Current Practice

PRACTICAL NEUROLOGY

Management of Virus Central Nervous System Disease

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Virus infections of the central nervous system (C.N.S.) still present a major problem of both diagnosis and management. As each year goes by more and more diseases of the C.N.S. are found to have a viral aetiology. Among the most recent is the subacute sclerosing panencephalitis of measles.[1 2] There are many others which are still borderline problems—for example, the progressive multifocal leucoencephalopathy occurring in association with certain types of malignant disease in which particles looking like virions of the papova group of viruses have been seen in large numbers in glial cells.[3] Kuru, the fascinating progressive neurological disorder of the Fore tribe in New Guinea, has now been transmitted to monkeys, particularly chimpanzees.[4] The agent responsible for this is of ultra-microscope size and may well be a virus.

Many other diseases, such as disseminated sclerosis and motor neurone disease, may be associated with some viral type agent. It is therefore somewhat difficult to generalize about the management of virus C.N.S. disease, but it is clear, however, that one must think in terms of acute viral C.N.S. disease and chronic "slow" or "latent" type virus disease. By far the most important is the acute viral C.N.S. disease.

Acute Viral C.N.S. Disease

This is seen all over the world as encephalomyelitis. This term is used as for practical purposes encephalitis (inflammation of the brain) or meningitis (inflammation of the meninges) or myelitis (inflammation of the spinal cord) does not exist alone as a clinical entity. The emphasis of the clinical disease may be on any one of these three, but all components are invariably present, and this affects prognosis. For example, what is thought to be a fairly simple case of aseptic meningitis may develop at a later date unpleasant psychological sequelae, such as changes in sleep rhythm, temper tantrums, and changes in personality. Yet at the time of the illness no obvious lesions indicating brain involvement could be detected by ordinary clinical examination. Awareness of this situation will affect management, prognosis, and the handling of relatives.

Acute C.N.S. viral disease is that in which clinical C.N.S. involvement occurs within one month of the primary infection. This is a somewhat arbitrary figure, based on personal experience of different types of encephalomyelitis seen both in Europe and the tropics. It ranges from infections with poliomyelitis, Japanese B virus encephalitis (insect borne), Coxsackie viruses, and those of the specific fevers such as chicken-pox, measles, and mumps.

The encephalomyelitic phase occurs as a second phase of the disease after the viraemia has finished. The length of time between this first and second phase varies with different viruses. It may be up to 14 days with members of the tick-borne encephalitic group, but only two to three days in poliomyelitis infection. It is of considerable interest that only a very small proportion of cases get this second phase with any virus infection—usually less than 0·1% of all those infected. However, when it does occur it is a serious illness and the patient should be looked after in hospital, as the illness can progress very rapidly. A child or adult approaching unconsciousness will have a much better chance of survival if he gets to hospital before lung damage has set in from inhaled vomit or there has been the onset of respiratory distress due to central or peripheral C.N.S. paralysis. Frequently, however, the disease is mild, and the only symptom may be severe headache following a "flu"-like illness some days or weeks previously.

In discussing management one is faced with dealing with the following problems: fever; headache; vomiting; restlessness and photophobia; skeletal pain, chiefly from muscle spasm; paralysis of muscles and limbs; coma; and respiratory failure.

Fever

The pyrexia is often quite low, though the state of consciousness is considerably depressed. When it is low no treatment is required. Just occasionally hyperpyrexia develops (temperatures of 105° F. (40·8° C.) and above), and this needs urgent treatment, particularly if it occurs in tropical climates. Dehydration and ketosis can occur very rapidly. Cooling is vital, and a simple method is to nurse the patient on a rubber sheet and cover him with a further damp cotton sheet and play a fan on it. Sometimes it is even necessary to put wet ice on the top sheet as well. It is only necessary to bring the temperature down to reasonable limits, to 100° F.–101° F. (37·8° C.–38·4° C.).

Headache

Headache can usually be controlled by simple analgesics such as paracetamol or salicylates. Codeine phosphate can be particularly useful for this purpose. Drugs which produce marked respiratory depression should be avoided.

