all that was necessary." Another envisaged "a full-time information officer," who would work in contact with all the Association's committees and "collect, correlate, and disseminate information." It was finally resolved that the Council should look into the arrangements for improving intraprofessional relationships and solidarity "in view of the approaching medico-political storm."

The R.B. gave its attention to a great many other matters, and in particular through the report by Dr. J. B. Tilley, Chairman of the Public Health Committee, showed its concern with the health of the community. Much of the discussion on several subjects was inaudible to many owing either to defective installation of microphones and loudspeakers or to the bad acoustics of an otherwise excellent hall. Dr. A. Beauchamp, the Chairman of the R.B., had his task made trebly difficult by this great acoustic disadvantage, and on occasion he had to repeat statements two or three times. All this undoubtedly added up to a considerable loss of time over the four days of the A.R.M., but in spite of this handicap the Chairman conducted the business with exemplary fairness and patience. Those Representatives who missed much of what was said from time to time will, it is hoped, be able to fill in the gaps by reading the account of the meeting in the *Supplement*. And if other members of the B.M.A. would read the account they would then be informed of the views on a variety of important subjects held by a representative cross-section of the medical profession.

RUSSIAN VACCINE FOR MULTIPLE SCLEROSIS

An important communication from Moscow appears in the correspondence columns this week (p. 245). It is on the Russian vaccine for multiple (or disseminated) sclerosis, and is signed by Professor George Dick, of the Queen's University, Belfast, who has recently visited the Soviet Union, and Professor A. K. Shubladze, Chief of Laboratory of the Ivanovsky Institute of Virology, Moscow. Professor Shubladze is in complete agreement with the findings of Dick and his colleagues, published recently in this *Journal*,[1] that the virus which is used to make the Russian multiple sclerosis vaccine of Shubladze and Margulis is similar to rabies virus. It is possible to go further than that, for the virus of the vaccine of Shubladze and Margulis is not only similar to rabies but is antigenically indistinguishable from it. This strain of rabies virus (which is apparently the so-called *street* virus), came from a strain of virus claimed to have been isolated from the blood of a patient with a peculiar acute encephalomyelitis syndrome.[2] We understand that the original isolates of this virus are to be reinvestigated, but there is no evidence that it is causally related to multiple sclerosis; indeed, there is no satisfactory evidence that any virus is. As to the vaccine, there is no significant evidence of its clinical value either in the U.S.S.R. or in other countries of Europe where it has been tried. Furthermore, as was pointed out in these columns recently,[3] the administration of it may possibly be harmful.

The marketing of this vaccine without any reliable evidence of its clinical value is unfortunate. Equally so is the publicity that must have raised the hopes of many sufferers from multiple sclerosis. Patients with this disease should be informed of the nature of the virus from which the vaccine is made, that the vaccine may be dangerous, and that it has not been shown to do any good. It is satisfactory that virologists in the U.S.S.R. and in Great Britain and Northern Ireland have reached such complete agreement on this vaccine and virus, an event that illustrates the great importance of personal exchanges of information between scientists of the two countries. It should also help to remove the vaccine from the political skirmishing that has been its lot in Britain.

[1] Dick, G. W. A., McKeown, Florence, and Wilson, D. C., *Brit. med. J.*, 1958, 1, 7.
[2] Margulis, M. S., Soloviev, V. D., and Shubladze, A. K., *J. Neurol. Neurosurg. Psychiat.*, 1946, 9, 63.
[3] *Brit. med. J.*, 1958, 1, 821.

TREATMENT OF CERVICAL SPONDYLOSIS

Cervical spondylosis is a term which is sometimes given a restricted meaning. But it is a useful term for all those chronic lesions of the cervical spine in which compression of the spinal cord or nerve roots is brought about by medial or lateral protrusions of the intervertebral disk, or by osteophytic outgrowths from the vertebral bodies and the neighbourhood of the joints of Luschka, where they may encroach on the intervertebral foramen and so compress the nerve roots. These outgrowths probably owe their origin primarily to disk degeneration, and have been found in 75% of a sample of hospital patients.[1] Cervical disk lesions are often associated with disk degeneration in the lumbar region, as might be expected, but the incidence of acute herniation of the nucleus pulposus is very much less in the neck. Not only is the disk much smaller, but the region is subject to very different strains and stresses. Acute herniation may be independent of cervical spondylosis. Because of the proximity of the spinal cord, the symp-

