source or occurring as part of a generalized tendency to thrombophlebitis is not very uncommon and frequently runs a benign course. Such cases in the past may have been erroneously attributed to arterial thrombosis or embolism, or to encephalitis. Some, especially those in which the onset has been with focal epileptic attacks, have doubtless been diagnosed as meningitis or abscess. The latter diagnosis has occasionally led to unnecessary and probably harmful operation. I can recall two cases in which I was responsible for this error, and in Case IV above the diagnosis was so much in doubt that it needed an exploratory craniotomy to satisfy physician and surgeon that the patient would make a spontaneous recovery. For these reasons, and in the hope that they may stimulate further inquiry, it has seemed worth recording these few observations.

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THE POSSIBILITIES OF NERVE GRAFTING *

BY

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AND

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The problem of bridging a nerve gap urgently demands an answer at the present time. The problem arose in the last war, and attempts were made, by means of multiple strands of cutaneous nerves or lengths of vein and other hollow tubes, to guide the down-growing axons from the proximal end of the nerve across the gap into the distal end. The results on the whole were disappointing, and nerve grafting was discredited until the work of Duel and Ballance (1932). These workers were interested in the problem of bridging a gap in the facial nerve in the Fallopian canal, and they were able to show, in animals and in man, that this gap could be successfully bridged by means of a nerve graft taken from the external cutaneous nerve of the thigh. Their work was fully reported, and it was obvious that they obtained brilliant success in restoring movements to a paralysed face.

In 1935 we started an inquiry, in collaboration with the late Sir Charles Ballance, to determine why there should be a divergence in the results of nerve grafting. Our experiments were carried out in cats and monkeys, and the early results were reported in detail (Bentley and Hill, 1936). They led us to believe that Duel and Ballance's success in facial nerve grafting resulted from the meticulously accurate fit they secured between the graft and the two ends of the facial nerve. They were aided in this by the size of the nerve, so that they were able to obtain a graft of approximately the same dimensions, and also by the helpful circumstance that the graft could be laid in a bony groove and accurate apposition obtained without the necessity for sutures. Our experiments taught us particularly the importance of endoneural scar at the two suture lines in preventing the down-growth of regenerating nerve axons. Any inaccuracy of approximation of graft to nerve or invasion of nerve tissue by sutures caused a great increase in the amount of scar at the anastomosis.

* Abridged from a lecture given at the British Postgraduate Medical School, University of London, July 26, 1940.

with proportionate obstruction to regenerating fibres. Particularly was this true at the distal suture line between the graft and nerve, in which the scar has some weeks to form a barrier before the fibres reach the suture line. It is probable that the disappointing clinical results of cable grafts and vein transplants reported by Platt and Bristow (1919-20, 1923-4) after the last war may be explained on the basis of scar-tissue formation. Our experiments suggest that under the conditions they describe fibrosis would be so extensive as to prevent any nerve fibres reaching the distal end of the nerve.

How a Nerve Graft Functions

We were interested in considering how a nerve graft functions in bridging a nerve gap, and histological studies of our nerve grafts at different periods after operation suggested to us that the graft formed a scaffolding along which the down-growing axons could grow. Duel and Ballance had had the conception of multiple neurilemmal tubes awaiting the passage of regenerating axons, and had believed that it was advantageous to allow the graft to undergo preliminary Wallerian degeneration before using it at operation, in order that the neurilemmal tubes should not be blocked by the products of axon degeneration. In a series of experiments designed to test this hypothesis we could find no difference in the rate of regeneration through fresh or degenerated grafts. The neurilemmal tubes certainly acted as a conducting medium for the new nerve fibres, but the presence of the products of degeneration seemed in no way to hinder the rate of axon growth. The importance of a nerve graft was that it provided the necessary scaffolding or framework along which nerve fibres could grow as easily and rapidly as along an ordinary piece of nerve after section and suture. It would be impossible, we believe, for anything other than nerve to provide this essential scaffolding.

It is possible, therefore, to bridge a nerve gap, given the essential scaffolding that a nerve graft provides and the minimum of endoneural scar at the suture lines. A certain amount of scar formation at the anastomosis is inevitable, but it must be kept to a minimum if a functional result is to be obtained, and we suggested that in order to obtain satisfactory results two things were essential: first, the greatest care and accuracy of technique in suturing, including only the nerve sheath in sutures of fine silk; and, secondly, employment of a graft of the same calibre as the nerve, so that accurate approximation of the cut ends of graft and nerve can be obtained.

Grafting Limb Nerves

How, then, can the problem of the limb nerves be tackled? Multiple strands of cutaneous nerve (cable grafts) do not provide the conditions essential for success, and no donor nerve of the same size as a main limb nerve is available from the patient himself. Nerve grafting in the case of limb nerves becomes impracticable unless it can be shown that a nerve taken from another individual can be used as a graft. This introduces a serious problem. Homeografts (that is, taken from another individual of the same species), in general, are reported not to survive in their new host. There is incompatibility between the cells of the graft and the tissues of the host, and such grafts excite connective-tissue reaction and are ultimately absorbed (Loeb, 1930). We thought it possible, however, that a homeonerve graft might, before it was absorbed, provide the essential temporary scaffolding along which the nerve axons could grow, and that a homeograft might prove successful providing the endoneural scar at the two suture lines was not too extensive. In our previous work (1936) we had shown in cats that a homeograft 3 cm. in length would successfully bridge a short nerve gap.