Vomiting

If vomiting is severe, absorption of drugs taken by mouth will be unreliable, and dehydration will set in. If drugs can be retained prochlorperazine is helpful. Antihistamines which are helpful in motion sickness are of less value in central vomiting induced by encephalitis. Prochlorperazine by intramuscular injection is as useful a drug as any for this type of vomiting.

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Restlessness and Photophobia

Irritability is helped by nursing in a darkened room with as little noise as possible. Sedative drugs must be used with caution because of respiratory depression, but again prochlorperazine and diazepam are helpful when given by intramuscular injection. Paraldehyde is still possibly the quickest-acting and safest sedative, but is very painful to give by intramuscular injection. Promethazine can be used, particularly to help sleep at night, but more powerful sedatives such as barbiturates should be avoided, because they cause confusion and increase restlessness in small doses. Chloral is also a useful hypnotic in these cases.

Skeletal Pain

Pain, chiefly from muscle spasm, is seen particularly in poliomyelitis and a few of the arbovirus infections. It may be very severe, but again analgesics which depress respiration should not be used. Drugs similar to those used for the headaches should be tried, and local warmth to the affected muscles is particularly helpful.

Paralysis of Muscles and Limbs

Paralysis of the respiratory muscles will be considered under the heading of respiratory failure. It is important that during the painful phase and the febrile period, which usually coincide, the muscles should be at rest. The limbs should be protected by cradles if necessary, and they should be immobilized in the position of maximum anatomical function—particularly the foot and wrist. As soon as the pain and temperature have subsided passive movements should be instituted. These should be carried out by both nursing and physiotherapy staff. Even relatives can be taught to be useful in this way. It is vital that no muscle of any part of the body gets overstretched or overcontracted. If this happens it will lengthen the convalescent period considerably and cause great distress to the patient. Though most people will remember about the optimum position for the hands and feet to be at rest, very few remember that a patient who always sits up in bed leaning over to the right will develop contractures of his long erector spinae muscles on that side and lengthening on the other side. A scoliosis will result. A kyphosis will result as well, particularly if he is allowed to sit bent forward uncontrolled. Repeated changes of posture are necessary to compensate one position with another. As soon as active movements become possible these should be instituted straight away. It is helpful if they are done in a bath or heated pool at first, so that the weight of the limbs is less.

Coma

Coma is dangerous to life and is often associated with respiratory distress and secondarily with cardiac failure. It is at this stage that the chance of survival decreases substantially if expert care is not available. The management of the unconscious patient has clear guiding lines.

The airway must be kept clear. The best position to achieve this is to have the patient lying on his side in such a way that the corner of his mouth is the lowest dependent point. During C.N.S. virus infections excess salivation may be a feature, and this fluid must be able to drain outwards and not into the lungs. A sucker should always be available by the bedside to deal with any mucus which may otherwise be inhaled. As these patients are particularly apt to vomit too, a sucker becomes an absolute necessity. Over-enthusiastic use of the sucker can cause trauma to the mouth. Salivation drainage by gravity is better than aspiration, provided it is effective. Careful oral hygiene should be carried out using glycerin and thymol mouth washes. If antibiotics are used for secondary infection monilial infection may develop in the mouth and upper gastrointestinal tract. Nystatin will usually control this.

Adequate fluid intake and output must be maintained. In the early stages the amount of calories given does not matter. This becomes important only if the coma persists for more than three to four days. As it is better to keep the stomach free of fluid because of the danger of vomiting, fluids should be given intravenously, at least for the first 72 hours. This has the great advantage that once the drip has been put up drugs, vitamins, and calories if necessary can be administered via this route with the least possible trouble. A small Ryle's tube should be kept in place to keep the stomach free of fluid and to use later for administering food. It is important to appreciate how much saliva is lost if the patient is kept in the correct position. It may be as much as 2 litres a day, which, of course, contains electrolytes also. Thus, though 3 litres a day is the intake of fluid for an average-size man, 1½ litres may need to be added for fluid loss by salivation. A careful eye should be kept on the electrolytes, potassium deficiency being the most important to combat. Potassium should be replaced intravenously, because frequently in encephalomyelitis there is atony of the gastrointestinal tract. This is a safe procedure provided that the kidneys are functioning normally and dosage is carefully controlled.

