orifice; (b) from the simultaneous and coincident rheumatic inflammation of the lungs.

Conclusion.

In a case of mitral stenosis the degree of dyspnoea should be looked upon as a measure of the efficiency of the circulation rather than of the efficiency of the myocardium.

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The Function of Complement.

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The study of the processes involved in general immunity has provided one of the most interesting fields of research in preventive medicine. The popularity of this problem among research workers was due to the fact that the defence mechanisms of the blood were regarded as closely allied to general bodily resistance and it was hoped that, from a knowledge of the substances involved in these reactions, a basis for the treatment and prevention of bacterial disease might be evolved. Immunity reactions have, however, proved to be complicated, involving the consideration of many factors about which there is very little knowledge.

Of the immuno-chemical substances present in the blood, complement—that non-specific labile substance of normal serum which is absorbed by the combination of an antigen (foreign protein, bacterium, toxin, etc.) and its specific antibody, and in this manner destroys the foreign cell—is probably of the highest importance. Ehrlich held that the complementary activity of sera observed in vitro had its parallel in the animal body, and now in the light of many experiments it may be taken as proven that complement action takes place in the blood, and there is every reason to believe that complement is indispensable to the animal organism in protecting it against the occurrence of infection. This was brought into prominence by Lister, who observed that blood removed aseptically from animals had no tendency to undergo "putrefaction," and that there was no detectable growth in the medium when bacteria were added. Lister was also aware of the importance not only of the purely bactericidal agents in serum, but also of phagocytosis by living cells.

The role of phagocytosis (cellular immunity) in the processes of infection is outstanding. The phagocytic power of leucocytes is dependent on a sensitisation of antigens (foreign substances, bacteria, etc.) by a humoral substance in serum termed opsonin. Opsonin has recently been shown to be complement minus one of its component parts, which is present in the white cells. The phagocytes, therefore, ingest cells "buttered" with opsonin and thus the complement reaction proceeds intracellularly.

In immune sera, besides the normal non-specific complement-opsonin, there are specific opsonins. One form—bacteriotropin—acts without complement, while in the second case the phagocytic power is brought about by a combination of an opsonic antibody and complement. We are thus forced to conclude that phagocytosis is but a manifestation of the complementary agents present in the blood.

The part played by complement in bringing about bacteriolytic and bactericidal effects is exemplified by Pfeiffer's reaction, and there is little doubt that the antibody-complement reaction is the chief mechanism contributing to natural and acquired immunity. Organisms such as B. typhosus, B. dysenteriae, V. cholerae and various members comprising these groups, are rapidly killed if normal or immune serum is added at body temperature, but not if the serum has been pre-heated to 56°C., owing to the thermolability of complement. The destruction of bacteria by normal serum is due to the co-operation of naturally occurring antibodies (probably non-specific in character) and the complement complex. The addition of an antiserum containing specific immune antibodies will merely enhance the action against the particular bacterium or toxin (*vide infra*). The lysis of sensitised red cells and other animal cells by normal sera and antisera has been generally accepted as a similar phenomenon, and there is evidence that

toxin-antitoxin and viral-antiviral combinations are bound by complement.

The complementary activity of a serum results from the interaction of certain fractions associated with the protein and lipoid constituents of the blood, and cannot be increased by any process of immunisation. In the kinetics of its action complement has characteristics common to many enzymes. The actual change produced by complement, after absorption by an antigen-antibody complex, is some digestive mechanism, suggested to be a hydrolysis of proteins and/or fats.

