this is present, treating it, perhaps curing it, or when the condition is grave and untreatable and in keeping with the unbearable anxiety that it generates in the mother, or better the parents, and in conformity with their wishes, terminating the undesired pregnancy at a stage when this is morally and legally acceptable. Disregarding the detection of gross developmental malformations by contrast radiography, ultrasonic scanning or fetoscopy, the favoured procedure for the detection of anomalies leading to serious and intractable handicap is early amniocentesis. The study of the fluid and cells is useful in respect of four main groups of anomalies.

First, study of the amniotic fluid and cells can be useful for the detection of mutants of large effect which are responsible for the severe inborn errors of metabolism, often untreatable and generally incurable and which have a high recurrence risk in certain families. Secondly, there is the detection of X-linked disease which often—but there are exceptions like Lesch-Nyhan's or Hunter's disease—is less precise because indirect. Thirdly there is the detection of chromosome anomalies of which the most relevant is trisomy-21(mongolism), because of the high prospect of severe subnormality and its frequency and the high risk of its recurrence in a few families. Fourthly, there seems to be now the chance of an early detection of anencephaly and some forms of spina bifida cystica by demonstrating in early pregnancy an excess of fetal α-protein in the amniotic fluid.

Prenatal diagnosis of chromosome and sex-linked disorders, and especially mongolism, will be discussed.

Symposium IV

Encephalitis and meningitis

Cryptococcal and Other Forms of Mycotic Meningitis

W. St. C. Symmers (Department of Pathology, Charing Cross Hospital and Medical School) What we conventionally refer to as fungal meningitis is, of course, meningoencephalitis. It is important to remember this as treatment that seems effective against the meningeal component of the illness may not sterilize lesions within the brain: these may subsequently be the source of reinfestation of the meninges.

Fungal meningoencephalitis may develop in the absence of apparent infection elsewhere, or it may be incidental in the course of a generalized haematogenous mycosis. It may occur without predisposing factors, or it may be an 'opportunistic' infection, predisposed to by the resistance-lowering effects of other diseases or of their treatment.

Some fungi have a predilection for the central nervous system—Cryptococcus neoformans, Cladosporium bantianum, the 'opportunistic' phycomycetes (species of Rhizopus, Absidia and Mucor) and Nocardia asteroides. Others (for instance, species of Aspergillus and of Candida, the histoplasmas and Coccioides immitis) have less affinity for the central nervous system and infect it comparatively seldom: when they do so, this may be the presenting or even the only clinical manifestation of the infection, or—usually as part of a generalized bloodstream infection—it may be accompanied by little or no evidence of neurological disturbance.

A series of cases, all seen in Britain, is presented, including actinomycosis, nocardiosis, streptomycoosis, madurellosis, aspergillosis, penicilliosis, phymycosis, candidosis, geotrichosis, cryptococcosis, North American blastomycosis, chromomycosis, and sporotrichosis. Some cases are also noted in which the microscopical appearances of the organisms were not familiar and cultures were not obtained: for the moment they must be added to the number of mycoses caused by as yet unidentified fungi.

Among the 'opportunistic' fungal infections of the central nervous system, special attention is due to naso-orbitocerebral phycomycosis complicating sustained acidosis, particularly in diabetes mellitus. The same sequence of nasal, orbital, and meningoencephalic infection is occasionally caused by aspergilli, particularly Aspergillus flavus: this species is a cause of infection of the nasal sinuses, particularly in hot, dry climates—its spread to the orbit and the brain is not necessarily related to predisposing factors, in contrast to the phycomycetes.

Double and multiple opportunistic fungal infections of the central nervous system are not infrequent. Any combination of 'opportunist' moulds, yeasts, and actinomycetes may be found, and opportunistic bacterial, viral, and protozoal infections—and even metazoan infestations—may coexist. As examples, two cases recently seen in Britain are presented: a case of meningoencephalitis caused by a free-living amoeba (Naegleria species) superimposed on cryptococcal meningoencephalitis complicating sardoidiosis; and a case of anomalous haematogenous infestation by larvae of Strongyloides stercoralis associated with septicaemic candidosis as complications of lymphatic laukaeemia under treatment with cytotoxic drugs and corticosteroids.

