DISEASE OR DEFENCE?

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Ever since medicine became systematised we have based our knowledge of disease on symptoms and signs. A patient has a sore throat, chills and malaise; we observe pyrexia, red tonsils with follicles; the laboratory reports streptococcus haemolyticus and we diagnose "tonsillitis" caused by these bacteria. But if we ask the laboratory to report again in one month's time when the tonsils are normal and the patient is healthy, the same type of bacteria are often found and the patient is now called a carrier, and is said to have acquired immunity. It is known that streptolysins appear in the blood after such an attack and these are supposed to maintain immunity: but their titres soon wane, yet the disease does not recur on this account. Some forms of sinusitis, otitis media, bronchitis, pneumonia and all broncho-pneumonias are associated with inflammatory catarrh apparently caused by the action of saphrophytic bacteria. Why do these saphrophytes become active, and how can we distinguish between a virulent and a quiescent saphrophyte? No one can give a factual answer. Why is a carrier immune from the influence of his bacteria one week and succumbs the next week? There is no definite reason based on the facts at present available.

The common cold, catarrhal fever, atypical pneumonias, and the catarrhal states of children are enigmas which have defied etiological classification. Attempts have been made to prove that the first three states are viral and can be transmitted. The causative agent can be measured by graded filters, cultured with difficulty in the amniotic sac of hens' embryos, but refuses to reproduce more than a pallid reflection of the original disease when inoculated into human volunteers. These volunteers cannot infect others exposed to them. In some way the agent has lost its virulence and its powers of passage from one host to another.[1] The intense and world-wide research which has produced these disappointing results leads one to search the well-trod paths again for hidden clues or misunderstood data which might help to reorientate our theories of the causation of some of these diseases.

The discovery of antibiotics and their use in the treatment of bacterial diseases has raised controversy which is closely associated with the questions mentioned. If tonsillitis, to take a single instance, is caused by a selected organism known to be sensitive to a chosen antibiotic, why is this organism often found at the site of the disease after the illness has subsided and in spite of an adequate course of the antibiotic? Bacterial saphrophytes are

known to be actively engaged in causing inflammatory foci in some cases of measles, yet there is division of opinion on the question of antibiotic therapy to suppress these complications. A boil caused by staphylococcus aureus will remit with adequate antibiotic therapy, but on withdrawal a series of these furuncles may develop over varying periods of time. In sinusitis, bronchitis and bronchiectasis the results of prolonged and heavy antibiotic therapy are disappointing and only palliative.

In the opinion of the writer the introduction of antibiotics, while providing a dramatic and heroic weapon against overwhelming bacterial infection, has revealed that these bacteria, when active only in moderation, are not the cause of any disease. They may antagonise another factor, possibly viral in origin. Let us take the easy example of measles. This disease is caused by a virus. If the natural immunity of the host fails to check the virus then the saphrophytic bacteria become active. These bacteria check and destroy the virus although the host is thrown into a more flagrant state of disease. This assertion is borne out by the fact that, in vitro, bacterial contamination of a virus culture will destroy the latter. Take another example: it seems possible that the inflammatory foci in the boil must contain foreign particles which the saphrophytes are mobilised to destroy, liquidate and evacuate from the host's tissues; a wooden splinter or a metal fragment embedded in the integument will produce a similar reaction. All recurrent bacterial inflammations of the respiratory tract can also be visualized as due to virual activity opposed by saphrophytic bacteria.[2] Antibiotics will curb the latter but only temporarily suppress the reaction and ultimately will enhance the invasive power of the underlying virus. Colds, catarrhal fever and atypical pneumonias are known to be caused by virus infections.[3] Yet it is curious that these diseases cannot be directly transmitted by controlled experiment and can only be reproduced in a subdued form after culture of the viral agent. Successive passages in human hosts are impossible.[4] The natural disease occurs sporadically, epidemically and explosively with no fixed incubation period. It is a common fault in all systems of thought to assume that knowledge based on observed and tested experience is always correct, and that facts which do not fit should be ignored or shaded in obscurity. In this way we assume that these catarrhal, viral borne conditions are always received from another case; that each case is infectious to all those around him; that there must be a regular incubation period; and that the virus, if cultured, should invariably reproduce the disease: this does not happen, therefore the hypothesis is wrong, and a new concept should be built up.

Phagocytes engulf dead bacteria, so why should not bacteria absorb virus.[5] The idea is not new. Pasteur and many succeeding pathologists believed in the existence of an ultravirus associated with the bacillus of Koch.[6] Pathologists working at the height of the influenza pandemic in 1918 wondered if that strain of virus emerged from symbiosis with H. influenzae.[7] Many strains of saphrophytic and pathogenic bacteria contain virus which is manifested as bacteriophage. If virus can parasitise saphrophytic bacteria and remain latent, changes in the human host or in his environment may release them in swarms, and it becomes clear that these states are being generated spontaneously in many people at once at epidemic times without any special need for contagion and infection to play more than a subsidiary role.

It is necessary to make a sharp distinction between the saphrophytic and the pathogenic bacteria. Such organisms as C. diphtheria, B. pestis, the dysentery bacilli and salmonellae, P. welchii and tetanus organisms are virulently antihuman, are not found as normal inhabitants in the average human host and provoke intense pathological states on contact with his tissues. The diseases caused by these foreign bacteria are excluded from the subject under discussion.

