

13. It is to be recognized that the majority of young doctors are already married by the time of qualification or marry shortly after. Even if they postpone having children, a measure of geographical stability is important if their wives are to get suitable employment (many are nurses, teachers, etc., for whom casual work is not really suitable, and who are needed in their own professions). Arrangements should so be made that wherever possible consecutive appointments in the same area can be offered. It is realized that there would be organizational difficulties and that there could not always be absolute guarantees, but it should be the aim of Regional Hospital Boards to provide plentiful opportunities for training in junior employment in which the movements of families are minimal.

Appendix to Part A. Aspects of General Practice Draft Syllabus

Many of the following topics could be brought into the M.B., B.S. clinical course but would, of course, need to be dealt with in much greater detail in any systematic vocational training for entry into general practice.

(a) The place of the general practice in systems of medical care and social welfare as a whole, not only in the U.K. but in other countries. The function and role of the State, the hospitals, insurance schemes, public health and welfare services, and general practitioners and their auxiliaries, in any pattern of medical care.

(b) Notions of illness and disease as held by individuals in different social settings. Diverse concepts of the role of the doctor, parson, chemist, and other sources of therapy and advice. "Normal" practice in self-diagnosis and self-medication. Acceptance and non-acceptance of the doctor's medicaments and instructions.

(c) Different sorts of populations; different organizations of general practice; different sorts of doctor. Different patterns of prescribing; different standards of equipment and facilities. Efficient and inefficient general practice.

(d) The concept of a health team based on general practice that includes nurses, midwives, social workers, mental health officers, and others. The medical secretary and other ancillaries. Nature of liaison with other community services. How social agencies affect the course of disease or moderate disability. The social problems of the elderly sick and infirm, and the incapacitated or chronic sick of all ages. Social emergencies and the principles of management in so far as they concern the general practitioner.

(e) The ethical and medico-legal aspects of practice. The relationship of practitioners with their colleagues in hospital, with the press, police, coroners, and lawyers. Medico-legal aspects of

accidents, sudden death, poisoning, suicide, intra-family strife, and violence. The responsibility of the doctor for his patient vis-à-vis his responsibility to society.

(f) The clinical material of general practice. The common diseases and the relative infrequency of rarer diseases. Major, minor, social, and undiagnosed diseases. Neurotic and psychomatic distress. The nature, volume, and distribution of the general practitioner's clinical work. The importance of the natural history of disease; different management in different phases.

(g) The principles applicable to the management of:

(i) Minor ailments of all types, including problems of minor surgery.

(ii) Major disease in general practice.

(iii) Terminal illness in the home.

(iv) The chronic sick and handicapped of all ages.

(v) Medical, surgical, and obstetrical emergencies.

(vi) Acute psychiatric emergency occurring in the family or at work.

(vii) Obstetrics: domiciliary or in general practitioners' units.

(h) The prevention of illness. The epidemiology of the common infectious illness and the roles of the general practitioner in restricting its spread. Immunization of the family. Health and education, health promotion and maintenance. The value and limitations of routine medical examination; different types of medical surveillance.

(i) The techniques of diagnosis as applied to the field of general practice with special reference to early and presymptomatic diagnosis. The special problems of screening tests and the discriminating use of the hospital pathological and radiological facilities.

(j) The way people actually live. Some in families, others in isolation of varying degree. The implications of differing material resources and differing capacity to make good use of such resources as do exist. The influence of these factors on the prevention, management, and course of disease.

(k) The general practitioner's role as the first and last person to whom the patient turns. The implication of the "front line" in terms of diagnosis and of personal availability. Equally the implication of this in terms of being an intermediary and "explaining" the patient's illness to him and of "translating" the hospital's treatment and advice into terms the patient can understand. The giving of prognosis to patient and family. The general practitioner's unique role, in our society, as a bridge of communication between social class subcultures. The importance of receptivity and of the uncritical non-directive role; the general practitioner's long-term relationship with families under his care.

