Changing patterns in diseases

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Disease is the interaction between a noxious stimulus or stimuli and a human being. Over the centuries we have learnt much about noxious stimuli, but our knowledge has not advanced much about the second factor, the human being. I shall consider the changes that have occurred during the last 50 years, since I started medicine in 1925.

The pattern of change is rather like a Bach fugue, that is, it consists of a central theme with numerous subsidiary themes around it. It has been said that Bach fugues do not follow any laws. Of course not, they themselves are the laws of music. It might appear at first sight that the best way of presenting the subject would be to offer the central theme first and then delineate the subsidiary themes. I propose, however, to do the opposite, namely, to describe the important subsidiary themes and then try to derive from them the central theme.

Subsidiary themes

The changes that have occurred during the last 50 years can be classified into: prevention, diagnosis, manifestations, management, and routine examination of normal people.

Prevention is the topic in which the greatest advances have been made, causing two changes in the pattern of disease. One is that many diseases which were common in my younger days are rarely or never seen now. The glaring examples are diphtheria, tuberculosis, smallpox, and beriberi. The other is in their presentation.

Pulmonary tuberculosis

Pulmonary tuberculosis used to be one of the commonest diseases and was often fatal. It was the dreaded disease of the eighteenth and nineteenth centuries and formed the subject of many authors such as the Brontë sisters and Mrs Henry Wood, who have given excellent descriptions of the history of the disease. The early symptoms were anorexia, loss of weight, lassitude, and slight fever, a difference of well over one degree F between the temperatures at 0600 and 1800 hours. The later manifestations were obvious fever, pleurisy, and spontaneous pneumothorax. In the 1930s every case of spontaneous pneumothorax would almost always be correctly diagnosed as pulmonary tuberculosis and was often complicated by pyopneumothorax and haemothorax. In many cases of the latter the blood loss could be so great as to need blood transfusion. Pyopneumothorax was treated with repeated aspiration and occasionally by surgical resection of the ribs and emptying of the pleural cavity. Most cases of spontaneous pneumothorax are now benign and due to the bursting of an emphysematous bulla. Today the disease is prevented by BCG vaccination in infancy, education of the people, better nourishment, and treatment mainly by antibiotics and surgery. When an expectant mother was on artificial pneumothorax the refills had to be made smaller and smaller and a big refill given immediately after delivery in case the lung expanded and caused severe relapse.

Malaria

Malaria was so common as to fill half the medical wards. It still occurs in Singapore, though rarely. Because of its rarity it is now easily missed. The history of the patient's stay during the fortnight preceding the onset of the illness is important, e.g. Johore and the surrounding islands are a common source. The disease presented generally with high fever, rigors, and sweats, but the manifestations are so variegated that it used to be said that malaria (and syphilis) could mimic any disease in the world. Expectant mothers with very few or no parasites in the peripheral blood would have the blood flooded with parasites in malignant tertian malaria on delivery and would often die unless the nursing staff and doctor were alert. I used to start them on intravenous drip and give ten grains of quinine hydrochloride while the blood films were repeated.

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Thus many lives were saved and this, as in the case of tuberculosis, emphasises the importance of co-operation between the physician and gynaecologist.

Beriberi

Beriberi is practically never seen nowadays except in chronic alcoholics who do not take an adequate balanced diet. Alcohol also interferes with the absorption of vitamin B. Forty years ago it presented in two forms, the wet and the dry. The wet form or cardiac beriberi consisted of right ventricular hypertrophy and failure with high cardiac output and enlarged liver, oedema of the legs, and congestion of the neck veins with marked dyspnoea. The knee jerk and the ankle jerk were absent except in children and the calves were tender. The dry or peripheral neuritic type had marked weakness of the legs, foot drop, a high steppage gait, and an inability to rise from a squatting position owing to the weakness of the muscles of the pelvis. The heart was normal. Mixed forms, however, occurred. The disease was common in the Chinese, but almost never seen in the Tamil labourer. Braddon, who among other things was the prison medical officer in Seremban, discovered this among the prisoners. He crossed over the diet, giving the Chinese (who ordinarily ate polished rice) parboiled rice, and the Tamils (who ordinarily ate parboiled rice) polished rice. Lo and behold! The Tamils got beriberi and the Chinese did not.

