a reproducible way if the diagnostic criteria listed are strictly adhered to. While the WHO classification of lung tumours, like any other, is concerned with names, it is important to remember that the name given to a tumour is of less importance than its safe recognition and the understanding of the biological implications of that name.

'Epidermoid carcinomas' are defined as 'tumours with keratinization or intercellular bridges'. This is a precise, but narrow delimitation, and some authorities would like to see tumours with a more or less 'transitional cell epithelium' included. 'Spindle-cell carcinomas' and 'carcinosarcomas' pose similar problems.

The term 'small cell anaplastic carcinoma' is used to include a number of subtypes (fusiform cell type, polygonal cell type, lymphocyte-like type or oat-cell type, and others) whereas some pathologists are inclined to regard the first two of these as undifferentiated epidermoid carcinomas.

The group of 'large cell carcinomas', defined as 'tumours composed of large cells without evidence of epidermization or formation of gland-like structures', embraces a number of different entities, many of which have been referred to as 'carcinoma solidum' in the older literature. Many of these tumours are not without a certain differentiation, manifested by the production of mucin-like substances, and special staining procedures are essential for their identification.

The term 'combined epidermoid and adenocarcinoma' has been applied to the 'comparatively rare tumour which should in some parts have definite evidence of epidermization as well as features that would qualify other parts unequivocally as adenocarcinomas'. Some pathologists designate these tumours as 'muco-epidermoid carcinomas', but in the WHO classification this term has been reserved for tumours where origin from bronchial glands is definite, or where goblet cells can be distinguished. The term 'combined' has been reserved for tumours containing two different kinds of differentiation from one and the same cell, while the term 'mixed' has been used in connexion with tumours with differentiation showing resemblance to epithelium as well as to connective tissue.

Changes in Sulphonamide and Antibiotic Resistance of *E. coli* in Urinary Infections outside Hospital during a 12-Year Period

W. A. GILLESPIE AND K. B. LINTON (*University of Bristol*)

The drug resistance was recorded of lactose-fermenting coliform bacilli (nearly all of which were *E. coli*) from urinary infections in pregnant women during the past 12 years. Sulphonamide resistance increased slightly, from an average of 6% of all strains during the years 1959-64 to an average of 12% during 1966-70. Ampicillin resistance rose from 2% in 1964 to 11% in 1970. Resistance to nitrofurantoin and nalidixic acid remained below 5% and 7% respectively probably because these drugs were rarely used. No trimethoprim-resistant strains were found since testing began in 1969.

The resistance patterns in *E. coli* urinary infections in non-pregnant women in 1969 and 1970 were similar to those in pregnant women during the same years. The resistance of the predominant coliform bacilli of healthy adults' faeces in the same population was also similar. Approximately 60% of the resistant strains from faeces and urine were able to transfer their resistance to a sensitive *E. coli* recipient.

Sulphonamides will probably retain their value for primary treatment of acute urinary infection outside hospital for some years to come.

Influence of Employment with Livestock on Antibiotic-resistant *E. coli* in the Faeces of Healthy People

K. B. LINTON, M. H. RICHMOND, AND W. A. GILLESPIE (*University of Bristol*)

Faeces of healthy adults and of children under the age of 5, none of whom were attending hospital nor receiving antibiotics, were examined for the presence of antibiotic-resistant coliform bacilli.

A higher proportion of children (73%) than of adults (49%) carried resistant strains and this difference was observed in both the rural and urban groups.

Rural members of both age groups more often carried resistant organisms than urban members. Among rural adults, the incidence of drug-resistant strains was 63% in those whose occupation involved close contact with farm animals, compared with 29% in those with other occupations. The survey took place before the implementation of the Swann Report could have influenced the use of antibiotics in animal foodstuffs.

Transmissible R-factors were demonstrated in 61% of the resistant strains.

The incidence of transmissible resistance was similar among adults and children in town and country.

Haematological Findings and Fits during the Prevention and Treatment of Folate Deficiency in Long-term Anticonvulsant Therapy

R. D. EASTHAM AND J. JANCAR (*Frenchay Hospital, Bristol*)

Folate deficiency has been frequently reported in epileptic patients treated with anticonvulsants and in psychiatric patients, and folate supplements have been reported as causing toxic symptoms in normal subjects, and as increasing fit frequency, whilst improving mental state in epileptic patients.

Yeast supplements, a natural source of folic acid, were given to both epileptic and non-epileptic, non-anaemic, mentally retarded patients. After three months of treatment with yeast, corresponding to the average normal red cell life, red cell and serum folate estimations were repeated in each clinical group. In the epileptic patients, on long-term treatment with anticonvulsants, both serum and red cell folate concentrations increased significantly, whereas in non-epileptics only the red cell folate concentration increased significantly in female patients. There was only a poor direct correlation between serum and red cell folate concentrations. The mean red cell volume was directly related to the daily dose of phenobarbitone, but red cell and serum folate concentrations were only poorly inversely correlated with phenobarbitone dosage, suggesting a different mechanism for the macrocytosis caused by phenobarbitone.

The number of fits recorded in epileptic patients during yeast therapy fell below the previous control period, and such yeast supplements have been effective in repairing folate deficiency without causing clinical trouble at very low financial cost, eliminating the need for costly and tedious laboratory estimations of serum and red cell folate concentrations in these patients. (The cost of yeast supplements per patient per three months of treatment is approximately 10p.)