(l) The special opportunities for research in general practice; its importance. Methods and techniques. Clinical records. Practice constituent records. Examples of general practice research. Contact with scientific and professional institutions. Continuing education, and learned contribution in general practice.

Work of Medical Research Council

The Report of the Medical Research Council for 1963-1965 (Cmd. 2787, H.M.S.O., 1965, price 20s. net) contains a review of subjects of current interest in the medical and biological sciences which have been under study during this period. The following is a short summary of some of the topics discussed.

Computers in Medicine

Although computers have become established as valuable research tools in biology, they are little used in medicine except in the processing of statistics. There are, however, promising opportunities related to non-numerical problems, particularly in the field of automatic analysis of photomicrographs. For this kind of work it is necessary to have an instrument that will describe a picture in terms of its constituent points—that is, "digitize" it—and a set of rules that will enable the computer to analyse the digitized picture. Instruments are now available

which will digitize film negatives by examining approximately 350,000 points on a film in a fifth of a second, code each on the basis of its light intensity in the range 1 to 7, and feed the information into a computer.

When automatic microscopy becomes available as a practical procedure, screening tests based on exfoliative cytology and on chromosomal abnormalities could be undertaken frequently and on a national scale.

Research on the Common Cold

Progress of work on common cold viruses (rhinoviruses) has been accelerated by the

discovery of a suitable culture medium in fibroblast cells from human embryo lung. Ultrafiltration and ultracentrifugation have shown that the particles are closely similar in size and density to those of poliovirus. The viruses have been shown to contain ribonucleic acid (R.N.A.), and in at least one rhinovirus the R.N.A. has been shown to be infective. In preliminary experiments on the possibility of protection, rhinovirus adapted to growth in tissue culture, and therefore likely to be attenuated in virulence, has been shown to produce a protective antibody response following intramuscular injection. There was, however, no protection

against infection by a serologically distinct virus. The Council is collaborating with three British pharmaceutical firms in research on methods of producing purified and concentrated vaccine preparations containing several strains of rhinovirus, which will be examined for their protective effect.

Experimental Carcinogenesis

The induction of cancer in experimental animals remains the central method of attacking the cancer problem. Thirty years ago it seemed that the main chemical carcinogens were the polycyclic hydrocarbons. A wide range of other chemical types, such as the carcinogenic amines and the nitroso compounds, is now known to be capable of inducing malignant changes.

The features in the chemical constitution of phenanthrene derivatives that were associated with carcinogenic potential had been known for many years; and it had been postulated that there was a reaction between the hydrocarbons and the nucleic acids of the cell nucleus. Recently attention has been directed to the possibility that hydrocarbon molecules become inserted between adjoining base pairs of nucleotides in the deoxyribonucleic acid (D.N.A.) of the chromosomes, with the result that the genetic "instructions" encoded in the D.N.A. are changed and malignant transformation is initiated. There is as yet no experimental evidence to support this hypothesis in the case of hydrocarbon carcinogens; but recent work with alkylating agents has shown that bisguanyl compounds are formed by the alkylation of D.N.A., and it seems virtually certain that the cross-linking process involves the twin strands of the D.N.A. helix, thus interfering with cell division. The oncogenic viruses, such as the Rous and Bittner viruses, and more recently the viral agents identified by Negroni in human leukaemia, probably act by transcribing "wrong" information on to the messenger R.N.A. From these different approaches investigators have reached the same conclusion—that the key event in the carcinogenic process is biochemical rearrangement of parts of the gene complex leading to mutation. Biological and other comparisons have been made for too long between the cancer cell and the corresponding normal adult cell. This comparison is misleading, and should rather be between the cancer cell and the embryonic cell, or perhaps the trophoblast.