Parboiling is the process of boiling the paddy in its husk and then milling it. This made the pericarp which contained all the Vitamin B in rice stick to the grain, whereas if freshly harvested rice is milled immediately or soon after, the pericarp is lost carrying with it all the precious vitamins. Parboiled rice is smelly and brown in colour, unlike fresh milled rice, which is polished white. The Brahmins in South India, however, got over the problem by storing the grain for a year before milling. The period necessary for the pericarp to adhere to the rice grain is in nature one year, but is cut down to one hour by parboiling. All this was done by the people themselves without scientific study or controlled experiments. The treatment and the prevention consisted in the administration of foods rich in vitamin B_1 such as soya beans, peas, *tauhu*, (bean curd), *taugay* (bean sprouts), green peas, and fresh milk. The non-Tamils, especially the Chinese, would not and still do not, take kindly to parboiled rice and milk. When vitamin B_1 was synthesised and became freely available about 1938, the treatment became simple. Vitamin B_1 was given in doses of between 20 and 100 mg intravenously for acute cardiac beriberi. Peripheral neuritis was treated with repeated injections and with vitamin B_1 by mouth. Twenty milligrams given daily is the normal requirement, but much larger doses were and still are being used.

Lobar pneumonia

Lobar pneumonia caused by pneumococci was a very common disease and had a mortality as high as 40 per cent among weakened labourers, though it has no particular respect for the rich. Heathcliffe in *Wuthering Heights* surely died of lobar pneumonia i.e. lobar pneumonia suddenly occurring in otherwise healthy strong adults. The clinical picture was one of a patient getting drenched in rain and 24 hours later developing a chill with rigors, raised temperature up to 40° C (106° F) a hot dry pungent skin (thus distinguishing it from malaria where sweating and often profuse sweating occurs) working of the alae nasi, rapid shallow respiration, with the pulse/respiration ratio altered from the normal one to four to one to two. Herpes labalis was common. Physical examination of the chest revealed dullness, tubular breathing, pleuritic rub and crepitations. Sometimes there was pleuritic pain. Serous membranes were often affected especially the pericardium. Pleural effusion was purulent and gave rise to empyema. Pericardial effusion was again prevalent and the only treatment we could give in these cases was drainage either by aspiration or rib resection or both. There were no antibiotics in those days.

The introduction of sulphonamides made a big difference especially sulphapyridine (M & B 693). This reduced the death rate in pneumonia from 40 to five per cent. The metastic complications arising from lobar pneumonia involving the serious membranes were arthritis, epidymitis, panotitis, meningitis, and peritonitis. Peritonitis, however, occurred sometimes in young girls independently of pneumonia. Symptoms and signs common to all pneumococcal infections were fever, dry pungent skin, herpes labialis, tachypnoea, with altered pulse respiration ratio, and pus formation.

Bronchopneumonia

Bronchopneumonia usually caused by pneumococci was common in the very young and the very old and often in the latter a common cause of death. Bronchopneumonia may be caused by

a variety or a combination of organisms. Before the second World War, there was no effective treatment and the mortality rate was high. The sulphonamide group of drugs had no great effect, but penicillin and the newer antibiotics were undoubtedly curative. A sputum culture may help if it shows up an unusual pathogen and the sensitivity has been determined.

One cause of error is aspiration pneumonia. In any upper respiratory infection, especially the common cold, mucopurulent secretion gets aspirated into the bronchopulmonary segments causing collapse and consolidation with varying degrees of inflammation. If only one segment is involved it is easily diagnosed on the x-ray, which shows a clearly outlined shadow with a slight shift of the trachea towards it and emphysema of the surrounding lung and sometimes an upward movement of the diaphragm. When a number of segments are involved, the physical signs simulate those of bronchopneumonia, in which case antibiotics have to be used, but the prognosis is excellent. To make a correct diagnosis lateral x-ray films are necessary.

