, which are uncommon, may take the form of claiming ownership of vast stores of sweets or toys. Reduced social standards, such as minor dishonesty or lack of personal cleanliness and tidiness, often presenting symptoms in adults, are likely to be less readily noticed in the juvenile age group. This is the picture given in the standard textbooks of neurology and psychiatry, though Ford (1949) and others mention a maniacal reaction as an occasional presenting symptom.

The following case is worth recording because juvenile G.P.I. is now an uncommon disease and because the

method of presentation was unusual. The sudden development of a hemiplegia drew attention to the disease, and shortly thereafter the patient developed an acute mania.

Case History

A National Service man, aged 19, was admitted to Wheatley Military Hospital in July, 1953. On the previous day, while picking peas on leave at home, he had suddenly "collapsed" in a semicomatose state, from which he could be roused only by repeated shouted requests. He was able to obey simple commands, but his answers to questions were incoherent and unintelligible. On examination he proved to have a right hemiparesis with dysphasia and right homonymous hemianopsia. There were some continuous clonic movements of the right face and hand resembling epilepsy partialis continua. The pupils were large, irregular, and did not react to light. The optic fundi were normal, as were other bodily systems. The blood pressure was 140/90. The urine was free from albumin and sugar. Lumbar puncture revealed a clear fluid under normal pressure, with a protein of 70 mg. per 100 ml. and 25 white cells per c.mm. (90% lymphocytes, 10% polymorphs). His electroencephalogram showed high-voltage delta activity in both hemispheres but focusing on the left mid-parietal electrode.

During the next 48 hours his comatose condition gave place to an acute mania. He would laugh and talk continually, and as he was still dysphasic a stream of jargon, often shouted at the top of his voice, resulted. Despite his hemiparesis he made continual attempts to get out of bed, and would keep on neither bedclothes nor pyjamas. He would try to attack anyone approaching him, and when restrained in bed made continual restless movements of his non-paretic limbs. He was incontinent of urine and faeces, and had to be tube-fed. In view of a possible left frontal abscess or tumour, a carotid angiogram was done, but this showed no convincing abnormality. By this time, some five days after admission, a strongly positive W.R. in the blood and C.S.F. had been returned, and the Lange gold curve was 4555555321. The diagnosis of juvenile G.P.I. was thus suggested, and he was given penicillin, and in view of a possible gummatous process this was combined with potassium iodide. During three weeks he had 22 mega units of penicillin and 30 gr. (2 g.) of potassium iodide three times a day. On the mental side the response was dramatic. Within a week his acute mania had subsided and he would remain in bed and feed himself. He was continent of faeces, though he still occasionally wet himself.

Four weeks later he was up and helping with ward duties, though still rather emotionally labile. His neurological condition had also improved. The involuntary movements lessened gradually and ceased after some seven days, the hemianopsia and hemiparesis also cleared, though pyramidal signs—increased tendon-jerks and an extensor plantar response—remained. Some dysphasia also persisted, and there was slight proprioceptive sensory loss in the right arm and leg. The pupils remained large and irregular. There were no other signs of congenital syphilis. His electroencephalogram became more normal, with an 11 c.p.s. alpha rhythm in the right hemisphere, and some low-voltage theta activity from the anterior leads on the left. He proved to be entirely right-handed. Three months after the onset of his illness he was well enough to return home and was invalided from the Army.

As his serology remained positive he was treated with two further courses of 20 mega units of penicillin at the Queen Elizabeth Hospital, Birmingham. In March, 1954, his C.S.F. showed a protein of 42 mg. per 100 ml., with 1 lymphocyte per c.mm., Lange 3211000000, and a positive W.R. He was still emotionally labile, had occasional dysphasia and also evidence of left parietal lobe dysfunction, such as visual and tactile inattention to the right half of the body and a disinclination to use these limbs. However, he was leading a normal social life at home and was hoping to restart work in his previous trade.