Biological Standards

The Council has always been associated with the introduction of biological standards, and Sir Henry Dale, when Head of the Department of Pharmacology and Biochemistry of the Council's National Institute for Medical Research, was instrumental in obtaining international recognition of the standards. There has been a rapid growth in the numbers of biological standards needed for the ever-increasing numbers of hormones, antibiotics, and immunological products whose activity cannot be determined by physical or chemical means. The Division of Biological Standards at the National Institute for Medical Research is engaged at the present time in attempting to create

standards for such substances as rheumatoid factor, erythropoietin, and plasminogen.

Although from time to time a biological standard is rendered obsolete by the discovery of processes for the manufacture of the pure substance, it seems likely that the responsibility that the Council has assumed for the establishment, maintenance, and distribution of biological standards is likely to increase.

Growth and Development of Children in the Tropics

The Council has four research units in the tropics, with broad rather than specialized functions. There has been increasing interest recently in the study of growth and development of children in their normal environment in an attempt to obtain better understanding of the origins of disease and malnutrition. Reports from all parts of the tropical world agree that even where poverty and disease are widespread, most babies grow well during the first few months of life—no doubt as a result of the almost universal practice of breast-feeding. The rates of growth may even exceed the rates found in Europe and the U.S.A. Fluorescent antibody studies by McGregor and his co-workers in the Gambia have demonstrated that a high level of passive immunity to malaria is transmitted by the mother, and protection against many other common diseases is thought to be provided in this way. From about six months of age the infants lose their early precocity and by the age of 2 are much smaller and lighter than their European counterparts.

An intensive investigation has been carried out in Keneba, involving co-operation between the Council's laboratories in the Gambia and its Obstetric Medicine Research Unit in Aberdeen. It has been shown that after the first few months of life growth depends almost entirely on the season. During the rains growth almost ceased, while during the dry season gains in weight were considerably in excess of those for British children of the same age. The dominant factor responsible for this fluctuation appears to be the prevalence of recurrent episodes of infectious disease during the rains. Mass prophylaxis of disease during the dangerous period of infancy may merely postpone the period to a later age. Further studies are being made.

Human Efficiency in Unpleasant Conditions

Although it would be tempting to believe that uncomfortable work conditions reduce efficiency, there has been little experimental work in this field. Heat, noise, and deprivation of sleep produce some deterioration in efficiency, but the critical levels are surprisingly high. Work at the Council's Applied Psychology Research Unit has shown the effect of sleeplessness to be brief periods of inaction in the course of continuous work. A very noisy environment, on the other hand, results in errors of commission rather than omission. Strikingly, the effects of noise and sleeplessness cancel each other out, so that there is less difference between the sleepless and the normal man when both are working in conditions of loud noise than there is in

ordinary conditions. The normal working state seems to depend upon the integrity of nerve pathways carrying non-specific information from the sense organs. A state of "arousal" or responsiveness of the nervous system is maintained by a steady flow along these pathways. This flow drops to a low level during sleep. Too high or too low level produces the effects described on working efficiency.

Accidents

Between the ages of 1 and 40 accidents are the commonest single cause of death. Environmental factors in the causation of accidents have been studied at the Department of Scientific and Industrial Research. When investigating road accidents, it was found that 76° F. is the temperature at which driving is performed best. Good street-lighting has been shown to reduce road accidents by 30%. The relation of road environment to accidents has been studied by "before and after" techniques. If there are adequate records of accident rates before and after road modifications valuable information is obtained for the assessment of the benefits likely to accrue from similar changes to other roads.

Diurnal Rhythm in Man

The Human Physiology Division of the National Institute of Medical Research has been investigating the fluctuations of physiological function that occur in sleep and wakefulness. Nocturnal sleep is a universally recognized feature of man's life, and under normal conditions the daily variations in heart rate, body temperatures, blood-pressure, and urinary excretion are synchronized so that they all show high levels in daylight and are at their lowest in the hours of darkness.

If a change is made in the time at which sleep is taken, some physiological trends immediately fall into phase with activity, but others remain in the original pattern for some time. Thus it would appear that there are in man intrinsic physiological daily rhythms which are maintained independently of his pattern of activity.