A special type of bronchopneumonia is that which follows near-drowning and this had a bad prognosis. Besides it may activate a focus of tuberculosis and cause a flaming tuberculous bronchopneumonia which will need the appropriate anti-tuberculosis measures. Aspiration of the stomach contents may simulate bronchopneumonia and is often fatal because of acid necrosis of the lung.

Syphilis

Syphilis was a common disease 40 years ago and all its manifestations were seen: the primary sore called the chancre with enlargement of the glands draining the area, a maculopapular generalised rash with generalised enlargement of the glands. Both epitrochlear glands were enlarged and this was often used as a diagnostic clinical point because they were rarely involved in other diseases. Later gumma could occur in any of the tissues including the heart and the brain.

Neurosyphilis presented in two main forms—meningovascular disease, which could occur after a varying interval, and tabes dorsalis and dementia paralytica, or general paralysis of the insane, which occurred only after about 15 years from the date of infection. Similarly with vascular syphilis, especially syphilitic aortitis and aortic incompetence. I have seen in the same patient and at the same time a chancre in which I demonstrated the spirochete pallida, a papular rash, and a centrifuged spinal fluid with pleocytosis and marked increase of globulin.

Until the first decade of this century syphilis and all its complications were treated somewhat inefficiently with mercury by mouth, by injection, and by application to the skin of an ointment containing mercury and mercurial baths. One aphorism was as " a few minutes of Venus and a lifetime of Mercury." Erhlich experimented with various substances till eventually the 914th experiment produced a drug called neoarsphenamine or 914, which was injected every week for 40 weeks with monthly intervals to prevent poisoning. The treatment was remarkably effective except where the central nervous system or the vascular system was involved. The former responded to pentavalent arsenicals, especially tryparsamide, and to repeated rigors produced by giving the patients B.T. malaria as an injection of 10 ml of blood from a proven case of B.T. malaria intramuscularly. Care had to be taken that the donor did not suffer from malignant tertian malaria as well. This position was changed with the introduction of penicillin which was effective against all forms of syphilis until recently when penicillin resistant strains began to appear. Today syphilis is a relatively uncommon disease and the management straightforward.

Yaws

Yaws is caused by a spirochete and was quite common in the peninsula of Malaysia, though not so in Singapore. It did not give rise to remote manifestations like syphilis and responded readily to 914.

Diphtheria

Diphtheria was very common 40 years ago and carried a high mortality. The patients would be brought late to hospital with laryngeal obstruction needing emergency tracheotomy and the insertion of a tube to promote free respiration. Antidiphtheria serum was of great value though liable to produce allergic reactions which could be serious or even fatal. Immediate contacts were also given antidiphtheria serum though the reasoning behind this was not quite clear. The advent of antidiphtheria toxin has altered the whole picture and now we rarely see diphtheria in general practice.

Smallpox

Smallpox was not common but epidemics sometimes occurred—they were limited from spreading because we have a largely immune population owing to compulsory vaccination within six months of birth and mass vaccination if it appeared that an epidemic might take place.

Chickenpox is important because of the liability for confusion with smallpox and, more important, vice-versa. The rash appears on the third day of the disease in smallpox and on the first day in chickenpox. There is high fever during the first few days of smallpox whereas in chickenpox fever starts on the fourth or fifth day. The essential difference is in the rash. In smallpox it undergoes a process of slow evolution, macular, papular, vesicular, pustular, whereas in chickenpox it is papular from the start and becomes pustular later. The distribution of the rash is centrifugal in smallpox and centripetal in chickenpox.

Deficiency diseases

Beriberi has already been described.

Pellagra

Pellagra used to be common 50 years ago and was manifested by a rash especially affecting the legs and the neck (rosary round the neck) mental symptoms (mainly depression) and signs of other deficiency diseases. Treatment consisted of a nutritious diet only. Today nicotinic acid 500 mg daily is curative. Some people are allergic to nicotinic acid and so the first dose should be small (50 mg) and subsequent doses gradually raised to obtain the desired effect.

