relief. This suggests that in some instances the efficacy of nicotinic acid is affected by repeated use, contrary to what is stated by Maisel. It is of course possible that the smaller dosage employed by me might in part explain this difference. Two cases were not improved at all by nicotinic acid. Neuwahl refers to severe exacerbations of asthma which occurred in 3 of his cases. This effect was also seen in 2 cases of this group. One case developed a status asthmaticus 24 hours after an intravenous injection which had given considerable relief and had been followed 20 hours later by an oral dose.

Flushing, tingling, and a feeling of heat appeared within a few minutes of the administration of nicotinic acid, and these symptoms were often pronounced and preceded improvement of the asthmatic attack. Occasionally headache, giddiness, depression, palpitations, and increased tightness of the chest were noted. As Maisel observed, improvement sometimes follows a bout of coughing.

Treatment between the Attacks

In 30 cases, many of which had severe and frequent paroxysms not controlled by ephedrine or stramonium, nicotinic acid treatment was given between the attacks for periods varying from a few weeks to several months. Of these patients 11 had received treatment previously during an acute paroxysm. The drug was given orally generally in doses of 50 mg. two or three times daily. Some cases received 100 mg., particularly on retiring. Children usually received half these doses. It should be noted that Maisel employed oral doses of 200 mg. 3 times daily before meals and once on retiring, but no mention is made over what period such dosage was given.

Results.—The results from this treatment were on the whole favourable. Sixteen cases showed definite improvement as compared with their recent condition before beginning nicotinic acid. This improvement was characterized by a definite reduction in either the frequency or the severity of the attacks and often by both these factors. The period of improvement varied considerably, from a few weeks to several months. Ten other cases showed slight improvement, assessed on the basis of a reduction in the frequency or severity of the attacks or upon the fact that relapse occurred within two weeks of starting treatment. In 4 cases no material change resulted from nicotinic acid therapy. In 9 cases courses of nicotinic acid were alternated with courses of citric acid tablets, the latter acting as a control. The patients were not informed that any change over to different tablets had been made.* In 6 of these cases the effect of nicotinic acid was definitely superior to that produced by the control tablets, the patients generally showing an early relapse when receiving the latter. Two cases, however, were maintained on the control tablets for many months with infrequent attacks. Six cases relapsed rapidly when they were taken off nicotinic acid and received no treatment.

Flushing and the other symptoms produced by nicotinic acid were often present in this group, and two patients abandoned their treatment because of unpleasant effects. It should be noted that several patients in whom the effect of nicotinic acid had worn off responded subsequently to adrenaline and ephedrine, but some were refractory to all treatment.

Conclusions

These results on the whole confirm those of Maisel and Somkin that nicotinic acid appears to be of value in the treatment of the asthmatic paroxysm. The drug when given over long periods also appears to be useful in diminishing the frequency and severity of the attacks. It is necessary to be cautious, however, in assessing the value of any treatment in this condition with such irregular incidence of attacks and susceptibility to psychological influence. Improvement after control injections and tablets illustrates this point. Nevertheless, in the majority of cases in which control therapy was employed, nicotinic acid proved much superior to the control measures in relieving the paroxysms and reducing their frequency. In view of the larger doses given by Maisel and Somkin, it would certainly seem an advantage to increase the dosage above 100 to 200 mg. daily in those cases which do not improve. Yet, although the drug appears to be non-toxic,

* The absence of flushing, etc., with citric acid did not appear to be regarded by the patients as indicating a change of treatment.

it can on occasion produce unpleasant symptoms, and the possibility of an exacerbation of the asthma (not noted by Maisel) must be borne in mind. I agree with Maisel and Somkin that at present nicotinic acid should only be regarded as an adjuvant in the treatment of asthma, particularly when adrenaline and ephedrine are proving ineffective or when ephedrine cannot be taken because of toxic symptoms. Further trials with the drug are obviously necessary.