[1] Pallis, C., Jones, A. M., and Spillane, J. D., *Brain*, 1954, 77, 274.
[2] Clarke, E. A., and Robinson, P. K., ibid., 1956, 79, 483.
[3] Cleveland, D. A., *Postgrad. Med.*, 1955, 18, 99.
[4] Spurling, R. G., *Lesions of the Cervical Intervertebral Disc*, 1956. Springfield, Illinois.
[5] Brain, W. R., *Ann. intern. Med.*, 1954, 41, 439.
[6] Mair, W. G. P., and Druckman, R., *Brain*, 1953, 76, 70.
[7] Scoville, W. B., *Conn. med. J.*, 1954, 18, 894.
[8] Odom, G. L., Finney, W., and Woodhall, B., *J. Amer. med. Ass.*, 1958, 166, 23.
[9] Haynes, W. G., *J. med. Ass. Ala*, 1956, 26, 261.

toms are severe and sudden in onset. There is no divergence of opinion about the need for surgical treatment in such cases. It is in the relief of chronic symptoms and signs that controversy has arisen.

The conditions of cord and root compression are best considered separately; one or other usually predominates. For the treatment of cord compression, E. A. Clarke and P. K. Robinson[2] concluded that conservative measures should be used at first, and continued if no further progression of symptoms has taken place. Failure to arrest the progress of the condition necessitates laminectomy and division of the dentate ligaments to allow the cord to ride freely over the protrusion. There is a large measure of agreement upon these principles, though some authors advocate traction,[3 4] while others prefer immobilization.[2 5] However, the socially unacceptable nature of most cervical collars limits their use to some extent. The most that should be hoped for from surgical treatment is that the progress of the disease may be arrested. W. R. Brain[5] has pointed out that arrest is often spontaneous, but with surgery it is hoped to bring this about more rapidly and also to prevent extensive cord damage.[6] He has also drawn attention to the danger of manipulation in these cases.

Many more operations are performed for cervical root compression in North America than in this country. Of 250 patients with cervical spondylosis operated upon by W. B. Scoville[7] in a period of eight years, all but six had lateral protrusions and osteophytes. G. L. Odom, W. Finney, and B. Woodhall[8] have just reported a similar number of patients treated over a period of 16 years, of which 72% were of this type. Though good or excellent results are claimed for 84% of lateral disk protrusion, and for 67% of those with foraminal spurs, the length of follow-up is not stated, and—as in some other papers advocating surgery[9]—it is not clear that a later return of symptoms has been excluded. There is a far from negligible risk of producing further damage to the cervical roots and cord when attempts are made to remove osteophytes. On this side of the Atlantic, operation is generally reserved for cases on whom conservative treatment has failed; spontaneous remission is quite common, and most surgeons are cautious in recommending operation. It is essential to differentiate other causes of pain in the upper limb, such as carpal tunnel compression of the median nerve, before concluding that the source is a cervical spondylosis, which may well be present, though unrelated to the symptoms. In the future more reliable operations may be devised, or, better still, means may be found of preventing the condition from developing.

TREATMENT OF IDIOPATHIC THROMBOCYTOPENIC PURPURA

The indications for splenectomy in the treatment of patients with idiopathic thrombocytopenic purpura have never been firmly established. Since the operation was first proposed by P. Kaznelson[1] in 1916, its frequent dramatic success in raising the platelet level and arresting haemorrhage made it the sheet anchor of treatment for many years. Cure rates of over 90% were reported in some early series of cases, but it later became clear that post-operative improvement might be transient and that relapse might occur months or even years later. A more recent review of the effects of splenectomy in 303 patients with idiopathic thrombocytopenic purpura whose subsequent progress was followed for several years showed complete and lasting remissions in 61%, partial remissions in 17%, and failure in 22%.[2] Attempts to select patients more likely to benefit from the operation have been made, but neither the presence of eosinophilia and megakaryocytic hyperplasia in the bone marrow nor the existence of detectable circulating antibodies active against the platelets has proved of consistent value in forecasting response.[2-4] Splenectomy has generally been avoided in purpura of acute onset, particularly in children and when there is any possibility that the condition might result from a recent infection or exposure to drugs, because spontaneous improvement is likely in these circumstances. In such cases transfusion with fresh, platelet-rich blood, preferably drawn into plastic or siliconized containers to improve platelet survival, and accompanied by administration of A.C.T.H., cortisone, or prednisone, provides the most satisfactory form of treatment. When purpura continues for several months, despite medical treatment, and in patients with a past history of bleeding episodes, splenectomy is commonly advised, since A.C.T.H. and cortisone, though improving capillary fragility, often fail to increase the platelet count and afford only temporary control of haemorrhage.[5]

