An Address

ON

CHANGES IN THE CLINICAL ASPECTS
OF DISEASE.*

BY

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CHANGES in the clinical characters of disease are interesting not only to those of us who from the passage of time have watched once familiar maladies alter their features, and become rare, and have seen new ones come on the scene, but to everyone, because different years often show differences in the occurrence or the prominence of certain characters and manifestations of the common epidemic diseases. This is particularly true of what we all, however much we may deplore it in others, are driven sooner or later to call "influenza." In one year it is mainly nasopharyngeal, in others pulmonary, gastro-intestinal, nervous, or, from the presence of a rash, may imitate scarlet fever, or, as in America in 1923, may be regarded as an epidemic of dengue (vide Hamer, 1923). On the other hand, it might be argued that what are called different types of influenza are in reality distinct diseases, as might be suggested by the separation of epidemic or lethargic encephalitis, which at its onset so often simulates influenza. During the war the virulence of influenza underwent a deplorable and dramatic increase in 1918, when there were two waves—the first in the spring with a comparatively low incidence of complications and deaths, and the other in the autumn, which was associated with *Streptococcus haemolyticus* infection and a high percentage of thoracic complications and mortality; this epidemic continued into 1919 and was world-wide. Thus within a short time there was a remarkable change in the character of a familiar disease, showing that this subject may be of immediate practical importance and not merely of historical interest.

Sydenham maintained that acute diseases showed (1) a long periodic evolution with a rise, decline, and fall extending over centuries; (2) seasonal variations with waves measured in months (as in the influenza of 1918) so that their character and reaction to treatment altered in a short time, a method successful in one epidemic becoming useless or even harmful in another; (3) that there was in his rather mysterious "epidemic constitutions" a special influence—telluric, as from the bowels of the earth, or climatic—which becomes dominant and by contaminating the atmosphere and acting on men's bodies disposes them to this or that disease, and impresses some definite character on the clinical manifestations of diseases prevalent at the time to the exclusion of other symptoms, the amplitude of this wave being measured in years. Major Greenwood explains the term "epidemic constitutions" as meaning that secondary infections, such as those familiar in influenza and measles, are just as important from the point of view of morbidity and mortality as the specific causes of disease. Sydenham, of course, had no knowledge of bacteriology, but Sir William Hamer, following in the footsteps of the English Hippocrates, has for years, with attractive eloquence and great ingenuity, argued the epidemiological relationship of diseases associated with different microbic agents—namely, that members of his "catarrhal group of diseases" (influenza, cerebro-spinal fever, acute poliomyelitis, and encephalitis epidemica) are variants of the same morbid process; at one time he ascribed them to the same virus acting under different conditions. Referring in 1924 to these and other acute diseases occurring in "the influenzal group of diseases," Hamer picturesquely wrote: "Surely we may recognize the protean influenza, now merely in mufti, but changing from one civilian garb to another under our eyes, and demonstrating unmistakably that the more it changes the more it is the same thing." In 1922 he argued that the hypothetical filter-passer determines the clinical manifestations which the *Bacillus influenzae* shall produce; and in

1925 he set out his thesis to the effect that in pandemic times the virulence of the influenzal germ was different from its activity in the intervals or trailing prevalences, giving rise in pandemics to a "shock attack" or influenza, and in the intervals apt to activate various secondary or associated micro-organisms—pneumococci, streptococci, meningococci. This is a much less iconoclastic view than that all the diseases in question are due to modifications of the same micro-organism, and narrows the gulf between the extremes of the epidemiological and bacteriological standpoints.

Recorded Changes in the Clinical Characters of Diseases.

There is now no need to insist that a change of type of disease does occur. A number of diseases are known to have changed their clinical characters; thus scarlet fever was very mild a century ago, fifty years ago it was extremely malignant, and now again it is a mild infection, although its prevalence cannot be shown to have diminished (Brownlee). Different types of the strains of the *Streptococcus haemolyticus* of scarlet fever have been described (Griffith), and it appears that these vary in different countries (James) so that clinical differences may thus be explained—for example, the extreme rarity of the disease in India. Though in addition to differences of virulence of the causal organism the resistance and antitoxin content of the individual must be taken into account, it would appear probable that simple mild scarlet fever may be due solely to pure streptococci, whereas the malignant forms are due to a secondary infection.

