form than in those who had not been vaccinated. It was further reported that the higher degree of protection shown by the live vaccine compared with the killed-and-live vaccines was statistically significant, a finding which correlates well with the results of the serological tests made in the small earlier study. It is interesting to note that a still further follow-up of this trial is to be made. This would seem to be essential, for it is important that information should be obtained on the duration of immunity into adult life and on the need for reinforcing doses.

The report concludes that there is a strong case for the use of live vaccine alone. This is the procedure which the Ministry of Health recommends for the immunization campaign which is soon to be launched in this country. The use of live vaccine alone entails only one injection, and the reactions which follow, though somewhat more frequent than after killed-and-live vaccines, are generally mild and should cause little concern, especially if parents are informed beforehand that they may occur. Further, as the report points out and as mentioned in these columns earlier this year, it would be unwise to use killed vaccine at present in view of the experience in the U.S.A. of local and systemic reactions which killed vaccine may sometimes cause when children are exposed to measles or given live vaccine a number of years later.

It may be argued that Great Britain has been slow in tackling the problem of prevention of measles by vaccination, for it has been going on in the U.S.A. increasingly since 1963, where already more than 20 million doses have been given. But Britain has always been cautious, and rightly so, in embarking on any large-scale programme of immunization, and the Medical Research Council trial reported in today's B.M.J. is an indispensable prelude to a national vaccination campaign. But, though the results of the trial have shown that live measles vaccine is effective, safe, and generally acceptable, it is nevertheless essential that a close watch should still be kept on the effects of vaccination once the campaign gets under way. Only in this way can a true assessment of the vaccine in general use be obtained, and it is therefore important that the Ministry of Health should include in its campaign a well-planned and long-term surveillance programme.

**Slow Progress in Cirrhosis**

Despite all the modern techniques of investigation about 40% of cases of cirrhosis in Great Britain remain of unknown aetiology. Some of these patients may give a history of an apparently uncomplicated attack of acute infectious hepatitis in childhood or adolescence. But follow-up of the large epidemics of hepatitis seen during the second world war or more recently in India has shown no increase in the incidence of cirrhosis alter them. Occasional cases of infectious hepatitis may follow a subacute course with the development of cirrhosis over three to six months. But even in these patients precise confirmation is impossible owing to the lack of a specific diagnostic test for the disease.

Alcoholic cirrhosis still poses many questions. Recent work has stressed the importance of alcohol as a toxic agent in the production of fatty liver or acute alcoholic hepatitis, though the link between these and cirrhosis has not been proved experimentally. The accompanying nutritional disturbance is now thought to be less important, but why does only one in 10 heavy drinkers develop cirrhosis? Genetic factors have been suggested as one answer, for there are reports of an increased incidence of blood group A and of colour blindness among patients with cirrhosis. Yet in one study the defect in colour vision was found to revert towards normal with treatment of the cirrhosis, and in some series no increase in incidence has been found. In the B.M.J. this week Dr. N. C. R. W. Reid and his colleagues report at page 463 interesting studies on Caucasian and Negro patients. They could find no increase in colour blindness in the Caucasian patients but they did find a higher incidence of brown hair and very light skin colour than among control subjects matched for age and race. There was no increase of blood group A in the cirrhotics of either race, but in the Negroes there was a significant increase in the proportion of patients with the Duffy blood group. The latter is one of the most sensitive of the blood group systems for showing racial differences, and the higher-than-average incidence of it among the Negro patients could be due to a greater White admixture in this group than in the Negro controls. The failure to find a significant difference with respect to the Duffy blood group in Caucasian subjects would suggest that the association is an indirect one rather than due to a linkage of the gene for cirrhosis with the Duffy locus. These results would suggest a multifactorial inheritance of susceptibility to cirrhosis with a greater frequency of these factors in Caucasian than in Negro people.

The role of autoimmunity in the pathogenesis of cirrhosis is also uncertain. Deborah Doniach and her colleagues have found non-organ-specific complement-fixing antibodies in the serum of 31% of patients with cryptogenic cirrhosis (i.e., without known cause), 85% with primary biliary cirrhosis, and 30% with active chronic hepatitis. The last is a variety of chronic liver disease of unknown aetiology which progresses to cirrhosis; it is accompanied by high levels of serum transaminase and globulin, hepatocellular necrosis and lymphocytic infiltration, and sometimes a positive L.E. (lupus erythematosus) test. The serum antibodies may simply be a reflection of heightened immunological reactivity of these patients.

Patients with active chronic hepatitis may develop lesions in other systems, with attacks of arthralgia, pleurisy, rashes, and ulcerative colitis. To this list Margaret Turner-Warwick has recently added fibrosing alveolitis. Five of the patients she described had active chronic hepatitis; the other three are described on pathological criteria as having “interlobular hepatitis.” In every case various non-specific serum antibodies were found like those already described, and the level of one or more of the circulating immunoglobulins was increased. The pulmonary signs and symptoms—cough, breathlessness, finger-clubbing, and widespread fine crepitations-dominated the clinical picture in six

patients, but it is of interest that in seven the course of the liver disease paralleled that of the lung. One patient showed a response in both organs to corticosteroids, but in three cases the disease advanced despite this therapy.