Summary

Nicotinic acid was given to 19 cases of asthma during one or more acute paroxysms in doses of 50 or 100 mg., as a rule intravenously. Definite improvement was obtained in 16 cases. Two cases had marked exacerbations. Control injections of sterile water were usually much less effective.

The drug was given over a long period in 30 cases, 11 of which had already received intravenous therapy. The frequency and severity of the attacks were definitely reduced in 16 of these. The doses used were 50 or 100 mg. 2 or 3 times daily. Half these doses were administered to children. The cases which improved on the drug frequently relapsed when it was discontinued or when they were receiving control tablets of citric acid.

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MENINGITIS DUE TO DIPLOCOCCUS MUCOSUS*

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McFarlan (1941) has recently described the characters of a capsulated Gram-negative diplococcus which had been isolated from the purulent cerebrospinal fluid of a young man. The man had been first seen on account of bed-wetting and slovenliness, and was found to have scanning speech and intention tremor. Pyrexia and signs of meningitis supervened, but he made a rapid recovery after sulphapyridine treatment. The organism was identified as *Diplococcus mucosus*, originally described by von Lingelsheim (1906, 1908) and isolated by him from the nasopharynx and cerebrospinal fluid. Cowan (1938) had described similar strains isolated from the cerebrospinal fluid of patients after operation for cerebral tumour.

While there is considerable evidence that certain of the nasopharyngeal *Neisseria* may under favourable conditions give rise to meningitis, the pathogenicity of the capsulated diplococci for man has not been conclusively proved. It therefore seems of interest to report a case in which the causative organism was almost certainly *Diplococcus mucosus*.

Clinical Features

The patient, a man aged 29, with two years' military service, is a driver attached to a field ambulance. On May 24, 1942,* he developed a slight sore throat, and the next day a pink macular and papular rash was noticed on the trunk. His throat improved, but he felt vaguely out of sorts during the whole week and the rash persisted. There was no fever during this period.

On May 31 he became suddenly ill with severe frontal headache, pains in the back and limbs, and fever. On admission to hospital a few hours later the temperature was 102° F. and pulse 100. The patient was confused and restless, and complained of intense headache. A profuse pink maculo-papular rash was present on the chest, abdomen, upper part of back, and proximal part of the limbs. No petechiae or purpuric patches were seen. Neck rigidity was present, but Kernig's and Brudzinski's signs were negative. A left divergent strabismus and left-sided ptosis were present, but it was subsequently

* A report to the Medical Research Council.

found that the strabismus had existed since childhood. The pupils were dilated but reacted normally to light. Abdominal and plantar reflexes were normal. There was a leucocytosis of 12,400. Lumbar puncture soon after admission yielded a turbid fluid under increased pressure.

Sulphapyridine was given by the mouth, the initial dose being 2 g. Oral administration was satisfactory, and 9 g. were given in the first 24 hours. The patient rapidly became quieter, and the temperature had fallen to 99.4° F. by the following morning. The general condition was better, the headache less severe, and the mental state normal. The rash had almost completely faded, but petechiae were noted on the anterior aspect of the legs and there was a circular purpuric patch an inch in diameter on the right calf. The ptosis persisted and neck rigidity was still present, but Kernig's sign was negative. Lumbar puncture again yielded a turbid fluid; the pressure was normal. Sulphapyridine was continued in a dosage of 1 g. every 4 hours.

Improvement continued, and during the next few days the rigidity, ptosis, and headache abated. The dosage of sulphapyridine was decreased and the drug was discontinued on June 5, a total of 22 g. having been given. A slight right otitis externa, noticed on June 8, responded quickly to treatment. Convalescence was rapid, and no abnormality was detected on routine examination on June 14.