Acute rheumatism, which eventually may, like scarlet fever, be proved to be of streptococcal origin, has become less acutely arthritic, though not less frequent than it was thirty years ago; widespread and excessively painful and swollen joints and profuse sweating causing the miliary eruptions once so familiar are seldom seen now. The pulmonary complications described by P. M. Latham in 1846 have become very rare, and hyperpyrexia is almost unknown.

Out of Latham's 136 cases of acute rheumatism the heart was attacked in 90, or 66 per cent., and among these 90 cases the lungs were affected in 24, there being pneumonia in 18 (6 double), pleurisy in 2, and much bronchitis in 4. Among the 46 cases in which no cardiac lesion was detected there were pulmonary complications in 5 (pneumonia in 3). It may well be that some or all of these complicated cases were different from what would now be regarded as uncomplicated acute rheumatism, and that they were actually pyaemic or septicæmic in nature.

Possibly the practical disappearance of these thoracic complications is connected with the alteration in the treatment—venesection in the past, salicylates during the last forty-five years. Secondary infections may have been favoured by the prolonged course of the disease in the pre-salicylate days, of which a verbal record remains in the answer of "six weeks" made by an authority to the question "What is good for acute rheumatism?"

Articular and tophaceous gout is becoming a curiosity, but we comfort ourselves by reflecting on our wise temperance as compared with our many-bottled predecessors.

Pneumonia has altered its character to a considerable extent since the reappearance of influenza in 1889, broncho-pneumonic forms being now perhaps as frequent as the frank lobar form; but this is only to say that there are several forms of the disease. Among the cases due to infection with pneumococci alone the pneumococcus types I, II, III, and IV differ in virulence, and accordingly the mortality varies, being highest in cases due to type III.

In the past the character of small-pox has varied, so that occasionally epidemics have been extremely mild, as was noted by Sydenham, Jenner, and others (see Newman). There has of recent years been a noticeably mild form of small-pox, both in this country and abroad, which is thought to come from North America; so mild, indeed, is it that in Switzerland the public expostulated against vaccination as more disagreeable than the disease, and some regard it as distinct from small-pox and would give it another name—such as *alastrim* (a Brazilian word derived from the Portuguese *alastra*—"something which burns like tinder, scatters, spreads from place to place" (Jorge)), *amaas* or *kaffir-pox*, *para-variola*, or *para-small-pox*. On the other hand, there are good grounds for the view that

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it is a mild form of small-pox due to a virus with suppression of its toxic properties for man, although its affinities for other animal species have not been appreciably changed (Ledingham). It occurs almost solely in the unvaccinated, and protects against small-pox and vaccinia; experimentally the viruses of the three diseases have been shown to be variants of the same virus (Blaxall; Ledingham; Gordon). As a rule, though not invariably, the mild form breeds true, but the mild and severe forms of small-pox may occur side by side. The objection to employing a special name, such as *alastrim*, is that this may make it more difficult even than it is now to maintain the necessary preventive measures of vaccination and isolation.

Acute *appendicitis* has undoubtedly become very much commoner since 1889, when influenza broke upon this country after a respite so long (since 1848) that its nature was not recognized for some little time.

The word "*appendicitis*," which has been criticized as barbarous on account of its Latin basis with a Greek termination, was constructed in 1886 by Reginald Fitz of Boston, Mass.; before that time it was called *perityphlitis*. Kelly and Hurdon unearthed a case reported in France by Meslivier in 1759. If we hesitate to accept this explanation of Erasmus's illness in 1530 and the necropsy mentioned by W. Musgrave in 1684, which may have shown evidence of past *appendicitis*, the first case in this country was briefly reported in 1812 as "Disease of the appendix vermiformis" by "James Parkinson Surgeon Esqr." (obit 1824), a general practitioner in Hoxton, who was also a palaeontologist, a writer of pamphlets advocating bloodless revolution, and the author of the famous "Essay on the Shaking Palsy" (1817) which has made his name familiar in "Parkinson's disease," "Parkinsonism," and "the Parkinsonian mask." In 1836 John Burne, physician to the Westminster Hospital (1835-42), in a paper read to the Medical and Chirurgical Society, referred to twenty cases he had seen, including three examined after death at Guy's Hospital; and in the same year Thomas Hodgkin, pathologist at Guy's Hospital, gave an account of the condition, which Thomas Addison probably drew on in his often quoted description (1839).