The human infant in the neo-natal state has a sterile respiratory and digestive tract, but acquires saphrophytes from (i) the maternal genital canal and (ii) the respiratory tract of the mother. Additions are made throughout life by casual contagion; in the writer's opinion they are all retained as domesticated defenders of the host against virus infections and are tolerated without evidence of the defence reactions we call disease. If these saphrophytes were even potentially virulent they would surely become so on first contact with the virgin soil of the new-born infant and fierce illnesses would rage soon after every birth. This does not occur. The new-born child will receive doses of viruses from parents and friends in the family circle and at school. These invasions into his system are countered by the stereotyped defence reactions we classify as coryza, bronchitis, otitis media and tonsillitis. The multiple factors which determine the focal point of the defence reaction are not yet well understood. But once the virus has gained a foothold the writer believes it can remain latent after the disease is over, ready to swarm and colonize deeper within the host when any change in the defence system favourable to the virus takes place. Perhaps they are latent in the saphrophytic bacteria, or perhaps within the tissues of the host? The lymphatic system appears to be integrated into most defence reactions and it is here that one should search for viral latency.

The family doctor spends years in close contact with patients of

all ages in the throes of minor and major illnesses. Equipped with a knowledge of modern clinical medicine, it is still a confusing scene he observes; there is no integration in the natural history of illness, and he has to plod blindly in the rear loaded down by massive pharmaceutical armaments. If the suggestions put forward are used to interpret the common diseases met with in general practice, a much clearer view of what is happening within the host emerges. The first signs of virus activity in the infant are manifested by coryzal defence. If this is insufficient, the defence system initiates headache, fever, malaise and increased catarrh of endothelial membranes. Deeper penetrations causing vomiting, diarrhoea and colic pains occur in infants, and disorders—gastritis, gastro-enteritis and enteritis—occur. Penetrations into the respiratory tract cause bronchitis and atypical pneumonias. The family doctor will be familiar with the fact that most of these conditions commence with a cold and that recovery is sealed by a cold in the head. Unfortunately, the virus is still latent in the host and in the opinion of the writer remains latent at any location it reaches until changes in the environment are favourable for swarming again even years or decades later. Generally speaking, the virus is opposed by saphrophytic bacteria wherever these are naturally resident or at sites accessible to them. Hence the tonsils, sinuses and middle ear infections are often " septic " defences. It is conceivable that lobar pneumonia is a very vigorous defence reaction to virus, with a definite conclusion in favour of the host if he survives, whereas broncho-pneumonia is not so conclusive and bronchitis favours the survival, by latency of the virus. Using a similar interpretation in terms of abdominal disease, the acute attack of appendicitis represents an allergic septic defence with a clean-cut result in favour of the host—providing a surgeon intervenes in time. Non-specific mesenteric adenitis is a milder defence of the abdominal gland-guards at a site not suitable for saphrophytic intervention. Gastritis, duodenitis, and colitis are catarrhal defences in the gut against virus invasion. When saphrophytes are mobilized the disease becomes ulcerative colitis. It is possible that the gastro-enteritis of infants is also a saphrophytic defence phenomenon when the gut is invaded by virus. A similar interpretation of some diseases in the genito-urinary tracts could be so assayed and would result in a clearer understanding of the dissimilar pathologies at present described as entities unconnected with each other.

If this interpretation of catarrhal and microbial diseases, as patterns of defence against a resident virus in the host or an invading virus from a carrier, is accepted, then a rational and uniform natural history will emerge in the case notes of any

individual from his birth to his death. Epidemics would be revealed as a mixture of new invasions and of exacerbations of resident virus in different hosts occurring at ambiguous anatomical sites. The common cold would be merely a stereotyped catarrhal defence of the upper respiratory tract to (*a*) new virus invasion or (*b*) resident virus activity. The bewildering assortment of apparently unassociated disorders which all crop up together during a coryzal or influenzal epidemic period would be explained. They are all caused by a viral agent, acting at different sites in different hosts who are employing a limited variation in defensive patterns in accordance with the resources available to them. Selye has investigated in great detail the physiological mechanisms of adaptation to stress and the pathological derailments which can occur.[8] The presence of resident virus may be a stress factor of importance. Many of the ailments and disorders met with every day in the consulting room or at the bedside could be regarded as the visible projections of the unending struggle of the human host to adapt his defensive power to check the virus resident in his system. Selye has introduced the concept of Stress into physiology and this requires a corollary in clinical medicine—Defence.

REFERENCES

[1]Blank, H., and Rake, G. *Viral and Rickettsial Diseases.* Boston, 1955., p 145.

[2]Stuart-Harris, C. H. *Influenza.* Edward Arnold, London, 1953.
[3]Zaiman, E., Balducci, D., and Tyrrell, D. A. J. *Lancet*, 1955, **2**, 595.
[4]Seiffert, G. *Virus Diseases in Man, Animal and Plant.* New York, 1944.
[5]Blank, H., and Rake, G. *Viral and Rickettsial Diseases.* Boston, 1955, p. 4.
[6]Ninni, M. D. *Annuls de l'Institute Pasteur*, 1933. **50**, 504.
[7]Croften, W. M. *The True Nature of Viruses.* London, 1939, p. 33.
[8]Selye, H. *Stress.* Montreal, 1950, p. 46.,

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