in order to calculate the P_{50} in these patients, before the results can be fully evaluated.

Symposium III

Chromosomes and disease

Leukaemia SYLVIA D. LAWLER (*Department of Clinical Research, Royal Marsden Hospital, London*) By using staining methods which produce characteristic banding patterns, it is now possible to identify precisely the individual chromosomes of the normal human set.

The components of structurally altered chromosomes can also be defined. For example, O'Riordan *et al* (1971) have shown that the Philadelphia chromosome, the deleted chromosome that is specifically associated with classical chronic myeloid leukaemia (CML), is a different member of the G group than the extra chromosome present constitutionally in Down's syndrome (Philadelphia chromosome = no. 22 with a deletion involving the long arm. Down's syndrome = trisomy 21).

Reeves *et al* (1972) have shown in four cases that the anomalous F group chromosome found in a variable proportion of cells in about 20% of cases of polycythaemia vera (PV) is a number 20, with a deletion involving the long arm, an observation which confirms the specificity of the anomaly in relation to PV.

The metacentric 'marker' chromosome of C group size, found not infrequently in the blast transformation stage of CML, has now been identified as an iso-chromosome of the long arm of a number 17 (Lobb *et al*, 1972).

The identification of supernumerary or abnormal chromosomes is also proving useful in a follow-up study that is in progress in patients with acute leukaemia first examined in the untreated state. A chromosomal pattern is becoming apparent in acute lymphoblastic leukaemia (ALL). At diagnosis the cases can be divided into three classes according to the karyotypes of the bone marrow cells: (1) predominantly hyperdiploid cells, (2) occasionally hyperdiploid or pseudoploid and normal cells, (3) not hyperdiploid.

During the course of treatment in ALL the bone marrow does not convert immediately to cytogenetic normality. If serial samples of bone marrow are examined cases frequently are seen to go through a phase of having the occasional hyperdiploid cell before becoming normal. Such hyperdiploid cells usually do not have the same karyotype as the original abnormal population. It remains to be seen whether relapse is associated with the reappearance of a population of cells that is chromosomally related to those found at diagnosis.

References

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Cancer of the Cervix A. I. SPRIGGS (*Department of Pathology, Radcliffe Infirmary, Oxford*) As a result of cervical smears, a whole range of conditions is available for study from normal through various presumptive precancerous stages up to fully developed invasive carcinoma of the cervix.

Established carcinoma shows chromosomal abnormalities comparable to those of other carcinomas; there is a stemline with a karyotype differing from the normal in ways which are unique to the particular tumour, with gains and losses of chromosomes and often recognizable markers. Counts near to diploid are the commonest, and counts above 92 are fairly rare. Most of the evidence favours the idea that the whole tumour originates from a single altered cell.

New karyotypically abnormal clones have also been found in microcarcinoma (microinvasive carcinoma).

Carcinoma *in situ* and severe dysplasia present variations which are less easy to describe. All observers have found aneuploidy, but there are conflicting reports about the presence or absence of associated diploid cells. *Cultures* of epithelium have produced diploid cells only. The commonest regions in chromosome count distributions have been around 46 and around 80. Sometimes the counts are consistent enough to suggest a clone. Similarity in the karyotypes from two separate areas, sometimes with the additional evidence of markers, confirm that clonal proliferation has occurred. In other cases there is a wide spread of counts with no obvious stemline.

The mildest dysplasias have been shown in a few cases to have counts near to 46, but even here abnormal karyotypes have been described. Very few analyses have been made from cells from normal cervices, and these have been found normal.

Taken together, the picture presented is of a tissue in which aneuploid cell lines compete for supremacy, and in which a dominant clone finally selects itself. At what stage spontaneous regression or rejection of the lesion is still possible remains to be found out.

Antenatal Diagnosis P. E. POLANI (*Paediatric Research Unit, Guy's Hospital, London*) Prenatal diagnosis follows a number of different approaches directed at preventing or detecting fetal abnormality and, when

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 reinfection 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 'opportunist' phycomycetes (species of *Rhizopus*, *Absidia* and *Mucor*) and *Nocardia asteroides*. Others (for instance, species of *Aspergillus* and of *Candida*, the histoplasmas and *Coccidioides 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, streptomycosis, madurellosis, aspergillosis, penicilliosis, phycomycosis, 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 meningocerebral 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 sardoidosis; and a case of anomalous haematogenous infestation by larvae of *Strongyloides stercoralis* associated with septicaemic candidosis as complications of lymphatic laukaemia under treatment with cytotoxic drugs and corticosteroids.

Meningococcal Infection: Serotypes and Suplhonamide 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