It can hardly be maintained that the condition was overlooked entirely by a generation less acute than ourselves; indeed, had it been as frequent before its operative treatment came in as it is now, it is obvious that the mortality from acute peritonitis would have been very high. For the increased occurrence of *appendicitis* various factors have been suggested, such as alteration in diet, greater consumption of meat—fresh, frozen, or tinned—fresh fruit, and antimony from the red rubber of bottle-stoppers. The association with the return of influenza, which has an intestinal form, is certainly significant.

A well established change in chronic disease within the lifetime of some of us is the great diminution of *chlorosis*, which may be contrasted with the, to my mind, increased incidence of pernicious (Addisonian) anaemia. The declension of *chlorosis* has been ascribed to several causes, such as better feeding, especially more meat, and to the change of fashion as regards tight lacing (F. P. Weber), the etiology of the disease being, according to Rosenbach and others, succinctly expressed as the corset. This explanation of the present rarity of the green-sickness of young women has not escaped adverse criticism (Elder; Waterhouse).

It is generally, though not unanimously, believed that *urinary calculus* in the Eastern Counties has undergone a well marked diminution; it must be remembered that fifty years ago operations for stone were among those most often undertaken, and therefore bulked more prominently than at the present day. The statistics collected by R. Smith and Yelloly make it clear that a hundred years ago *urinary calculus* was much commoner in Norfolk than in other parts of England and Wales.

R. Smith, making considerable allowances so as to avoid minimizing the incidence of calculous disease, estimated that in 1819 there were not more than 200 cases annually in the whole of the British Empire, and that there were as many cases in the Norfolk and Norwich Hospital as in either Scotland or Ireland. Yelloly found that from 1772 to 1827 inclusive there were 649 lithotomies in the Norfolk and Norwich Hospital, or one in forty admissions, and on an average $11\frac{1}{2}$ a year; that stone occurred in one out of every 34,000 persons in Norfolk as compared with one out of 108,000 persons in the rest of England and Wales, with a population of nearly twelve millions; and that it was less rare in Norwich, London, and other towns than in the surrounding country districts.

The reason for this relatively high incidence of *urinary calculi* in Norfolk is obscure. Dr. John Yelloly, who was

physician to the London Hospital from 1807 to 1818, and in 1805, when the Medical and Chirurgical Society was formed in opposition to the Medical Society of London, then under the blight of Dr. James Sims's long presidency, was with Dr. A. J. G. Marcet one of the founders and first secretaries of the new society, of which he was later treasurer, was also physician to the Norfolk and Norwich Hospital from 1820 to 1832, and in 1829 and 1830 wrote on the tendency to calculous diseases. He very tentatively put forward the view that the "large employment of ill fermented farinaceous food" was, by the resulting indigestion, *a*, if not *the*, cause of the prevalence of stone in Norfolk.

Syphilis, when it breaks out in a previously uninfected race, is much more virulent than in civilized and syphilized countries; but the much milder type of the cutaneous and bony lesions of syphilis in this country can hardly be ascribed solely to some approach to relative immunity, as the influence of more general early recognition and efficient treatment must be taken into account.

The diminution of malaria, yellow fever, plague, and enteric fever, and the practical disappearance of hydrophobia and scurvy in this country, have been determined by administrative and hygienic measures. It has been suggested that the milder small-pox at the present time is due to the better hygienic conditions, thus corresponding with the lower fatality of typhus and relapsing fever when these rare diseases occur in this country, and their increased mortality in conditions of famine, as in Serbia during the war. No doubt this factor is important, but it is not the whole story, for in the past small-pox and scarlet fever have had their mild interludes. Pasteur's explanation, which takes into account both a change in the virulence of the infective agents and altered conditions of environment, seems nearer the mark, but there may be some further and obscure factor to account for these long-spaced variations in virulence.