The existence of intrinsic diurnal physiological patterns in lower animals has been demonstrated on many occasions. The periodicity of the rhythms is approximately but not exactly 24 hours—and hence is called "circadian," from *circum diem*—but these rhythms can be made to take on a periodicity of exactly 24 hours if short periods of light are introduced in an otherwise dark environment every 24 hours. The light acts as a *Zeitgeber* or time clue. Study of human subjects under conditions of isolation suggest that the intrinsic rhythms in man are circadian and that the normal periodicity is produced by the action of a *Zeitgeber* in the natural environment. In men who spend long periods in the high latitudes of the Arctic, where the normal daily alternation of light and darkness is absent, daily rhythms of urinary excretion are less marked or absent. Support for the hypothesis that the regular alternation of light and darkness plays the major part in the initiation and maintenance of daily physiological rhythms is provided by the disorganization of these rhythms that is

found in people who become suddenly blind. Subjects who live in isolated communities in continuous daylight on a routine of 21-, 22-, and 27-hour "days" show rapid adaptation of their body temperature rhythm to the new time routine, but their urinary rhythms adapt slowly if at all. When the activity pattern is reversed in relation to the solar time pattern and subjects are awake during the true night-time and are sleeping during the

day, production of urine is low during the period of activity. Although man adapts slowly to an abnormal time routine, reversion to normal is almost immediate when a normal pattern of activity is resumed.

The association of the natural physiological rhythms with the normal 24-hour day clearly has a bearing on abnormal work schedules. Daily patterns in levels of efficiency and performance that correspond very

closely to the physiological rhythms have been demonstrated. Studies of performance in travellers by jet flight show that a minimum of three to five days is required for a tolerable adaptation to a new time scale. If members of civilized communities are to be asked to work efficiently at unusual times, as in factory shift-working, then alteration in the pattern of activity should be made as infrequent as possible.

Early Stages of Chronic Bronchitis

[FROM A SPECIAL CORRESPONDENT]

A one-day symposium on the early stages of chronic bronchitis was held by the College of General Practitioners at the Postgraduate Medical School of London on 30 September. The chairman was Dr. H. N. LEVITT and the meeting was sponsored by Beecham Research Laboratories. It was attended by a number of doctors from the London area.

The programme began with a film "Chronic Bronchitis—a Team Affair," which was introduced by Mr. G. J. WILKINS, chairman of Beecham Research Laboratories. This film stressed the importance of morbid anatomy and bacteriology both in the management of patients with chronic bronchitis and in research. The film opened with a necropsy attended by those who cared for the patient in life, and digressed into various aspects of the pathology, bacteriology, medicine, and physiotherapy. Pathological changes in the bronchi and lungs were illustrated and good clinical examples of the emphysematous "pink puffer" and the bronchitic "blue bloater" were shown. The commentary stressed the importance of looking at the sputum for purulence and described the part played by *Haemophilus influenzae*.

Unanswered Questions

Professor J. G. SCADDING spoke on the many unanswered questions about chronic bronchitis. He said that the diagnosis of early bronchitis, defined in terms of hypersecretion of mucus, was easy, and only a matter of listening to what the patient said. It was less easy, however, to quantitate the symptoms, and we did not know yet how closely they correlated with the morbid anatomical findings. The role of air pollution and cigarette-smoking was well established, but we were not sure of their relative importance and how far they were synergistic. Other questions concerned the possible part played by heredity and what happened to chronic bronchitics when they were removed to a more favourable environment. Was the rate of physiological deterioration really due to recurrent bacterial infections? What was the exact role of viruses in bronchitis? In the present state of our knowledge the most important thing the practitioner could do in the field of prevention was to attack the causes he knew to be important—by trying to stop patients from smoking cigarettes and devising ways of reducing air pollution. He mentioned incidentally that the clinician should not be afraid of diagnosing emphysema

in patients with increasing breathlessness, a deep chest, low diaphragm, and long thin heart in the chest film, and almost no breath sounds on auscultation. Many of them were not bronchitics.