Certain recent observations, however, strongly suggest that splenectomy should no longer be regarded as the treatment of choice in chronic idiopathic thrombocytopenia. Disseminated lupus erythematosus has been reported to develop after splenectomy in patients who before operation showed the clinical and haematological pictures of idiopathic thrombocytopenia or acquired haemolytic anaemia, with no manifest evidence of lupus,[6] and W. Dameshek and his colleagues[7] now claim that approximately 25% of all patients with apparently typical idiopathic thrombocytopenic purpura in whom the spleen is removed will eventually develop systemic lupus erythematosus. They think it possible that splenectomy in some way aids dissemination of the lupus process, which they believe to be present, in occult form, in many cases of thrombocytopenia. For this reason, and because the effects of splenectomy are in any case poorly predictable, he and his associates carried out a fresh assessment of medical treatment in thrombocytopenic purpura, with particular reference to the effects of prednisone on the bleeding tendency and the platelet count. Thirty consecutive patients, 11 with "acute" and 19 with "chronic" thrombocytopenia, were treated with prednisone in initial doses of 20 to 150 mg. daily. In 22 cases the platelet count rose to normal in 6 to 150

[1] Kaznelson, P., *Wien. klin. Wschr.*, 1916, **29**, 1451.
[2] Lozner, E. L., *Bull. N.Y. Acad. Med.*, 1954, **30**, 184.
[3] Harrington, W. J., *Sang*, 1954, **25**, 712.
[4] Stefanini, M., ibid., 1955, **26**, 83.
[5] Robson, H. N., and Duthie, J. J. R., *Brit. med. J.*, 1950, **2**, 971.
[6] Dameshek, W., and Reeves, W. H., *Amer. J. Med.*, 1956, **21**, 560.
[7] —— Rubio, F., Mahoney, J. P., Reeves, W. H., and Burgin, L. A., *J. Amer. med. Ass.*, 1958, **166**, 1805.

days, and remained well above haemorrhagic levels on maintenance doses ranging from 2.5 to 15 mg. daily. The dosage of prednisone was frequently altered to find the lowest effective dose in each case, and the drug was withdrawn entirely from eight patients without relapse. Prednisone appeared to be much more effective in raising the platelet count than either A.C.T.H. or cortisone in comparable dosage, and the authors now regard it as the treatment to be preferred in both acute and chronic forms of the disease, splenectomy being reserved for the occasional severe cases that fail to respond. The use of prednisone and of splenectomy in the treatment of idiopathic thrombocytopenic purpura offers a close parallel with their use in idiopathic acquired haemolytic anaemia. In both diseases splenectomy is variably and unpredictably successful and has possible concealed risks, and is therefore best postponed until prednisone has proved ineffective or effective only in doses too high to be tolerated for long periods. Provided control can be achieved and maintained with doses of prednisone small enough to avoid serious drug toxicity, this approach seems eminently sensible.

BYSSINOSIS

For nearly two hundred years Lancashire has been identified with cotton manufactures. While these brought wealth and industry, now unfortunately declining, to the population of the crowded mill towns, they also caused an inordinately high morbidity and mortality from chronic respiratory disease. The whole community suffered excessively from bronchitis, which was non-occupational but due to pollution of the atmosphere by the acrid smoke of house and factory chimneys.[1] Certain groups of workers, notably those employed in the processes of preparing the cotton and in the cardrooms and blow-rooms suffered additionally from "asthma," which was occupational and popularly attributed to the irritation of cotton dust. J. Leach,[2] a certifying surgeon of Heywood, Lancashire, described the disorder in 1863. Since then the disease, byssinosis, has continued to occur, causing chronic ill-health, disablement, and death. In recent years byssinosis has been the subject of extensive researches—clinical, pathological, and epidemiological—by R. S. F. Schilling and his co-workers,[3] who have been admirably assisted by the mill owners and by the trade unions. In seeking ways of preventing this disease, or at least of minimizing its effects, occupational health workers must first estimate its prevalence and identify its cause or causes, and this entails a critical differentiation of occupational from non-occupational cases of chronic bronchitis. Schilling and his colleagues concluded that the symptom complex of chronic bronchitis is not the same as that of byssinosis, for whereas men with chronic bronchitis develop tightness of the chest whenever they are exposed to an irritating concentration of any dust, in the early stages of byssinosis the workers are affected only by cotton dust and only on Mondays or on the day immediately following absence from work. They divided the disease into two stages—grade I in which chest tightness and/or breathlessness occur on Mondays only, and grade II in which chest tightness and/or breathlessness occur on Mondays and other days. But even in grade II the symptoms are worst on Mondays. This means that the occurrence of Monday symptoms,[4] previously called "Monday feeling," is the specific characteristic in the diagnosis of byssinosis.