Hydatid disease has become much rarer in England and commoner in the Argentine Republic, but this is dependent on variations in the source of infection—namely, from dogs attendant on cattle. Forty years ago *hydatids* were by no means rare around Cambridge, now the disease is most exceptional; possibly, like the extinction of malaria in the fens, this is connected with the draining and reclaiming of the land. Conversely, the influence of certain industries in producing disease, such as silicosis; carcinoma (sweeps', paraffin workers', mule-spinners'), anaemia (benzol), and jaundice (trinitrotoluene and tetrachlorethane during the war), have attracted more, and more skilled, attention. It is rather remarkable that chimney-sweeps' cancer and mule-spinners' cancer are practically confined to this country. On the other hand, the effect of prophylactic measures is well shown in the great diminution of lead poisoning during this century.

Effect of Treatment.

It may be interesting to mention incidentally an artificial factor which had modified disease as many of us see it—namely, the influence of early and efficient treatment. The modification of syphilis so that the terrible tertiary lesions of bone are now seldom seen may be in part due to more thorough treatment. Enteric fever has become rare, and diphtheria has lost much of its terrors, thanks to prophylactic and curative measures. The influence of Jennerian vaccination is too obvious to labour, but attention may be drawn to an incident in connexion with inoculation in the eighteenth century: an uneducated Shetlander, John Williamson, practised inoculation with small-pox crusts which he dried and kept for years before using; with this attenuated virus he never failed to obtain protection and never had any bad results.

Surgery, too, had not been idle; thus early laparotomy for perforated or leaking gastric ulcer has made subphrenic gas-containing abscesses extremely rare. As the result of improved methods of diagnosis, and so earlier operations on cholecystitis, the character of gall-stone cases has undergone some change, and in Paris at any rate cases of stones in the common bile duct have become rare (Petit-Dutaillis and Mestrezat).

Disease: A Reaction, not a Morbid Entity.

It would indeed be strange if diseases always remained the same, for a disease, as the late Sir Clifford Allbutt insisted, is not a fixed morbid entity, such as might perhaps be visualized by the entry of an evil spirit into a man, but the reaction of that complex organism the body to some infection or injurious influence. There have been many definitions of disease, but Adami's (1910) gives a good impression of the potential variability in the reaction we call disease, and runs as follows: "Disease is a process or succession of disturbances induced by any agent which disturbs the normal activities of the organism as a whole or of its constituent parts." It is clear that the character of the reaction must depend on the condition of the individual host and on that of the cause—of the soil and the seed. Both of these may vary; for example, the difference in the manifestations of infections at the various periods of life shows how the state of the soil modifies its reaction. Variations in the virulence and doses of pathogenic organisms, supposing that the resistance of the host remains the same, would lead to changes in the reactions. With variations in the conditions of both the soil (the host) and the seed (bacteria and other environmental influences) it is clear that the clinical reactions and manifestations must alter in a corresponding degree. A highly virulent strain of micro-organism falling on a group of men whose resistance is either inherently weak or has been lowered by adverse influences should lead to an epidemic with fulminating attacks; whereas an attenuated infection acting on persons with fair powers of resistance would cause mild attacks, or fail to produce any recognizable result except to confer immunity. Further, a greatly lowered general resistance might allow micro-organisms ordinarily harmless to become pathogenic.

Experimental Epidemiology.

The experimental methods applied to epidemiology by Topley (assisted in the statistical aspects by Major Greenwood) in this country, and by Flexner, Webster, and other workers at the Rockefeller Institute, New York, who produced epidemics in laboratory animals, are throwing much light on the problems of spontaneous epidemics in man—such as the virulence of micro-organisms, the factor of the doses of micro-organisms, the susceptibility of the host, and, what is apparently a different problem, that of the herd. The variations in these factors give rise to permutations and combinations in the causation of epidemics, and further, "it is probable that additional factors not connected with the dosage of the parasite, nor with variations in the biological characters of the parasite or hosts, play a part in the spread of an epidemic" (Topley); and, though secondary infections, the part played by bacteriophages and by diet may possibly affect the relations between the parasite and the host, little is known about the additional factors. These problems of epidemics obviously bear on those of a change of type of disease, but at present they await a final solution.