Meningococcal Infection: Serotypes and Sulphonamide Sensitivity J. D. Abbott (Public Health Laboratory, Withington Hospital, Manchester) In recent years sulphonamide resistance of meningococci has become a problem in the USA and elsewhere. Since
1966 cultures of meningococci isolated from patients in different areas of England and Northern Ireland have been sent to the Manchester Public Health Laboratory for serotyping and for testing for sensitivity to sulphonamides. From 1966 to the end of April 1972, we have typed 342 cultures isolated from blood or CSF: 27 strains were group A (8%), 185 group B (54%), 113 group C (33%), one strain each group X and Y, and 15 were untypable (4%). The majority of untypable strains (13/15) were received before 1970 and had been stored for long periods before typing. During the same period 370 cultures were tested for sensitivity to sodium sulphadiazine. The majority of cultures 319 (86%) were inhibited by 0.16 mg% sodium sulphadiazine, and a further 18 (5%) by 0.32 mg%. Thirty-three strains (9%) had a minimal inhibitory concentration of 0.64 mg% or greater, and these we have classed as resistant; 12 of these (3%) had a minimal inhibitory concentration of 0.64-1 mg%, and 21 (6%) a minimal inhibitory concentration of 5 mg% or more. The proportion of resistant strains isolated recently appears to be increasing—22% of those isolated in the first four months of 1972 compared with 7% of those in 1971. Resistant strains were isolated from different areas of England and Northern Ireland. The proportion of resistant strains amongst different serotypes varies—6% of group B, 8% of group C, and 44% of group A strains. These findings and the report of sulphonamide-resistant strains in Scotland (Fallon, 1971) clearly indicate that sulphonamides alone cannot be relied upon for the treatment of meningococcal infection in this country, and the efficacy of sulphonamides for chemoprophylaxis may be affected by the presence of sulphonamide-resistant strains.

Reference

Meningococcal Infection: Serological Studies D. M. JONES (Public Health Laboratory, Withington Hospital, Manchester) The recrudescence of interest in meningococcal disease, particularly in the United States, has resulted in much progress being made towards the understanding of immunity in this disease (Artenstein et al, 1971). A variety of serological techniques have been used to study the antibody response in the carrier state, in disease, and after administration of the recently developed meningococcal polysaccharide vaccines. The indirect haemagglutination technique has been found to be very sensitive, and to detect type specific antibody. This method has been used to investigate the normal antibody responses in carriers and cases in a small outbreak of meningitis in a school in the north west of England. With this basic information it has been possible to assess situations where multiple cases occur in one family and where there may be a deficiency in immunity. The occurrence of a community outbreak of group B meningococcal meningitis in Bolton and district during 1970 and 1971 enabled the incidence of antibody in the general population of epidemic and non-epidemic areas to be compared. The incidence of antibody was found to increase with age but no significant differences were found in antibody distribution between Bolton and elsewhere in NW England. The distribution of type-specific antibody was found to differ from that reported from the United States; this may be related to the differing distribution of serotypes causing disease in the US compared with England and Wales (Abbott and Graves, 1972).

Aspects of the Epidemiology of Haemophilus Meningitis D. C. TURK (Bacteriology Department, Radcliffe Infirmary, Oxford) The incidence of this disease has increased greatly in the past 30-40 years, notably in N America but also in Britain and many other countries. It is now, at least in those countries, the commonest form of meningitis in childhood. Mortality, almost 100% without treatment, can be reduced to 5% or so with suitable antibiotics, but residual disability is common. Virtually all cases are caused by capsulated type B strains of Haemophilus influenzae—a type carried in the nasopharynx of some 1-3% of the general population. The disease occurs as sporadic cases, with some seasonal concentration but no true epidemics and seldom with demonstrable case-to-case spread. A personal study of the families of 17 affected children confirmed the high frequency of carriers of type B strains in the environment of the children, and provided serological evidence that, in most cases at least, the strain had been in the family for some weeks before the child (usually the youngest) became ill. Little information about precipitating factors is available; evidence about the influence of social and economic factors is conflicting. The age incidence was explained in 1933 by demonstration that bactericidal antibodies for H. influenzae type B are commonly to be found in blood from newborn babies or older children or adults, but rarely in blood from children in the usual age range for the disease. Whether this pattern still applies is a matter currently under dispute—