equal in efficiency, though not superior, to the hydantoinates. Robinson (1957) reports a downward trend in the frequency of attacks in 8 out of 11 (73%) patients to whom nydrane was administered over a period of five months. Sharpe *et al.* (1958) found 17 patients out of 25 (68%) improved, 3 (12%) worse, and 5 (20%) unchanged over a period of six months; they noticed an increase in the frequency of attacks during the changeover period. These workers used a dosage comparable to our own.

By contrast, only 3 out of 27 (11%) of our patients showed a sustained improvement, according to the criteria used, 6 (22%) became worse, and 18 (67%) were unchanged. Two others improved temporarily, for two weeks and 24 weeks respectively, the latter ultimately becoming worse than before. Particular benefit has been claimed for patients with temporal lobe seizures, but only one of our patients in this category improved. In only 2 out of 10 patients where nydrane was added to the former treatment did improvement occur; where it was substituted for part of the former treatment only 1 out of 17 improved.

Where nydrane was substituted and deterioration did not occur (11 patients), it may have been responsible for maintaining the former level of control. The improvement in three patients, taken together with the findings of other clinicians and of laboratory experiments, indicates that nydrane probably has some anticonvulsant effect, but from a practical point of view we feel that the results are disappointing and do not justify its use as a routine. On the other hand, occasional patients benefit and relatively few deteriorate, so that its addition may be tried where dangerous amounts of the more established, but more toxic, drugs would otherwise be necessary. It may be useful to try the effect of much higher dosage.

Six patients showed little difference in response whether on active or inert tablets. This is interesting in view of the common finding that many epileptic patients respond temporarily to any new treatment which may be prescribed. In some this is undoubtedly because they take a new remedy with fresh enthusiasm and regularity. In others, however, the benefit may be similar in origin to that obtained by many people from a placebo.

Claims made for the low toxicity of nydrane are upheld by our findings. Two of our patients developed a rash, but no other side-effects were noted. The psychotic episode in one patient did not have a proved relation to the drug. The danger of status epilepticus when changing to nydrane is mentioned by Hoenig *et al.* (1956) and is illustrated by one of our patients; it indicates that the severe case should be admitted to hospital if this procedure is contemplated.

Summary

Nydrane was used in the treatment of 27 patients with severe epilepsy during the routine work of a neurological department: 3 (11%) improved, 6 (22%) were worse, and 18 (67%) remained unchanged.

In six in-patients inert dummy tablets were interchanged with nydrane; no change resulted in the frequency of attacks, unless the dosage of other drugs was altered.

Claims for the low toxicity of nydrane are supported.

On the basis of these findings it is suggested that nydrane is less useful clinically than the more established

anticonvulsants; but where exceptionally heavy medication is necessary for control it can occasionally be helpful by reason of its low toxicity.

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Medical Memoranda

Partially Treated Meningitis in Infants

Meningitis caused by pyogenic bacteria is always a dangerous disease, especially in infancy. The danger lies in the possibility of early death or of permanent damage to the brain or to the pathways of the flow of cerebrospinal fluid. Early diagnosis is therefore of the greatest importance, but unfortunately is often very difficult. Thus many infants with meningitis are treated empirically at home with sulphonamides without a definite diagnosis being made. This treatment modifies the clinical picture of the illness and may make an accurate diagnosis increasingly complex.

In order to try to demonstrate some of the diverse clinical pictures that can be presented in partially treated meningitis, the following cases are recorded.

CASE REPORTS

Case 1.—A female infant aged 15 months was admitted to hospital on October 9, 1950, with a history of sudden onset of fever eight weeks previously. Apart from the fever, she was irritable, and vomited some feeds. After a six-day course of sulphonamides she improved but remained irritable, had anorexia, and continued to lose weight. The family doctor thought she had pink disease. On admission she was a wasted, irritable baby who resented being handled. She had photophobia but no evidence of infection, no neck stiffness, and no rise in fontanelle tension. Her appearance was that of a baby with pink disease. A lumbar puncture, however, showed a purulent fluid from which *Haemophilus influenzae* was grown. After treatment with sulphadiazine and systemic penicillin for 10 days she rapidly improved, and at the time of discharge was a normal baby. Four years later she was a healthy, intelligent child.

Case 2.—A male infant aged 19 months was admitted to hospital on January 21, 1951, with a history that 18 days previously he had suddenly become febrile and irritable and had vomited some feeds. A short course of sulphonamides brought only slight improvement, and he continued to be irritable and had severe anorexia until the time of admission. When admitted he was ill; temperature 102° F. (38.9° C.). Slight neck stiffness was present, and there was evidence of considerable loss of weight but no other abnormalities. A lumbar puncture showed a purulent fluid, but no organisms

were cultured. After receiving sulphadiazine and systemic penicillin for 10 days he made a good recovery. Five years later he appeared to be a normal child.

Case 3.—A male infant aged 4 months was admitted to hospital on June 2, 1953, with a history that three weeks previously he had become suddenly febrile and irritable, and resented being handled. Over the next two days he had become drowsy and vomited his feeds. He was treated with sulphonamides for several days at home. On admission he was an unwell, wasted baby with a temperature of 100° F. (37.8° C.). There was slight fullness of the fontanelle but no other abnormality. A lumbar puncture showed a purulent fluid from which meningococci were grown. He was treated with sulphadiazine and systemic penicillin for eight days. Progress was satisfactory, and six months later he appeared to be normal.