In 1956 the Industrial Injuries Advisory Council reported that although an experienced observer visiting the cotton mill on a Monday might be able to decide with some assurance whether a person was experiencing the symptoms of byssinosis (grade I), there was no simple objective test by which the disorder could be distinguished. C. B. McKerrow and his colleagues[5] have recently sought to discover such an objective test. In a carefully planned study, which is another example of the excellent scientific work initiated by Dr. R. S. F. Schilling and supplemented by the Medical Research Council's Pneumoconiosis Research Unit at Cardiff under the direction of Dr. J. C. Gilson, they measured respiratory functions by the accepted modern methods; these included indirect maximum breathing capacity (M.B.C.), maximum voluntary ventilation (M.V.V.), and peak inspiratory and expiratory flows coupled with an airways resistance (A.W.R.). The results showed distinctive specific patterns for both grades of byssinosis and for the controls. McKerrow and his colleagues concluded that the mill dust—quantitatively as well as qualitatively—is the cause of the respiratory impairment and that it contains some pharmacologically active constituent. This work marks an important advance towards the establishment of a practical objective test for the detection of the earliest stage of the disease, especially as the specific changes in M.B.C. and A.W.R., but of less degree, were discovered among cotton workers without clinical byssinosis.

DIAGNOSIS OF ACUTE PANCREATITIS

The consensus of opinion at the present time is that operation should be avoided in acute pancreatitis.[1] Such a view presupposes a correct diagnosis. Unfortunately this is seldom easy, especially since the disease is uncommon compared with such conditions as perforated peptic ulcer, gall-bladder disease, intestinal obstruction, and myocardial infarction, from all of which it has to be differentiated. The most widely used laboratory aid in diagnosis is the level of the serum amylase, but this test has several disadvantages. Normal values do not necessarily imply the absence of acute pancreatitis, while levels above 200 Somogyi units, which can be regarded as the upper limit of normal, may occur in a variety of conditions, including those already mentioned.[2] Never-

[1] Lane, R. E., and Campbell, A. C. B., *Brit. J. industr. Med.*, 1952, **11**, 118.
[2] Leach, J., *Lancet*, 1863, **2**, 648.
[3] Schilling, R. S. F., Hughes, J. P. W., Dingwall-Fordyce, I., and Gilson, J. C., *Brit. J. industr. Med.*, 1955, **12**, 217.
[4] Report of the Industrial Injuries Advisory Council, *Byssinosis*, 1956, Cmd. 9673, H.M.S.O., London.
[5] McKerrow, C. B., McDermott, M., Gilson, J. C., and Schilling, R. S. F., *Brit. J. industr. Med.*, 1958, **15**, 75.

[1] Richman, A., *Amer. J. Med.*, 1956, **21**, 246.
[2] Burnett, W., and Ness, T. D., *Brit. med. J.*, 1955, **2**, 770.
[3] Cherry, I. S., and Crandall, L. A., Jr., *Amer. J. Physiol.*, 1932, **100**, 266.
[4] Keith, L. M., Jr., Zollinger, R. M., and McCleery, R. S., *Arch. Surg. (Chicago)*, 1950, **61**, 930.
[5] Pfeffer, R. B., Mixter, G., Jr., and Hinton, J. W., *Surgery*, 1958, **43**, 550.

theless a serum amylase concentration above 400 units is strongly suggestive, especially when accompanied by hyperglycaemia (which is seen in about half the cases) and by a leucocytosis with a relative lymphopenia. The rise, however, is short-lived and seldom lasts longer than 48 hours. An increase in blood lipase occurs later and is more persistent; this enzyme is relatively simple to estimate.[3]

Various other tests have been used. The serum calcium concentration is said to fall, presumably owing to combination of calcium with the fatty acids liberated by hydrolysis, but this usually implies a very poor prognosis. Some help may be obtained by radiography of the abdomen, especially if dilated loops of jejunum are seen round the area of the pancreas. A procedure which has recently been used with some success is to attempt to aspirate fluid from the peritoneal cavity.[4] For this purpose a trocar and cannula are inserted into the flank, and a fine polythene tube is threaded through the cannula as far as possible in a cephalic direction.[5] The cannula is then removed, so that the patient can be turned into various positions while an attempt is made to aspirate fluid. A positive diagnosis depends on the withdrawal of a haemorrhagic exudate with a very high content of amylase. This method too has its drawbacks, the main one being failure to obtain a sample, but it is at least simple and free from danger. It is worth considering in any patient in whom the question of acute pancreatitis arises, but it cannot yet be said that there is a reliable way of confirming the diagnosis of this serious disease.