Changes in the State of the Soil (the Host) as Responsible for Alterations in the Clinical Manifestations.

That continued exposure may be followed by a greater or less degree of immunity, as the result of unrecognized vaccination, in exposed persons is suggested by several observations: the increased resistance of laboratory animals who have survived an epidemic; the growing immunity in schools and institutions to diphtheria and to scarlet fever, as shown by the Schick and Dick tests; the acquired immunity to malaria and yellow fever shown by natives (who may also have had the disease); and in an indirect manner by the severity of epidemics of measles among the inhabitants of isolated countries where the disease rarely occurs—for example, the Faroe Islands (1781 and 1846), Fiji (1875 and 1907) and the neighbouring island of Rotuma (1911), and the Shetlands; the ravages of the common cold when introduced into St. Kilda; and the rapid and fatal course of tuberculosis in persons coming from regions where the disease is unknown. On the other hand, the long persistence of epidemic diseases, especially measles, shows that any racial immunity that can be thus produced is very slow. Webster, however, has brought forward experimental evidence of its occurrence, and on clinical grounds there

is some reason to believe that a gradual racial immunity may be developed in the course of years.

Changes in the constitution or make-up of the members of a race must exert some influence on the liability to special diseases, and as the structural architecture of a nation becomes modified by admixture with other races, some alteration in the prevalent chronic disorders would be anticipated. The Jews are particularly prone to some common pathological states, such as diabetes mellitus, obesity, and arterio-sclerosis, and some rare conditions occur chiefly among them, such as amaurotic family idiocy, obliterating thrombo-angiitis, pentosuria, lipodystrophia, and the recently described Niemann's disease (Bloom) which had previously been included in Gaucher's splenomegaly. Draper, who holds that the association of certain diseases with special anthropometric types is as distinct as the anthropometric racial types, speaks of the incidence of the above diseases in the Hebrew race as evidence of "a pathological tendency of physiological nature."

Environment, hygienic conditions, alcoholism, food supplies, and so forth, influence the general resistance and so the susceptibility to disease. It would be interesting to know which of the two factors, the variations in the host's resistance and the pathogenic power and the dosage of the microbe, is more important in the production of infection. According to Webster the mortality of an epidemic depends less on fluctuations in microbic virulence than on variations in the susceptibilities of the hosts; but Topley's critical conclusion is to the effect that in laboratory epidemics the existence of innate differences in the resistance of the hosts is non-proven. In human disease, however, it would seem reasonable to anticipate that impaired resistance would play a more dominant part in favouring infection than microbic fluctuations.

From investigation of the streptococci constantly present in dental root infections Knott and Spencer-Payne conclude that the production of systemic and metastatic infections depends more on diminished local resistance than on the specificity and selectivity of the streptococcal strains.

The increased frequency of subacute and chronic bacterial endocarditis, and of pernicious anaemia if this be accepted, raises the question whether or not this can be correlated with correspondingly great incidence of focal infections, such as dental, tonsillar, or intestinal, which in their turn are due to a widespread diminution in resistance allowing micro-organisms, such as strains of streptococci, usually saprophytic to become pathogenic (Horder; Dawson). The definite increase of subacute and chronic bacterial endocarditis, especially in ex-service men, since the war, with its infecting and depressing conditions, is an argument in favour of the view that a diminished resistance is the probable responsible factor. War has always altered the bills of mortality more by spreading epidemic diseases, such as dysentery, enteric, typhus, cholera, and malaria, than by wounds, though in the great war there were exceptions to this rule on the Western and other fronts. Malaria, which had become extinct in Flanders, reappeared after the advent of infected Portuguese troops and flooding of the country to arrest the German advance, thus recalling the disastrous Walcheren expedition of 1809; the extremely resistant character of malaria to quinine treatment during the war in the Macedonian area is another noteworthy incident.