Sensitisation by the appropriate antibody confers on the antigen the property of absorbing complement, and thus leads to the resulting destruction or lysis of the foreign organism. Recent investigations have shown that the amount of antibody removed by an antigen is a constant fraction of the amount with which the antigen is treated, and that the greater the quantity of antibody absorbed the greater is the proportion of complement absorbed from any complement concentration, with enhanced bactericidal or lytic activity. An antiserum will therefore produce a high degree of sensitisation of the bacterial organism, so that a smaller quantity of complement will be required in the humoral process of destruction. A deficiency in the blood complement concentration, on the other hand, may predispose an individual to serious infection even if antisera are injected, since complement is, as has already been described, the final link in the process of foreign cell destruction. In the presence of a low concentration of complement the foreign organisms may therefore be insensitive to its action; this may explain the poor reaction after antiseral injection which occurs with some frequency. Such deficiency may well be responsible for a lowered resistance to infection and for a poor response during the course of acute diseases; indeed a low complement during an acute infection is a bad prognostic sign.

While there is little evidence that nutritional defects disturb the antibody-forming mechanism, there is ample proof that resistance both to spontaneous and induced infection is profoundly affected, and that the blood complement tends to be lowered. The precise functions played by particular vitamin deficiencies in producing this state of affairs is not yet clear. With regard to vitamin A this is regarded by Mellanby as an anti-infectivity vitamin; Osborne (1936) found that vitamin A deficient rats had a low complement and that feeding cod-liver oil to humans raised the blood complement above its normal level.

However, it must be realised that the effects of complement on foreign cells observed in vitro will not be fully attained in the living organism. A study of the effects of the various physical and chemical agencies present in blood on complement has led to the conclusion that complement is acting under adverse conditions in the blood due to the presence of the following inhibitory factors:—

1. *Carbon dioxide*—The presence of carbon dioxide in serum has been found to decrease its complementary power up to 40% of its original activity; this effect is not due to the formation of bicarbonate since this has been found to increase the complementary activity. As the carbon dioxide tension in the serum is increased from 0 mms. Hg. to 60 mms. Hg., so is there an increasing inactivation of the complement, until at blood carbon dioxide tensions the inactivation of serum complement is maximal.

2. *Haemoglobin and serum proteins*—The blood proteins, owing to their high concentration of 7%, have been found to be strongly anti-complementary. Haemoglobin within the red cell has no effect on complement, but in solution or in the form of breakdown products has an extremely inhibitory influence on complement.

3. *Chemical and organic constituents of blood*—Apart from a few isolated substances practically every constituent of serum tested has been shown to inhibit complement, as judged by comparison with its activity in normal saline.

Although it is some fifty years since complement was first described, few satisfactory methods of increasing the complementary activity within the body have been discovered; they are limited to the injection of bicarbonate, adrenaline and thyroxine, and the ingestion of large quantities of cod-liver oil (vitamins A and D). Further, despite our knowledge that the liver is the site of formation of the component parts of complement, we have yet to discover a method of stimulating its formation. The fact that we are unable to concentrate or isolate complement by any means, owing to its unstable nature, has proved a great stumbling block in the investigation of its properties and function.

We are faced with the realisation that the tangible results of the therapeutic value of complement will be few, until we are able to

THE IMPORTANCE of MINERALS IN ANIMAL NUTRITION . . .

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It has long been known that the vital processes of life are dependent not only on the presence of various mineral salts, but also on a proper relationship between them. At the present time the importance of mineral matter for livestock is receiving much popular attention, due chiefly to striking results which have been secured in recent experiments by nutrition experts. Particular attention is being paid to the deficiency of minerals in animal nutrition. Such experimentation in the past has established the fact that Lamsiekte in cattle and Rickets in pigs fall in the class of deficiency diseases.

Among the minerals which should receive especial attention by all progressive farmers, Calcium and Phosphorus have first claim. The particular deficiency of these two minerals is greatly accentuated by their paucity in certain South African soils.

Dairy cattle in particular are affected by the lack of these minerals, and it has been shown that for every 2½ gallons of milk withdrawn from the cow the lime equivalent of 1½ ounces of first-grade bone meal is also withdrawn. The cow, in order to keep up the production and composition of her milk, must eventually deplete the reserves of Lime and Phosphorus in her skeleton. Such a condition can be likened to a banking account—funds, unless replenished, soon become depleted.