HORMONE-INDUCED SEX CHANGES

The theory of sex determination by hormonal control is as old as Voronoff, but direct experimental evidence of this possibility is comparatively recent. Foetal intersex of various types can now be produced relatively easily in most laboratory animals by the administration of androgens to the mother, and there is accumulating evidence that similar effects may be reproduced inadvertently in the human female. G. Nellhaus[1] reports the case of a woman who had received a total dosage of 2 g. of methyltestosterone for habitual abortion, and who subsequently delivered a typical female pseudohermaphrodite, and he cites five other cases from the literature. Similar results are described following progesterone therapy for the same condition by other authors.[2 3]

Up to the tenth week of gestation the two sexes share the common indifferent genitalia, differentiation into male and female appendages taking place within the next six weeks. A. Jost[4] has shown that before this stage the genitalia are particularly susceptible to hormonal influence. The normal basic neutral structure is female, as in the ovum, future differentiation being directed by the testis, acting mainly through its testosterone secretion. Androgens administered to the mother at this crucial stage pass easily through to the foetus in rather high concentration, and any excess may cause changes in its sensitive external organs. If the genetic sex is male, the added androgen will have little effect beyond reinforcing the natural testosterone and perhaps producing temporary genital hypertrophy. If, however, the sex chromosome addition is female, such treatment may easily simulate the hormonal effects of normal testicular development, with the production of a type of intersex such as pseudohermaphroditism. The same effect may be produced with progesterone (which is used much more widely than the androgens for threatened abortion) through its partial conversion into testosterone during normal metabolism. Here, however, the total amount of androgen released is relatively small, 1 mg. of progesterone being equivalent, according to J. K. Lamar,[5] to 0.03 mg. of testosterone, so that its administration in the usual therapeutic dosage should be fairly safe. This cannot, however, be said for testosterone itself. Experimental and clinical observation shows that pregnant women taking large amounts of the hormone, particularly during the third and fourth months, may deliver a baby with abnormal external genitalia. Such treatment is anyway of doubtful therapeutic value, and in view of the inherent dangers it is probably unwise in any circumstances during early pregnancy.

[1] Nellhaus, G., *New Engl. J. Med.*, 1958, **258**, 935.
[2] Reilly, W. A., Pickering, D. E., and Crane, J. T., *Amer. J. Dis. Child.*, 1958, **95**, 9.
[3] Wilkins, L., and Jones, H. W., *Pediatrics*, 1958, **21**, 513.
[4] Jost, A., in *The Comparative Physiology of Reproduction and the Effects of Sex Hormones in Vertebrates*, p. 237, ed. I. C. Jones and P. Eckstein, Cambridge, 1955.
[5] Lamar, J. K., *Anat. Rec.*, 1937, **70**, Suppl. 45.

MORE POLIO VACCINE

The Medical Research Council has produced compelling evidence[1 2] that a third, or booster, dose of poliomyelitis vaccine is needed to maintain circulating antibody at levels likely to confer protection. Its results agreed with those of several American studies, which were discussed last year in these columns,[3] where the suggestion was made that children who had had two doses should be offered a booster in the spring. Unfortunately this apparently was impossible. The Government's hope that supplies for this purpose will be available in the autumn, expressed by the Minister of Health last Monday, is therefore welcome. The offer of vaccination is also to be extended to people aged up to and including 25, and to a wider range of hospital staffs and their families. The Minister and the Secretary of State for Scotland are to consult with the B.M.A. and local authority associations on the details of continuing this elaborate campaign in preventive medicine.

Whether further doses beyond the third will be needed to maintain immunity has yet to be discovered, for much mystery still surrounds the nature of immunity and the relation between level of antibody and the protection it confers.[4] The studies that are now being carried out may throw light on that within the next year or so. But, owing to the complex administrative arrangements that must of necessity be made to give these injections, it is a possibility worth keeping in mind. If the disease is to be reduced drastically, as diphtheria has been, for instance, very large numbers of inoculations may have to be performed, at least for some years.

[1] Report to the Medical Research Council, *Brit. med. J.*, 1957, **2**, 1207.
[2] —— ibid., 1958, **1**, 1206.
[3] Ibid., 1957, **2**, 1229.
[4] Ibid., 1958, **1**, 1227.