Care of the bladder.—There is some difference of opinion among experts here. It is my contention that if a patient has become potentially incontinent and unable to control this function he is much better catheterized. By so doing nursing is made much easier, the risk of bedsores and skin contaminations much less, the regulation of fluid intake and output is made easier, and the risk of getting over-distension of the bladder from neurological retention is excluded. On the other hand there is a risk of causing an urinary infection and of this progressing to a pyelitis. I believe that the advantages of catheterization considerably outweigh the risk of infection, which can be reduced to a very low potential by using adequate sterile techniques. If the urine is frequently monitored for bacterial infection the correct antibiotic can be used as required.

Care of the bowel is always difficult. Constipation is a major factor in long-term illness. Enemas tend to be retained, and faecal impaction may occur, needing manual removal. From a very early time glycerin suppositories and compounds such as Agarol and liquid paraffin by mouth are helpful. Both can be put down a Ryle's tube. Enemas should be tried early, but if not easily returned may need to be abandoned.

Care of the eyes.—Great care should be taken that corneal abrasions do not occur. Pads are not the answer, because the eyes may become open under them, which may pass unnoticed, and the dry cotton wool or gauze pad will scratch the eye. It is much better to use a small strip of very light tape to close the eyes so that if they open it will be noticed immediately. Saline wash-outs should be given once a day at least. It is not advisable to use oil, as it can cause a conjunctivitis.

Care of the skin.—The patient ought to be turned two-hourly and if possible nursed on a ripple bed. Rubbing the skin is not as valuable as care to relieve pressure points by regular turning. On each occasion the patient must be left in a position in which he is not traumatizing himself, as can occur by finger nails piercing the skin over the chest when hands rest on the anterior chest wall, or hard objects coming up against limbs, such as screws from the attachment of a monitoring E.C.G. machine.

Care of the limbs should be as stated above, with the nurses, physiotherapists, and relatives putting joints through a full range of passive movements as often as possible.

Respiratory Failure

Respiratory failure may arise from central brain-stem damage or intercostal paralysis or both. It is very important that it

should be recognized early. If possible the patient should be transferred to a unit which has facilities for intermittent positive pressure ventilation (I.P.P.V.) and the expertise and nursing staff available to manage such problems. Endotracheal intubation is often necessary to prevent inhalation of saliva and stomach contents and to allow artificial respiration, should this be necessary. It is wrong for the inexperienced "to try to manage" if expert assistance is available. A lung which is clear of aspirated mucus and vomit is much easier to control on a mechanical respirator than one which is already infected, consolidated, and partly collapsed. The clinical indications for mechanical respiratory assistance are very important to recognize. It is too late if you wait for the patient to become hypoxic, restless, and hypercarbic.

The earliest clinical signs are:

(1) Hyperventilation. This occurs sometimes to the extent of tetany. Overbreathing happens when patients begin to experience anoxia when completely relaxed and not thinking about their breathing. Fear, a feeling of general weakness, and an inability to cough makes them overbreathe. To measure arterial carbon dioxide tension at this stage and make decisions from the results would be positively dangerous.

(2) Stopping to take a breath in the middle of a sentence.

(3) The inability to make an adequate noise coughing. In normal respiration the resting tidal volume is about 500 ml. To cough efficiently one needs an inspiration of three times this amount, 1,500 ml. Serial vital capacity as measured on a volumeter is clearly valuable. The normal vital capacity lies between 4·5–5·5 l. Anything below 1·5 l. is dangerous because of the inability to cough adequately. A reliably measured vital capacity below 1 l. is very dangerous. The above clinical signs are at least as useful as any more sophisticated measurement. In fact, people with a permanent vital capacity below 1·5 l. survive only because they learn to "frog" breathe (glossopharyngeal breathing) by swallowing air into their lungs. In this way they can get up to 2·5 l. under pressure behind the closed glottis. They can then cough.

If artificial ventilation is required then it is better to overventilate than to underventilate. A minute volume of 8 l. is the average normal. Provided that the patient gets to the unit with clear lungs the minute volume requirements for each individual patient can be assessed on a weight/height basis from a Radford nomogram.[5] It becomes more difficult to estimate ventilatory needs with rise in temperature from infection or central C.N.S. involvement.

There are few real dangers from hyperventilation. Patients who have been hyperventilated tend to go on doing so for a short time after removal from the respirator, but this is quite useful. Tetany is an obvious symptom of excess overventilation.