Short nerve gaps, however, are not a problem of human surgery, and in addition do not test out the utmost limitations of the homeograft. We considered it necessary to determine the fate of grafts at least three inches long in order that the results might have more direct application to the surgery of man.

We therefore carried out a series of experiments in monkeys, the results of which are being recorded in detail elsewhere. Briefly, in eight monkeys three inches of the external popliteal division of the sciatic nerve in the upper part of the thigh was removed and the gap bridged by a similar length of external popliteal nerve from the thigh of another monkey.

The extent of regeneration through the grafts was determined at different periods after operation by noting the results of electrical stimulation of the nerves and by histological study of the graft and the nerve distal to the graft, as in our previous work in 1936. We found, much as we had expected, that the graft excited a connective-tissue reaction, but that fibres were able to grow through it to the distal end of the nerve, and that about 250 days after operation motor response was obtained in the extensors of the foot. At 500 days there was a very satisfactory motor response, and histological study showed large numbers of fibres in the external popliteal nerve as low down as the ankle. Endoneural scar at the suture lines was more severe than when autogenous grafts were used, and we believe it would be advantageous to employ the technique described by Davis and Cleveland (1934) and excise the distal suture line at a time when it was estimated that nerve fibres had reached this level, and so give the nerve fibres a better chance of reaching the distal end of the nerve.

Commentary

Our experiments showed without equivocation that a three-inch gap in a main limb nerve of a monkey can be bridged with a homeograft. A nerve graft does not solve the problem of the incomplete recovery that follows nerve suture as a result of axon crossing. It probably intensifies it compared with simple nerve suture, but it is the only way to get even a partial result when a length of nerve has been lost. We believe that where a nerve gap exists in a limb nerve of man a homeograft from a fresh cadaver should be employed, since the results in monkeys are so encouraging and there is no other satisfactory method of treatment. The greatest accuracy in suturing, followed by careful recording of the result, will give us an answer to whether the homeograft can solve the problem of the limb-nerve gap in man.

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FULMINATING SEPTICAEMIA ASSOCIATED WITH PURPURA AND ADRENAL HAEMORRHAGE (WATERHOUSE-FRIDERICHSEN SYNDROME)

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Fulminating septicaemia associated with purpura and adrenal haemorrhage forms a clinico-pathological syndrome which is so striking and so characteristic that it may be considered a definite clinical entity. The earliest case reports of the condition are by Garrod and Drysdale, Still, Batten, Talbot, and others (Sacks, 1937). In 1911 Waterhouse reviewed the cases up to that time, and this was repeated by Friderichsen in 1918. In 1916 MacLagan and Cooke established an infectious origin and emphasized the significance of the meningococcus. Since then other cases have been reported, and by the beginning of 1940 these had reached a total of 70 (Carey, 1940).

Case Report

The patient, a well-nourished female child aged 10 weeks, had, apart from a slight cold for one day, been perfectly well until 6 o'clock on the evening of admission to hospital. At 6 p.m. the mother noticed that the child had suddenly become very pale. Its bowels then acted once, the motions being a little lumpy and slightly green, but containing no blood, pus, or mucus. There seemed to be no abdominal pain: there was no screaming, only slight whining. The other systems appeared normal, and no history of contact with meningitis was elicited.

Examination at 11.30 p.m. showed an extremely shocked cyanosed child—stuporous, whining, with updrawn legs—presenting almost a complete Hippocratic facies. The temperature was 98° F., the pulse rate 140, and the respiratory rate 20. The throat and ears appeared normal. There was no bulging of the fontanelle, but there was a minimal degree of neck stiffness, associated with slightly positive Kernig's and Brudzinski's signs. The heart and lungs presented no abnormality, but a moderate degree of abdominal rigidity was observed. There were a few purpuric haemorrhages on the trunk.

Diagnosis was therefore made of acute fulminating meningococcal meningitis, and appropriate treatment was administered. The child's general condition, however, rapidly declined, extensive generalized and diffuse purpuric haemorrhages appeared, and death occurred four hours after admission.

Necropsy revealed the brain to be of soft consistence, with an increased amount of cerebrospinal fluid and a moderate degree of meningeal congestion. There was no exudate, either on the surface of the brain or in the ventricles. The tonsils were not enlarged. Heart, lungs, and gastro-intestinal tract presented no abnormality except for hyperplasia of the lymphoid nodules of the intestine. The liver was enlarged, pale, and flabby; the spleen was also enlarged, and the kidneys were somewhat pale. The pelvic viscera appeared normal. Both suprarenal glands were dark red in colour, and the cortex and medulla were haemorrhagic.

Microscopically both suprarenals were intensely congested, and were diffusely and completely infiltrated with blood. Only cells of the cortical glomerular zone remained. The thyroid was congested, but to a lesser degree, and presented a few haemorrhages. The pituitary was slightly congested, and had some small haemorrhagic areas. The lungs also were slightly congested, and the spleen appeared normal. A smear of the splenic pulp revealed Gram-negative diplococci, morphologically compatible with the meningococcus.

Clinical Features

The clinical picture is so characteristic that if the condition be borne in mind diagnosis during life should be possible. 70% of the cases occur in infants under the age