The adverse circumstances of war, entailing deficiency of food, destitution, overcrowding, and insanitation, may so reduce the resistance of those concerned that diseases not usually prevalent or sometimes previously unrecognized come into prominence. This, as Dr. Horsley Gantt has shown, was particularly the case in Russia, where rickets, famine or hunger oedema, famine cachexia (without oedema), acute enteritis and peptic ulcer, and typhus and relapsing fever (immediately due to animal vectors) became rampant. War oedema occurred during the Napoleonic campaigns and the siege of Paris, and, it is said, in the concentration camps during the Boer war, under the name of epidemic oedema (Maliwa); it has been seen apart from war. Scurvy on land has been a feature of wars since the Middle Ages, and out of 143 epidemics analysed by Hirsch 55 were during hostilities. In Russia recently scurvy was the least frequent of the deficiency diseases, probably because the very great food scarcity led to the consumption of bark

and leaves (Gantt), but it was prominent in some other theatres of the great war, especially in Mesopotamia, where 11,445 cases occurred in the second half of 1916. Tuberculosis increased in all the combatant European nations. In Germany and Austria rickets became extremely common, and keratomalacia and blindness appeared; in Germany there was an increase of jaundice and acute yellow atrophy, quite apart from the factor of syphilis and its treatment by salvarsan preparations. Epidemic encephalitis, which was practically a new disease described by Economo in Vienna in 1917, soon, like influenza, spread over the world, and is still with us. The environmental conditions of stationary warfare created trench fever and trench nephritis, the latter having been seen seventy years before in the War of the Rebellion in North America, and made spirochaetosis ictero-haemorrhagica common instead of a curiosity. But from their etiology these conditions were more of the same nature as the epidemic infections—enteric, dysentery, cholera, malaria, and in Russia syphilis—which are an outcome of circumstances favouring mass infection, and they were not, in the main, the outcome of changes in the resistance of the troops.

Enforced moderation in diet was naturally followed by a diminution in disease due to excess (in a sense the reverse of deficiency diseases); thus in Russia Gantt reported a fall in chronic alcoholism, adiposity, appendicitis, and diabetes; the incidence of cholecystitis and gall stones gradually fell from 4.7 per cent. of all out-patients in 1914 to 4 per cent. in 1917, and then dropped suddenly to 1 per cent. in 1918 and 0.8 per cent. in 1919, thus suggesting the importance of overeating as a causal factor. In Germany the war showed a diminution in diabetes, in acute pancreatitis (Wilms), and in arterio-sclerosis, but the last became more frequent in Russia.

It is tempting to associate with the popular cry of "the wear and tear of modern life," and the nervous strain entailed by the more rapid fashion of existence, an increase of functional and organic nervous diseases, of diabetes, high blood pressure, and arterio-sclerosis. Thus in the United States of America, where intensity and "hustle" are characteristic features of life, the death rate of cardio-renal disease far exceeds that due to any other cause, and was responsible for the deaths of the last two Presidents (F. M. Allen). On the other hand, the frequency of functional nervous disease is no new phenomenon, for George Cheyne, in *The English Malady* (1733), estimated that one-third of the upper classes were thus afflicted, and Thomas Trotter, in his *View of the Nervous Temperament* (1807), went one better by putting the incidence at two-thirds of all civilized communities, poor as well as rich. It is difficult, therefore, to be certain, probable as it may appear, that neurasthenia and functional disease are so much commoner now than in the past, for statistics, as apart from impressions, such as those of Cheyne and Trotter, are hardly available, and in the comparatively short period covered by a medical generation or two it is far from easy to estimate accurately the degree of change that occurs. Although telephones, motors, and aeroplanes increase the rate of living, they also have compensating advantages, and wars and alarms were more constant in the past. It is impossible to be certain that there has been an increase of high blood pressure on account of the recent introduction of the sphygmomanometer and the absence of any statistics in the past on this point. The indirect evidence that might be sought from arterio-sclerosis is rendered doubtful by want of exact correspondence between the two, high pressure being only one, and not the sole, cause of arterial change; but arterio-sclerosis was common in ancient Egypt. The greatly increased expectation of life, which is a noticeable result of public health activities, has altered the forms of disease responsible for the bills of mortality; malignant disease, arterio-sclerosis, and chronic cardio-renal disease have become more prominent, whereas tuberculosis has declined.

Changes in Bacteria as Responsible for Alterations in Clinical Manifestations.