Underventilation is characterized by restlessness and nightmares in sleep and a persistent tendency to breathe spontaneously with or against the respirator. The arterial carbon dioxide should be kept below 40 mm. Hg, so that the patient, if he has any respiratory capacity left, does not try to breathe and resist the machine.

All the time nurses and physiotherapists should work closely together, particularly concentrating on keeping the chest clear. Mucus can be moved from the smaller bronchi by turning the patient from side to side and then suitably pummelling and squeezing the thoracic cage. Strong hand inflation of an anaesthetic reservoir bag by the nurse to get full inflation of the chest, followed by a strong squeeze of the chest by the physiotherapist, will bring the mucus up for the sucker to remove.

It is not easy to gauge exactly when a patient should be removed from the respirator. Sometimes it has to be done by trial and error. However, if one takes as an example a patient with polyneuritis who has been on a ventilating machine and begins to recover, the inflation pressure begins to fall as the patient begins to assist the respirator and the pressure pattern of the I.P.P.V. machine in the oesophagus begins to flatten out. This is an indication to start weaning the patient off the ventilator. It is very important not to remove the patient from the ventilating machine too early. During the trial periods of removal from the machine it should always be close at hand so that the patient can be quickly reattached if necessary. One can lose the benefits of weeks of care in six hours of non-ventilation if during this time there is aspiration into the lung of mucus and stomach contents. Pressure to return the patients to the ordinary ward too early must be strongly resisted, because it is not an investment in time and labour.

During these illnesses patients lose a lot of weight, particularly at the expense of muscle bulk. It is therefore wise to put them on a high protein diet as soon as possible to try to rebuild this muscle loss.

General Management

In an intensive care unit there should be enough staff available to provide continuous observation of the patient, with half-hourly checks on the pumps. The staff must learn to talk to the patient as if he was normal. Because the patient is tracheotomized and intubated and unable to speak he must not be considered mentally confused. In fact, the medical staff are usually much worse about discussing inappropriate medical details by the bedside of this type of patient than the nurses. It is the latter who are left with the ghastly job of trying to reassure the patient after the doctors have left.

It is important to talk to the relatives and to prevent them getting too exhausted by too frequent visiting. Prognosis must always be guarded when mechanical respiration has had to be used, because the mortality from this alone is 5% if required for more than 72 hours. The longer the nursing and physiotherapy care is required the more obsessional and good it should be to keep the mortality and morbidity rate to its lowest. It is very demoralizing to have a patient recover and find he has contractures of his fingers and feet and curvature of the spine because this aspect of his care has been neglected.

These types of patients very rarely get pulmonary emboli. Anticoagulation as a precaution should not be considered, particularly in the presence of a tracheostomy and oesophageal intubation.

Special Drugs

There is a strong school of thought which supports giving steroids in large doses for a short time at the onset of the encephalomyelitic phase. The logic of this lies in trying to reduce the intense oedema and inflammatory reaction which are known to be present at that time. Steroids such as dexamethasone are particularly useful because of their anti-inflammatory and diuretic effect, and up to 4 mg. q.d.s. can be given for three days and then reduced over a further 10–14 days.

It would be dangerous to give a steroid before the onset of the encephalomyelitic phase as a possible protective agent. Steroids are probably not of much value given three to four days after the encephalomyelitic phase has started, unless the illness is still getting worse. The object of the therapy is to prevent a further fall-out of neurones from anoxia caused by cerebral ischaemia secondary to oedema occurring within a rigid cavity.

The introduction of antiviral agents such as N-methylisatin-β-thiosemicarbazone (methisazone) and 5-iodo-2-deoxyuridine (I.U.D.R.) is of great interest. The latter has been shown to be of value in the treatment of skin and eye lesions of herpes simplex. It has now been tried in several cases of herpes encephalitis with varying degrees of possible success.[6–8]

I.U.D.R. has some hepatotoxic effects and produces a leucopenia, and at the moment there is no convincing scientific evidence that it is beneficial in encephalitis. It is certainly an antiviral agent and from it may be developed something that is useful.