Foetoprotein Estimation in the Diagnosis of Hepatoma

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Alpha₁ foetoprotein (α_1 FP) is a normal

constituent of foetal serum, but it virtually disappears from the circulation very soon after birth and is not detectable in normal adults. The only conditions where α_1 FP has been found in the sera of adult humans in significant quantities are primary hepatocellular cancer of the liver and teratocarcinomas. It has been shown that the demonstration of α_1 FP in the serum of adult patients can be regarded as a reliable indicator of the presence of primary carcinoma of the liver. Synthesis of α_1 FP by liver cancer cells is believed to result from derepression of genes which had been, in turn, activated and then repressed during ontogenesis. Techniques most commonly used for the detection of α_1 FP are bidimensional immunodiffusion (Ouchterlony), counter-current electrophoresis, followed by complement-fixation tests, haemagglutinin inhibition and more recently radioimmunoassay and latex agglutination. The relative merits of these techniques, as well as the problems of quantitation, standards, and availability of suitable antisera, will be discussed. The importance of good quality specific high titre antisera is emphasized. The interpretation of results and main sources of error will be considered, including the occurrence of α_1 FP in conditions other than hepatoma. Statistical and epidemiological data available to date regarding results obtained in various centres will be presented, as well as our own findings.

Antibody Protein Levels in Maternal Sera in Rh Haemolytic Disease

I. D. FRASER AND G. H. TOVEY

(Regional Blood Transfusion Centre, Bristol)

An automated haemagglutination technique was used to estimate antibody protein levels, in the maternal sera, in 600 pregnancies complicated by Rh incompatibility. Good correlation was found between the maternal antibody protein level and the subsequent severity of haemolytic disease in the baby. The method was found to be very reliable for selecting cases for amniocentesis. In 325 pregnancies (group I) where the mother developed Rh antibodies for the first time, amniocentesis was indicated if the antibody protein value reached or exceeded 1.5 μ g/ml before the end of 34 weeks' gestation. In 275 pregnancies (group II) where the mother had had a previously affected baby, amniocentesis was indicated if the antibody protein level reached 1.0

μ g/ml or more before the end of 34 weeks' gestation. If the automated technique was employed instead of manual antibody titrations, the proportions of mothers requiring amniocentesis in group I fell from 45% to 35% and the proportion in group II fell from 56% to 50%.

The maternal serum of two of the 600 mothers contained a bromelain inhibitor; pre enzyme treatment of the test cells in the automated procedure overcame this problem.

A Mortality Study of Sickle Cell Anaemia in Central Africa 1968-1971

G. P. T. BARCLAY (Kitwe, Zambia)

In our community of Zambian mine workers and their families, the total population of some 60,000 has a sickle cell carrier rate of 18%. In three years, 246 cases of sickle cell anaemia have been found and a closely supervised screening programme has revealed 49 of them to have died in childhood. In only seven of these cases was the diagnosis of sickle cell anaemia offered clinically. Most were discovered by typing everyone born in and admitted to the community hospital, some direct to the necropsy room.

The age range of these fatalities is of particular relevance clinically and offers a clue to the reason for the paucity of adult homozygote sicklers in this country.

The now traditional classification of crises into occlusive, haemolytic, and aplastic is meaningless in the form of the illness seen in Zambia. The clinical course of many of these fatal cases of sickle cell anaemia has been dramatic. Death occurred most commonly after a relatively short period of oligaemic shock and central cardiac failure following a rapid worsening of the anaemia, the result of acute hepatosplenic sequestration, in turn, associated with the metabolic acidosis of an infection. The key to the successful management of sickle cell anaemia is the prevention of infection.

Necropsies were performed on 21 of this series. The results further elucidate the nature of the sequestration syndrome and indicate the urgent necessity for a rational treatment regime which is simple and is proving increasingly successful.

The Spread of Cholera to and within Nigeria 1970-71

A. M. M. WILSON (University of Edinburgh)

The seventh pandemic of cholera started

from an endemic focus in the East Indies in 1961. Its westward spread came to halt in the Middle East in 1966. In August 1970, the disease was reported from southern Russia, previously uninfected parts of the Middle East, Libya, and Guinea. From Guinea it spread east along the coast to Nigeria in December and Cameroun in February and inland more slowly to reach Mali in November and Chad in May. No northward spread occurred along the coast, but eventually inland spread from Mali to Mauritania was reported in June, and subsequently to Morocco, Spain, Senegal and Algeria.

Within Nigeria the spread was general, all but one of the 12 states reported the disease within three months. Explosive outbreaks were few and small, except for that in Ibadan at the end of Ramadan.

Total figures are unknown. Most cases were in adults. The case mortality in Lagos fell from over 50% in the first week to under 5% two and a half months later.

The passage of *V. cholerae* in the stool of a demographically randomized sample of the population of the Lagos area was carried out between February and April. No clinical cholera or contact with a case was found but five persons per thousand were asymptomatic excretors. They lived mainly in the areas where the concentration of population had outstripped the public services.

The spread and retreat of cholera are unpredictable; some of the factors will be discussed.

The Effects of Centralization in Haematology

A. A. SHARP (Radcliffe Infirmary, Oxford)

Expansion of laboratory haematology has necessitated the introduction of mechanical and automated equipment to contain the ever increasing workload. This revolution has shown the value of these machines both in terms of speed of working, numbers of tests handled, and accuracy. Further expansion is possible today and greater use of automated equipment is inevitable.

In terms of economics and availability of staff, centralization of this equipment in large, centralized laboratory areas appears inevitable. Considering the capital investment, machine potential, and the need for duplication of certain equipment, it would appear that the central laboratory should serve a population of 500,000 and receive between 500 and 1,000 tests per