Variation and mutation are more readily and rapidly produced in bacteria than in higher animals and man, and

serological research has shown the perplexing differences that may thus occur, for example, in the salmonella group (Andrewes, P. Bruce White). Different strains which are morphologically and culturally identical vary in their serological reactions in a remarkable manner; thus *Bacillus paratyphosus* B and *Bacillus aertrycke*, which are indistinguishable morphologically and culturally, are serologically different and also distinct in their clinical effects, the first causing paratyphoid fever, the second acute food poisoning. Differences in virulence may, as Pasteur showed long ago by growing anthrax bacilli at 40° C. and producing a relatively non-virulent strain, be modified by environment, nature of nutrient material, temperature, and possibly other factors.

As a rule, however, the influence of culture media and other laboratory methods is in the direction of diminishing, not of increasing, virulence; there are exceptional instances of increased pathogenicity induced by culture—for example, of the pneumococcus (Felton and Dougherty) and of the meningococcus (E. G. D. Murray); and Flexner and Amoss observed revival of the poliomyelitis virus after being in glycerol for several years. According to Webster, virulent strains come into being by some means more subtle than animal passage.

Associated with the known different types of the typhoid-paratyphoid group, dysentery bacilli (Shiga and Flexner), and to some extent of the pneumococci, there are correlated differences in the clinical manifestations; in cerebro-spinal fever the different types of meningococci have been connected with different clinical reactions; thus, according to Dopter, the predominant infective meningococcus before the European war was Type A (Gordon's Types I and III), whereas later it became Type B (Gordon's Types II and IV); Netter correlated the greater frequency of cases of septicaemia and of lesions, such as rashes, arthritis, and irido-cyclitis, with this change to Type B. Thus changes in the clinical aspects, for example, of enteric fever and cerebro-spinal fever, may be due to infection with different types of the typhoid-paratyphoid group and of the meningococcus. It is reasonable to believe that further evolution of such varieties might be accompanied by such alterations in the clinical picture as to constitute new diseases, as indeed has occurred in the differentiation of typhoid and paratyphoid fevers. The adaptability of bacteria to altered conditions so that a harmless saprophyte living on the surface of the body can be changed, in the laboratory or outside, into a pathogenic micro-organism which invades the body and gives rise to disease was emphasized by the late J. G. Adami (1918), who instanced as a probable example the transformation of some previously harmless diphtheroid bacillus into the virulent diphtheria bacillus to account for the appearance at the beginning of the last century of diphtheria, a disease so sharply cut that it could hardly have been overlooked by all physicians until Bretonneau of Tours gave his classical description in 1821. Among animals hog cholera, unknown before the sixties, when it appeared in the United States, is another example in support of the view that bacteria can and do undergo evolution from a saprophytic to a pathogenic state. As has been mentioned above, the occurrence of secondary infections is a factor of importance in altering the clinical manifestations of an infective disease.

The two variations—in the soil and in the seed—though mentioned separately, must often be combined in varying degrees, and must play an all-important part in the changes in the clinical aspects of disease.

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GLEANINGS FROM THE STORY OF THE THYROID GLAND.

AN ADDRESS DELIVERED TO THE SOUTH-WEST WALES
DIVISION OF THE BRITISH MEDICAL ASSOCIATION

BY

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THE accounts of the physiology of the thyroid gland and the surgery of goitre given in the textbooks of my early student days took less than three hours to read and study; it is, however, necessary to point out that this apparent cramming course was not so intensive as it sounds. In the index to the fourth edition (1883) of the standard *Textbook of Physiology* by Michael Foster there is no reference to the thyroid gland. Incidentally, it was in this year that attention was drawn in Switzerland to post-operative myxoedema, as will appear later from the very interesting note sent by my friend Dr. Albert Kocher in reply to a request to let me have an epitome of the work his father, the late Professor Theodor Kocher, had done as regards the subject-matter of my address to you. I am glad to recall that both Professor Theodor and Dr. Albert Kocher visited the area of our South-West Wales Division many years ago and saw examples of our thyroid troubles, to my edification.