There are other drugs, too, at the experimental stage in animals, such as daunomycin, which inhibits DNA synthesis and synthesis of DNA-dependent RNA. Actinomycin D, an antibiotic derived from *Streptomyces antibioticus*, also inhibits DNA viruses because it has an affinity for guanine. Because of this it attaches itself to the DNA, and, possibly by altering the molecular configuration of the nucleic acid, it blocks the action of DNA-dependent RNA polymerase. There is also rifampicin, which is believed to act directly on the DNA-dependent RNA polymerase enzyme. So there is some hope that there may be an effective and safe antiviral agent in the not too distant future.

Chronic Encephalomyelitides

Lastly, one must consider the management of the chronic encephalomyelitides. So little is understood of the aetiological factors in these conditions that apart from symptomatic therapy the rest is guesswork. If there is a proliferative phenomenon at work, as denoted by the intense gliosis seen in many of these diseases, then it would be reasonable to try drugs such as vincristine, 6-mercaptopurine, and methotrexate, as in malignant disease generally. This would also apply if immunological mechanisms were concerned in the slowly progressive disease.

In both acute and chronic encephalomyelitis changes of personality, depression, and other psychiatric disturbances occur. They should be treated on their own merits. E.C.T. and antidepressive drugs are frequently helpful in treating depressions after a viral C.N.S. disturbance. These forms of therapy are not contraindicated even though one feels the psychiatric disturbance has been induced by organic brain damage. Treatment is frequently very helpful.

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TODAY'S DRUGS

With the help of expert contributors we print in this section notes on drugs in common use.

Drugs for Diarrhoea

The physician who is called upon to treat a patient with diarrhoea may elect to do so in one of several ways. Firstly, he may elect to treat the diarrhoea as such, administering a drug designed to reduce the number of bowel actions. Secondly, he may elect to treat the cause of the diarrhoea by administering an antibiotic or antiamoebic drug; or he may feel it necessary to treat the results of the patient's diarrhoea by replacing abnormal losses of water, electrolytes, protein, or blood. Finally, he may adopt a therapeutic regimen which combines two or more of these aims, his final decision being based upon his assessment of the cause of the diarrhoea and the clinical state of the patient.

Non-specific Therapy

Whatever the cause of diarrhoea, it is an unpleasant state of affairs for the patient, and one well worth symptomatic treatment in its own right. A variety of drugs exist which, though they have little or no effect upon the cause of the patient's diarrhoea, have the effect of reducing the number of bowel actions. They are classified for convenience according to their mode of action as adsorbent powders, opiates, and anticholinergic drugs—though many preparations contain combinations of these types of drug.

Adsorbent Powders.—This group of antidiarrhoeal drugs is so named because it is claimed that they adsorb harmful substances within the lumen of the bowel, though it is far from clear that this is in fact their mode of action. Charcoal, for example, which is occasionally used, is a highly effective adsorbent of gases in a dry state. But whether it can materially affect the gaseous content of the distended bowel is another matter entirely. Kaolin, which may be administered either as a compound powder (adult dose 2–10 g.), or as a mixture (adult dose 15–30 ml.), is another adsorbent which is effective against bacteria and toxins, though what degree of activity it retains by the time it reaches the large bowel is debatable. One of the very few side-effects reported following the use of kaolin is granuloma of the stomach.[1] Another adsorbent sometimes used is pectin, a carbohydrate product containing polygalacturonic acid, which is found in raw apples and the rind of citrus fruits. The mode of action of the drug is again unknown, though it has been suggested that large amounts of unchanged pectin reach the colon in patients suffering from diarrhoea, and that its subsequent breakdown to various acid products provides an unfavourable environment for the invading bacteria[2]. None the less, despite the uncertainty surrounding their mode of action, the adsorbent drugs often have an undoubted antidiarrhoeal effect.

Opium Derivatives.—Opium and a number of allied drugs may be valuable in the treatment of diarrhoea by virtue of their action on the smooth muscle of the bowel which leads to a reduction in peristalsis. They are often given in combination with other drugs, such as kaolin, and this applies particularly to both opium itself and morphine. On the other hand, codeine is often administered on its own as codeine phosphate in a dose of 15–60 mg. Pethidine has little effect upon diarrhoea and should not be used in this context.

The clinical usefulness of this group of drugs in the treatment of diarrhoea depends upon one feature—the dosage