Laboratory Findings

The cerebrospinal fluid obtained on May 31 was turbid. There were 330 cells per c.mm., mainly polymorphs; protein 240 mg. per 100 c.cm. Fair numbers of Gram-negative diplococci were present, sometimes intracellularly. The opposed sides of the cocci were flattened, but the organisms were on the whole rather larger and more irregular in size than meningococci. Culture of the deposit on blood agar aerobically produced in 24 hours a profuse growth of yellowish mucoid colonies consisting of encapsulated Gram-negative diplococci. The characters of these organisms were as follows:

Morphology.—Gram-negative cocci occurring in pairs with the opposed sides flattened. A capsule was demonstrated by nigrosine and Muir's method.

Growth in Broth.—Diffuse turbidity in 24 hours at 37° C. aerobically.

Agar and Blood Agar, 24 Hours Aerobically.—Abundant growth of low convex, opaque, greyish-yellow, round colonies, 2 to 3 mm. in diameter, smooth surface, entire edge, mucoid consistency, undifferentiated. There was no true haemolysis, but the blood underwent a brownish discoloration. Growth was slightly better at 37° C. than at 22° C.

MacConkey's Agar, 24 Hours Aerobically.—Good growth of similar colonies, tending later to develop an effuse periphery and a finely crenated edge.

Gelatin Stab.—Growth along the line of the stab and on the surface. No liquefaction in 3 weeks.

Biochemical Reactions.—Acid, without gas, was produced in glucose in 24 hours, but not in lactose, mannite, sucrose, or dulcitol. Litmus milk was unchanged, indole was not produced, and the M.R. and V.P. reactions were both negative.

Pathogenicity.—1 c.cm. of a 24-hour broth culture was injected intraperitoneally into a guinea-pig without effect.

The cerebrospinal fluid obtained on June 1 was still turbid and contained smaller numbers of pus cells, but no organisms were seen in direct films. No growth was obtained on culture. Protein was 80 mg., chlorides 700 mg. per 100 c.cm.

The organism agrees in all respects with the type A form of *Diplococcus mucosus* described by McFarlan, who has discussed the systematic position of these strains and suggests that they are probably variants of the *Neisseria pharyngis* group. Though the evidence points strongly to the present strain being the cause of the meningitis, it would have been more conclusive if the isolation had been made on more than one occasion. Response to sulphapyridine was so prompt, however, that no organisms were found in the second specimen.

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MULTIPLE MUSCLE HERNIAE

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Although from time to time one sees simple muscle herniae, usually of the tibialis anticus, they give rise to little comment, as frequently they cause only slight if any trouble. In most standard textbooks the subject is dealt with very briefly, and few references can be found to it in recent literature. The cases that have been described are mostly those of fairly large single hernia, but bilateral herniae of the tibialis anticus have been recorded.

Ihde (1929), in a comprehensive review of the literature, himself reports 12 new cases, but all those mentioned in the review, including his own, were either single or single bilateral herniae. No case of multiple or multiple bilateral herniae of the lower leg was mentioned. Neither have we been able to find any reference to this condition in later literature. We therefore consider the following three cases of multiple herniae of the tibialis anticus worth recording.

All three patients were soldiers and had been engaged in strenuous training in rough hilly country, and it seems possible that both the nature of the training and that of the country

were contributing factors in producing the herniae. This is in accordance with the experience of Hesse (1921), who found muscle herniae rare except in mountainous districts, and of Pichon (Ihde, 1929), who found 39 cases in 217 Alpine soldiers, but only 1 in 1,000 Russian recruits. The herniae we have seen were small—about the size of a pea. All were reducible, and they disappeared when the muscle was contracted, leaving no palpable thickening. The splits in the fascia were distinctly felt. The openings were round and had quite sharp defined edges.

Records of Three Recent Cases

Case 1.—An infantryman was referred to hospital because of aching in both legs, which started during an intensive training course and was attributed to small varicose veins. Previously he had had no trouble, and was not a recent recruit. In addition to the varicose veins, three small reducible muscle herniae about the size of peas were present in the left leg, situated over the belly of the tibialis anticus muscle. The herniae were not tender, and disappeared completely on pressure and when the muscle was contracted.