On the question of the surgery of goitre I have to confess that for a few years after qualifying I deprecated operations except in emergency—in fact until I visited the great master and pioneer at work in Berne. This attitude, I may add, was due almost entirely to the teaching and practice at my school, for I, being imitative, had operated on a Gasserian ganglion and did an experimental decompression on acromegaly years before I felt justified in doing a thyroidectomy. My view was nurtured in my nonage by reading the seven pages devoted to diseases of the thyroid gland in the standard work *A System of Surgery* (Holmes, vol. 3, 1883), and was fortified years later by witnessing a brilliant surgeon attack a bronchocele and wallow in an operation masked with blood and many sponges, and constantly harassed by a Clover's bag—one special sponge was conspicuously held over the field to deliver fluid if necessary; later he descended on its value should a gurgling sound be heard indicative of air

being drawn into one of the veins! He also pooh-pooled the adoption of an innovation which he flippantly described as a "cut-throat" incision.

When I witnessed the first Kocher operation performed by its originator with deliberation and care, without unnecessary spilling of blood, with unsurpassed surgical cleanliness, with non-variable speed, neither slow nor quick, but a safe "Kocher speed," I instantly became a convert. I was astonished and impressed with the novelty and value of the Kocher screen which completely safeguarded the field of operation from infection from the patient's mouth, from the anaesthetist, and from interested onlookers; the patient's hands also were secured from doing harm.

We re-read to-day, with gratitude to Professor Theodor Kocher, the nightmare which appeared under "treatment" in the *System of Surgery*, and obsessed so many like myself, knowing that it is now gone for ever; there we read such statements as that "fibrous bronchoceles are best treated by setons"; that "the best treatment for cystic bronchoceles is . . . tapping the cyst with a trocar and cannula, emptying it, injecting a solution of perchloride of iron (two drachms to an ounce of water) . . . to be repeated if necessary until suppuration is established"; and that "removal of a bronchocele is usually a grave operation . . . the danger of haemorrhage is considerable." Nevertheless, the volume contains shrewd clinical observations, and exhibits discernment and the true scientific outlook in not accepting as truth that which is not proven. For example, it is said:

"The endemic form of bronchocele, or goitre, occurs chiefly in association with cretinism and seems to have some hitherto unexplained connexion with geographical conditions . . . the cause commonly assigned—namely, the use of melted snow, or of water impregnated with calcareous or earthy particles—is unsatisfactory. . . . Although the Korrawurrees can get nothing but snow for some months in the year, they are not so subject to goitre as those who live at the foot of hills where there can never be any snow water."

The importance of this quotation will be seen when I come to discuss Professor Kocher's views as to the causation of goitre. From that time to the present the literature on thyroid gland and goitre has grown so voluminous that I can only attempt to bring to your notice a few gleanings, after reading to you the most valuable and interesting *aperçu* by Dr. Albert Kocher of his father's work on the subjects.

NOTES ON THEODOR KOCHER'S WORK ON THE THYROID GLAND.

BY

DR. ALBERT KOCHER.

From 1866 to 1872 Theodor Kocher was assistant of Professor Lucke in Berne. During that time Lucke performed ten goitre operations; of the patients nine died. Two years after having been elected Lucke's successor in the chair of surgery at the University Theodor Kocher, in 1874, published his first paper on the thyroid gland—on the pathology and treatment of goitre. In this paper he published his first thirteen goitre operations, with two deaths only. In this paper he said that there were three forms of operation for goitre: total thyroidectomy, partial thyroidectomy, and enucleation. He said that the total thyroidectomy was an easier procedure "than partial thyroidectomy, but it is a question whether there is any connexion between the total extirpation of the thyroid gland and the altered mental condition I have noticed in one of my cases of total thyroidectomy." His goitre operations were already at that time done on a preconceived plan—he sought in each case to ligate the arteries first. A few years later (1887) he published his first operations for malignant goitre, describing a method of "évidement" of soft malignant tumours, especially intrathoracic ones.

In 1883 he published the results of his first 101 goitre operations. He gave at the same time a list of all the goitre operations done down to 1883. He found that with his own 101 cases 240 goitre operations had been performed. In this same paper he detailed his exact method of operating, and then described the consequence of total thyroidectomy. He had reviewed all the cases he had operated on, and in the eighteen cases where total thyroidectomy had been done he found the typical picture of myxoedema. In April, 1883, he read a paper on the consequence of total thyroidectomy at the German Surgical Congress, calling the disease "cachexia thyreopriva."