Farmers whose every care is closely linked up with the welfare of their cows should take warning. They should feed balanced rations to replenish the depleted reserves, and so prevent mineral starvation. The feeding of "Vebros" Milk and Beef Meal will ensure not only a balance of Protein and Vitamins, but also a balance of the necessary minerals. Our "Vebros" Mineral mixtures and cattle licks are likewise scientifically balanced and consequently guaranteed to meet all the requirements in mineral nutrition. They will therefore insure your animals against such mineral deficiency diseases as e.g., anaemia and "hairless" goitre in young pigs.

In conclusion, a warning against the use of mineral licks is not out of place in this article. Mineral mixtures which contain high percentages of Fluorine have been shown to be disastrous to stock in that they cause deformities in the bones, particularly the jaw-bone, and similarly they lead to improper mastication in that the teeth become tender and loose. The danger of chronic Fluorine poisoning has only lately gained prominence and it is on that score that we repeat our warning against the use of high percentage Fluorine mixtures. Fluorine is particularly associated with Raw Rock Phosphate in chemical combination.

handle the "labile" protein molecules of the blood and to understand the mechanism of action of complement. The necessity for a better knowledge regarding complement lies in the fact that the present day tendency in treating bacterial disease is to assume that complement is present in sufficient quantity and to increase the antibody concentration of the blood. There is indeed some evidence contrary to such an assumption.

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Constitution and Disease.

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It is a common and ancient conceit that man can know his fellows not so much by their fruit as by their form. "Just as observers of mankind," says Hutchinson in "The Pedigree of Disease," "have from time to time strained their faculties in the endeavour to find in the external lineaments of a man some clue to his mental power and moral habits, so have physicians sought to find in parallel indications the means of predicting his tendencies in reference to disease." To the ancient physicians the relationship of physical habit and temperament to health and disease formed an integral part of their system of medicine. "Persons who are naturally fat die earlier than those who are slender" (aphorism of Hippocrates).

For Hippocrates, constitution was a vague and comprehensive term and for some 2,000 years after his time the concept of constitution was bound up with the theory of humours, four types of men being recognised, viz., the phlegmatic, the plethoric, the bilious and the melancholic types, in whom one or other of the humours predominated. The recognition of the type was important for diagnosis, prognosis and treatment. Up to modern times the four temperaments received ample and elaborate discussion in text books. When the humoral theory went out of fashion the types established remained as the basis of the modern concept of constitution.

Towards the end of the nineteenth century Hutchinson and Heuppe tried to maintain interest in the constitutional factor of disease in the face of the terriffic onslaught of bacterial investigation. But it was not long before bacteriologists themselves found that the microbe was not the whole answer to disease. A similar fate has overtaken physiological and biochemical investigation.

The concept of constitution implies that the man is as worthy of study as the disease with which he is afflicted—a concept which must of necessity keep the practice of medicine more at the bedside than in the laboratory. Unfortunately there has been little agreement as to what is meant by the term. Some stress the hereditary qualities, others the personal or acquired peculiarities. Some adopt purely morphological criteria, others functional or physical standards. Bochardt defines constitution as the status of the organism as conditioned by hereditary and environment, while for Draper it is the summation of the morphological, physiological, immunological and psychological qualities ("panels") of the individual, influenced more or less by the environment, which determine his reactions to his environment. Petersen's description of constitution recalls the Hippocratic *physis* implying the total organism in its environment. The term constitution must embrace, says Petersen (1932), "not only the quality of the protoplasm in its form and structure, but the functional status as made apparent in the physiological and pathological reactivity—in adaptability to change in the environment—in modifications produced by season, climate, diet, age, endogenous and exogenous irritants, disease, physical and mental trauma and the varying forces of the universe of which the individual is a part."

With the development of Physical Anthropology, the methods of this science were applied to the study of constitution; attempts to differentiate man on morphological grounds were made. Beneke, de Giovanni, Viola and others correlated physical habitus with different diseases. Draper extended these methods and coupling clinical observation with anthropometric technique has described