Case 4.—A male infant aged 15 months was admitted to hospital on November 6, 1953, with a history that five weeks previously he had suddenly become febrile and extremely irritable and had vomited profusely for 24 hours. Sulphonamides were given for several days. There was some improvement, but he continued to be irritable and showed anorexia until his admission. When admitted he was a wasted, irritable baby, with a temperature of 101° F. (38.3° C.). Slight fullness of the fontanelle was present, but there were no other clinical abnormalities. A lumbar puncture gave a purulent fluid from which *Haemophilus influenzae* was grown. Sulphadiazine and chloramphenicol were given for eight days. Progress was satisfactory, and three months later he appeared to be normal.

Case 5.—A female infant aged 8 months was admitted to hospital on November 10, 1953, with a history that five weeks previously she had become irritable and had developed a cold and cough, with marked anorexia. Although some improvement occurred after a six-day course of sulphonamides, she continued to be listless and irritable. Eight days before admission she became drowsy, and a further four-day course of sulphonamides was given. The family doctor thought she had pink disease. On admission she was a wasted, ill-looking baby with a temperature of 101° F. (38.3° C.), but there were no other specific abnormalities and no fullness of fontanelle or neck stiffness. She resembled a case of pink disease so closely that lumbar puncture was not carried out until two days after admission. It showed a clear fluid with 230 cells, 80 mg. of protein, and 37 mg. of sugar per 100 ml., and was sterile on culture. After chloramphenicol and sulphadiazine for nine days she made a good recovery. Two months later she appeared to be quite normal.

Case 6.—A male infant aged 18 months was admitted to hospital on July 19, 1954, with a history that three weeks previously he had suddenly become feverish and irritable and had vomited his feeds. He also had a cold and cough. After sulphonamides for several days he improved, but continued to remain irritable and had anorexia. On admission he was afebrile, showed evidence of considerable wasting, and had slight terminal neck stiffness, but there were no other abnormalities. A lumbar puncture showed a purulent fluid but no organisms were cultured. After sulphadiazine and systemic penicillin for nine days he made a good recovery.

Case 7.—A female infant aged 2 months was admitted to hospital on May 15, 1956, with a history that two weeks previously she had become febrile, irritable, and had vomited her feeds. After sulphonamides at home for six days she had improved considerably, but remained irritable and had anorexia. On admission she had a temperature of 101° F. (38.3° C.), showed wasting, and disliked being handled. Slight fullness of the fontanelle was present, but there were no other abnormalities. A lumbar puncture showed a clear fluid with 517 cells, 70 mg. of protein, and 26 mg. of sugar per 100 ml.; no organism was cultured. She was treated with chloramphenicol for eight days and sulphadimidine for eight days. Progress was good, and when seen one month later she appeared to be quite normal.

Each of these cases also showed a normal x-ray picture of the chest, a negative Mantoux test, and normal urine.

COMMENT

These case histories show the alteration in the clinical picture of purulent meningitis in infants treated with sulphonamides. Unfortunately it has not been possible to find the exact dosage that each infant was given, although in each case it was the small dosage normally used for the treatment of minor infection, and the sulphonamides were not given continuously for longer than six days.

Meningitis in an infant nearly always has a sudden onset and should always be suspected in a sudden febrile illness when the following features are present: anorexia and vomiting of feeds; irritability and dislike of being handled; episodes of crying for no apparent reason; and a dulling of the infant's intellect showing itself in a lack of interest in the surroundings.

If untreated, the infant deteriorates rapidly and becomes quite obviously seriously ill within a matter of hours or at least a day or two. When, however, a short course of sulphonamides is given the clinical picture seems to change very considerably. The devastating nature of the illness is altered and the infant continues in a chronic state of ill-health in which irritability and anorexia appear to be the predominant features. Should these symptoms persist over a period of several weeks, as in Cases 1 and 5, the illness in many ways resembles pink disease, and this similarity is so striking that it would be wise always to regard this as a differential diagnosis to pink disease.

Clinical findings of the modified illness consisted essentially of a wasted, irritable baby, often with a slight rise in temperature. Signs referable to cerebral irritation, such as bulging of the fontanelle or nuchal rigidity, were present in only a few of the babies, and then diagnosis was relatively simple. If these signs were not seen the differential diagnosis tended to rest between other conditions presenting this clinical picture of a wasted irritable baby, such as a chronic urinary infection, pink disease, or idiopathic hypercalcaemia.

An interesting and surprising feature of these cases is that, even though the diagnosis is not made until some weeks later, a total recovery seems to occur when energetic treatment is given, and in none of these cases has any neurological sequelae occurred.

In a busy general practice the temptation to treat an undiagnosed febrile illness with chemotherapy is understandable, but I would make the plea that, if chemotherapy is used in such an illness, a non-thecal-passing drug such as oral penicillin should be used rather than a sulphonamide. The diagnosis will then not be obscured.

As medicine advances and more antibiotics are discovered, a distinct possibility arises of many infective disease processes being modified by incomplete treatment; thus it may well be that medical teachers will have to describe not only the clinical picture of an infective disease but its pattern when modified by partial treatment.

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