Dr. W. W. HOLLAND described the natural history of chronic bronchitis. He contrasted the high mortality rates in industrial areas of north-west England with the lower rates in agricultural areas of the south. Provisional results in a new study showed that the peak expiratory flow rate (Wright meter) was significantly lower in children living in industrial areas than in rural areas. Admissions to hospital were well known to rise after episodes of high atmospheric pollution and falls in temperature, but there was no evidence that humidity, rainfall, or hours of sunshine had any effect. Heavy smoking was, however, a prevalent factor in all areas and very few non-smokers produced more than 2 ml. of sputum a day. Of all the factors at work in chronic bronchitis, the most important was smoking.

Pathology of Early Changes

Dr. B. E. HEARD said that although the pathologist was more familiar with the late results of chronic bronchitis as seen in the post-mortem room, something was known of the early changes from surgical material and animal research. The normal airways were protected by a thin layer of mucus; this was propelled by cilia upwards to the throat at a rate of about 1 cm. a minute and swallowed asymptotically. Inhaled cigarette smoke and other irritants caused more protective mucus to be produced by the goblet cells, and in chronic bronchitis the goblet cells were increased in number and the bronchial glands enlarged. If the concentration was high enough to penetrate the mucus and kill the ciliated cells, the overlying mucus sheet came to a halt in those areas and the mucosa became even more susceptible to damage. Squamous metaplasia was common, and atypical cellular changes could lead on to carcinoma. Episodes of inflammation were encouraged by the mucosal changes and inflicted more damage, including emphysema. There was evidence that mucous changes in the epithelium and glands were reversible, so that attempts to treat the early bronchitic by stopping him from smoking and reducing his exposure to air pollutants were worth while. The onset of permanent structural damage to

the lungs with resulting disability could be delayed or prevented and his life prolonged.

Dr. P. A. EMERSON said that an increase in the residual volume was one of the earliest physiological findings in chronic bronchitis, and Dr. G. GOMEZ showed how the general practitioner could easily measure the peak expiratory flow rate with the Wright meter or, if he wanted a graph and more information, the Vitalograph. Precautions should be taken to avoid leaks at the mouth, as well as the restriction of chest movements by excessive winter clothing. It was also necessary to encourage the patients to use their full effort. He had had little success with the De Bono whistle. The other tests were of great value and a useful guide to treatment. Dr. W. E. H. FIELD described clinicopathological correlations in smokers. Male smokers had significantly enlarged bronchial glands, and the effects of cigarettes were greater than those of pipes. She had been unable, so far, to demonstrate similar findings in women smokers.

Structural Damage to Bronchial Tree

Dr. I. M. GREGG thought that the cardinal feature of chronic bronchitis was not hypersecretion of mucus but structural damage of the bronchial tree, which was frequently associated with destructive emphysema. A productive cough was common in his practice; if he included throat-clearers, 42% of his practice was affected. He recommended measuring the peak expiratory flow (Wright meter) and described the normal gradual fall in values through the years. Smokers with throat-clearing and sputum production had lower readings, especially over the age of 40 years. Ex-smokers mostly lost their coughs and their readings were often satisfactory, but some showed evidence of permanent damage. Readings varied with patients' sizes, but he regarded a value of less than 450 litres/min. abnormal for any size.

Dr. D. H. TRAPNELL described bronchograms in chronic bronchitis. Uncomplicated chronic bronchitis was usually associated with a normal chest film. Bronchography was undertaken only in certain selected cases. It revealed diverticuli of the bronchi and loss of parallelism of the walls; also pinching, pooling, and blocks. The severity of the bronchial changes was found to correlate with the peak expiratory flow readings.

Dr. J. R. MAY stressed the importance and persistence of *H. influenzae* in chronic bron-