Ariboflavinosis was characterised by perleche (angular stomatitis) ulcers of the medial conjunctiva eczema of the scrotum and evidence of other deficiency diseases. Now it occurs with pellagra and other deficiency diseases only in chronic alcoholics who do not take an adequate nutritious diet. Treatment is by stopping alcohol and giving a balanced and adequately nutritious diet and the administration of riboflavine.

Scurvy

Scurvy was common, especially in children, because of the use of artificial milk and still is in old people living alone who do not buy fresh food, but find it convenient to live on canned food. It was common in the sailing days and even later if they were unable to obtain fresh food. We saw several cases in hospital in the early days of the Japanese occupation in 1942. We dealt with the problem by giving every patient a glass of tapioca leaf and spinach juice. The main manifestations were swollen bleeding gums and haemorrhages anywhere in the body, especially persistent haemorrhage on the anteromedial surface of the tibia. Treatment consisted of giving lemons, oranges, and fresh food. In the later 1930s ascorbic acid was synthesised and became available in the forms of tablets and injections. Ascorbic acid is both preventive and curative.

Rickets

Rickets was thought not to occur in Singapore because we had an abundance of sunlight. Cicely Williams showed, however, that this did not protect our children from getting rickets, since our atmosphere is moisture laden and prevents the ultraviolet light from getting to us. In an article in the *British Journal of Paediatrics* she wrote a paper describing a long series of rickets in children fully supported by laboratory findings. The treatment then was cod liver oil and fresh milk. Now the answer is calciferol and in resistant cases A T 10.

Protein deficiency

Protein deficiency occurred owing to an inadequate intake of protein and in cirrhosis of the liver owing to an inability to synthesise the protein from the aminoacids absorbed. Treatment was unsatisfactory mainly because we did not recognise the cause, but later, when we did, the administration of large doses was curative.

Liver disease

Cirrhosis and primary cancer of the liver were both common, and they were connected diseases because both were due to malnutrition and cancer of the liver patients invariably had cirrhosis of the liver as well. Alcohol played little or no part in the disease, because those affected were those Chinese who did not drink, or Malays who as Muslims were forbidden by religious laws to take alcohol.

The real cause, as we now know thanks to Himsworth and others, was an inadequate intake of proteins.

Main theme

The remarkable point that stands out in the last half century is the astonishing speed that has been developed in every sphere of human activity. Speed is a catalyst and the advance in each century is usually much greater than in the previous one. The focal point of this web is progress and the main factors responsible for medical progress in the first half century are as follows:

Rise in the standard of living

Through the increasing affluence in the country, people can earn much more than before. For instance, an unskilled worker who received ten dollars (S) a month (£2 sterling at the present rate of exchange) now receives $200 per month. Because people earn more they can spend more on food, and this reduces the incidence of deficiency diseases and diminishes the incidence of diseases which flourish in a body with low resistance such as is produced by inadequate foods. The best example, of course, is pulmonary tuberculosis.

The improved economy not only prevents the incidence of organic diseases, but subdues psychoneurosis. The dissatisfied person is more prone to neurosis than the well satisfied one. There is practically no unemployment in Singapore.

Education has made a great difference to the incidence and pattern of disease. Before 1941 there were very few schools compared with now, especially those teaching in the English stream, and few of these were filled because there was no compulsory education and no propaganda to explain to the people the advantages of education. Now there are numerous schools, English stream, Chinese stream, Malay stream, and Indian (Tamil) stream. The English stream is the leader. The various communications media especially the press, radio, and the television, are enthusiastically informing the public of how to keep well physically and mentally. The general economic improvement during the last 20 years is phenomenal. The gross national product indicates the human activity useful to the country, the income per head, the general affluence of the community, and the total budget, the benefit accruing to the Government. The figures speak for themselves:

GNP. PER CAPITA GNP$ AND GOVERNMENT BUDGET—1956, 1960, 1968, 1975

	1950	*1956*	*1960*	*1968*	*1975*
Gross national product at current market prices	NA	S$1,596,000	S$2,193,000	S$4,568,000	S$13,430,000
Gross national product per head at current market prices	NA	S$1,144	S$1,331	S$2,270	S$5,969
Price	NA	S$164 M	S$383 M	S$943 M	S$4,335 M
Government budget					

Source: GNP 1956—National Income of Singapore 1956—Frederick Benham
GNP 1960, 1968, 1975—Statistics Department
Budget Estimate 1950 to 1975/1976

Prevention

Singapore is an island and a city state with an area of about 250 square miles and a population of about two and a half million people, not counting the tourists who number more than a million each year. The water is clean and wholesome, so that surgical operations could, though they are not, be carried out only by thorough washing with soap and scrubbing the hands with running water from the tap. There is practically no risk of infection as asepsis is punctiliously maintained. By proper antimosquito measures such as an adequate drainage system and the prevention of collection of water in houses and elsewhere, mosquito-borne diseases such as malaria, dengue, haemorrhagic fever, and filariasis are prevented. The general cleanliness of the

city prevents the breeding of flies and therefore the occurrence of fly-borne diseases common in the tropics, such as dysentery and other gastrointestinal infections. The credit goes to the City Health Department and the co-operative public.

Treatment

Therapeutic measure have advanced here as elsewhere. The use of the sulphonamide group of drugs and antibiotics has reduced human suffering and death and altered the manifestations of disease. To take two examples: the enteric group of fevers no longer presents the clinical picture described by Osler as they used to 50 years ago. Typhoid is now a somewhat moderate fever not going up above 40°C (104°F). There is no clouding of the mind and no semi-consciousness; rose spots are uncommon, and haemorrhagic perforation practically unknown; the heavily furred tongue with raw and red edges is practically never seen. The mortality of this condition with chloramphenicol treatment is nil. The bacillus has undergone mutation under the repeated onslaught of antibiotics. Again we are seeing a new disease due to mutation under the onslaught of powerful drugs. These changes in the character of disease took place well before the advancement of medicine which has been described.

Immunisation

Fifty years ago no immunisations were available except vaccination against smallpox. Now immunisation is carried out almost routinely for tetanus, diphtheria, whooping cough, poliomyelitis, and when indicated, typhoid, measles, and cholera (we sometimes get cases of El Tor, and we vaccinate with specific El Tor vaccine). If a vaccinated person gets the disease, as sometimes occurs, the disease is modified and much milder.

Examination of normal people

Routine examination of normal people is a new concept in medicine and is practised, of course, in Singapore.

Conclusion

The changes have taken place because the outlook in the world has changed in many fields, including science, finance, politics and society in general. Therefore the medical philosophy and behaviour must be part of the symphony of life; witness the blind girl in André Gido Pastoral Symphony, who, after hearing it for the first time, asks her adopted father who is her mentor whether she is beautiful, because she does not want to be a blot on the beautiful symphony of life.

A BLOOD TEST FOR MULTIPLE SCLEROSIS BASED ON THE ADHERENCE OF LYMPHOCYTES TO MEASLES-INFECTED CELLS

The increased capacity of lymphocytes from patients with multiple sclerosis to adhere to human epithelial cells persistently infected with measles virus has provided an accurate blood test for multiple sclerosis. When lymphocytes from affected patients were mixed with measles-infected human epithelial cells, the lymphocytes formed rosettes around a mean ($\pm$S.E.) of $69 \cdot 2 \pm 1 \cdot 7$ per cent of the measles-infected cells. In contrast, lymphocytes from controls, either healthy or with other neurological and non-neurological diseases, formed rosettes around a mean of only $28 \cdot 2 \pm 2 \cdot 1$ per cent of the measles-infected cells. Of greater importance was the complete absence of overlap between multiple sclerosis and control values, thus indicating the diagnostic potential of the rosetting phenomenon. The severity, duration, and activity of the disease had no effect on the degree of rosette formation.

REFERENCE

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