Corticosteroids and more recently immunosuppressive drugs (6-mercaptopurine and azathioprine) have been tried in the treatment of various cirrhosis such as active chronic hepatitis when there is evidence of continuing inflammation and hepatocellular necrosis. The results, as in the recent report of S. Mistlel and C. R. B. Blackburn, include some improvement in the symptoms and biochemical changes but little effect on the hepatic lesions or even on the patient's survival. Controlled trials at present in progress may throw more light on this.

The prognosis in cirrhosis as a whole is worse than in many forms of cancer. In a series of 156 patients with cirrhosis seen in a general hospital in Birmingham between 1959 and 1965 W. D. Stone and his colleagues found a five-year survival rate of only 14.3%. The patients with alcoholic cirrhosis lived longer than those with the cryptoegenic variety, though W. J. Powell and G. Klatkin, from Yale, New Haven, paint a brighter picture. The survival of patients with ascites was no different from that reported by O. D. Ratnoff and A. J. Patek in 1944—an indication that the undoubted efficacy of present-day diuretics may be balanced by complicating electrolyte disorders. The incidence of hepatic coma also appears to be increasing.

A true picture of the natural history of cirrhosis will be obtained only when the incidence of asymptomatic disease in the community can be established. The exciting possibilities raised by recent accounts of hepatic transplantation must not be allowed to divert too much attention from these gaps in our knowledge of the basic epidemiology of cirrhosis and of the value of medical treatment.

Brunner's Glands

Brunner's glands are coiled tubules that lie below the muscularis mucosae of the duodenum. They are lined by epithelial cells containing mucous substances, and their secretion is slimy, slightly alkaline, and mucoid. The late Lord Florey, who was interested in mucus secretion in the gut both before and after his wartime work on penicillin, demonstrated that secretion from Brunner's glands could be provoked by stimulation of the vagus and by a hormone that was extracted from duodenal mucosa. At the time he thought that this hormone was secretin, but recently it has been shown that a purified extract of secretin does not stimulate Brunner's glands, and probably another hormone from the pyloroduodenal mucosa is concerned.

The exact function of these glands remains an enigma. Though the juice is slightly alkaline it does not contain nearly as much bicarbonate as pancreatic juice, which is able to neutralize gastric acid as it enters the small intestine. Furthermore, the secretion from Brunner's glands does not appear to aid digestion, for it contains only peptic and this is small amounts. Probably the main function of these glands is to secrete mucus which may protect the duodenal mucosa against acid-pepsin attack from the stomach. Possibly, therefore, the glands may be important in the pathogenesis of duodenal ulcer, but there is at present no evidence for this.

Diseases of Brunner's glands are extremely uncommon. Large single adenoma occur and may cause intermittent obstruction of the pylorus. Hyperplasia of the glands is recognizable macroscopically by a cobblestone appearance of the duodenum. This has been claimed to be a cause of coarse duodenal folds seen on barium-meal examination, though another explanation is that this is due mainly to hypersecretion of gastric acid. Patients with coarse duodenal folds may have dyspepsia, which is best treated as if they had a duodenal ulcer, particularly if gastric acid secretion is high. Hyperplasia of Brunner's glands is not a precursor of cancer, but there are reports of its causing gastrointestinal bleeding and duodenal obstruction.

Management of Strokes

"Stroke" was an adequate diagnosis as long as there was little that could be done to affect the outcome of cerebrovascular accidents. When more effective treatments became available the differentiation of haemorrhage, thrombosis, and embolism ceased to be just an academic exercise, and it soon became apparent that the clinical features traditionally used in diagnosis were unreliable. Cerebral haemorrhage is not necessarily limited to the hypertensive patient with degenerate arterioles. It does not necessarily occur during activity; there may be little headache or disturbance of consciousness, and the condition can have a good prognosis. Primary cerebral thrombosis is not found only in elderly arteriosclerotic patients, nor does it always occur during periods of inactivity. Cerebral thrombosis may result in such massive infarction as to simulate a haemorrhage in symptomatology and prognosis. An embolism need not arise from a heart valve or chamber; auricular fibrillation is not essential; and the onset need not be dramatically abrupt. It may indeed be extremely difficult to distinguish these events at the bedside. Furthermore, the use of arteriography and the careful examination of thousands of well-fixed brains have shattered many illusions, and in particular have shown how rarely is that most favoured diagnosis—middle cerebral thrombosis—accurate. A small intracerebral haemorrhage can mimic the classical picture of a thrombosis; a large infarction may behave like a haemorrhage; emboli may arise from atheromatous plaques or clots in the great vessels in the neck, and may at times find their way to the brain from thrombosed veins elsewhere in the body if a patent foramen ovale in the heart permits them to bypass the lungs.

Another change of mental attitude has become necessary. When a blood vessel is blocked it is not the presence of the clot in the arterioles which is the direct cause of the patient's symptoms; it is the inadequacy of blood flow to a particular part of the brain. If there are healthy collaterals to give an alternative flow then a thrombus can be present in a major vessel—vas is often the case in internal carotid thrombosis—with no referable symptoms. On the other hand, if a proximal vessel is narrowed and the collaterals are inadequate or