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Man is not Sick by Germs alone-South East Asian Ovalocytosis, G6PD Deficiency, Erythrocyte Deformability and Experiments on Plasmodium Knowles Prove Germ Terrain Duality Theorem

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Introduction

South East Asian Ovalocytosis, G6PD deficiency and erythrocyte deformability are three conditions/factors/properties that alter cell anatomy/physiology consequently affecting susceptibility to disease [particularly malaria] hence proving the Germ Terrain duality theorem. Experiments done on plasmodium Knowles also prove the theorem. According to the Germ Terrain Duality Theorem of Disease there are two causal agents the micro organism and the anatomical/physiological terrain. BOTH are equally important and neither factor is primary or secondary. Disease is caused by a complex interplay between germs and the inherent anatomical/physiological integrity of the body cells. Every disease is associated with a particular micro-organism AND condition/set of conditions [1].

To be precise the theorem states: "the etiology of certain diseases/diseased states is better explained as a complex interplay between germs and the inherent anatomical/physiological integrity of the body cells. The etiology of certain diseases is not fully explained merely by the presence of germs (Germ Theory) or by a mere loss of cellular integrity (Terrain Theory). As a result the prevention and treatment of such diseases should focus not just on fighting germs but on maintaining/restoring the anatomical/physiological cellular integrity [2].

Peruse the following quotations from reputable works that buttress the theorem

Experiments done on plasmodium Knowles prove germ terrain duality theorem. Plasmodium [Knowles] metabolism is affected by changes in osmotic pressure and ion content of the fluid bathing red blood cells. Blood from Macaques rhesus monkeys infected with Plasmodium Knowles. Consumes oxygen and destroys glucose in vitro with great rapidity as compared with blood from normal monkeys. Parasitized red cells account for the unusual activity. Approximately half of the destroyed glucose is converted to lactic acid; the remainder is only partially oxidized. Anaerobiosis stimulates glycol sis by infected red cells, but has no effect upon normal erythrocytes. Under comparable conditions of pH, lactate and glucose are equally good substrates for respiration. Lactate, like glucose, is incompletely oxidized. Parasitized blood to which nothing is added consumes oxygen for many hours, although it becomes free of glucose, if heavily parasitized, within 30 minutes or an hour [3-6]. Fortifying infected blood with several hundred mg per cent of glucose leads to rapid fall in pH and decline in oxygen consumption and glycol sis. Both metabolic processes cease at pH 5.5. Other factors which are unfavorable to preservation of active metabolism in vitro are addition of phosphate, cyanide, and oxalate, hypertonic solutions of neutral salts, replacement of serum with physiological salt solutions, and spontaneous clumping of red cells. Favorable to prolongation of active parasite metabolism are low degrees of parasitization of specimens, dilution with serum, and neutralization of the accumulated acid. Factors which usually have no significant influence upon respiration or glycol sis are brief centrifugation, moderate dilution of blood with physiological salt solutions, and the addition of heparin, citrate, malamute, sulfanilamide and ethylene blue [7-15].

Plasmodia normally inhabit red cells, at the expense of which they undergo rapid and extensive changes in size and structure. Such a relationship suggests a dependence of the parasite upon constituents and perhaps, metabolic processes of the host cell [16].

Southeast Asian Ovalocytosis [SAO] proves germ terrain duality theorem

Southeast Asian Ovalocytosis is a form of hereditary elliptocytosis common in some communities in Malaysia and Papua New Guinea, as it confers some resistance to cerebral

Falciparum Malaria. It is hereditary hemolytic anemia in which the red blood cell is oval-shaped. The primary defect in SAO differs significantly from other forms of elliptocytosis in that it is a defect in the gene coding for a protein that is not directly involved in the cytoskeleton scaffolding of the cell. Rather, the defect lies in a protein known as the band, which lies in the cell membrane itself. The band 3 protein normally binds to another membrane-bound protein called ankyrin, but in SAO this bond is stronger than normal. Other abnormalities include tighter tethering of the band 3 protein to the cell membrane, increased tyrosine phosphorylation of the band 3 protein, reduced sulfate anion transport through the cell membrane, and more rapid ATP consumption. These (and probably other) consequences of the SAO mutations lead to the following erythrocyte abnormalities [17].

1. A greater robustness of cells to a variety of external forces, including:

a. Reduction in cellular sensitivity to osmotic pressures.

b. Reduction in fragility related to temperature change.

c. Greater general rigidity of the cell membrane.

d. Loss of sensitivity to substances that cause speculation of cells.

2. Reduced anion exchange.

3. Partial intracellular depletion of ATP.

4. A reduction in expression of multiple antigens.

These changes are thought to give rise to the scientifically and clinically interesting phenomenon that those with SAO exhibit: a marked in vivo resistance to infection by the causative pathogen of malaria, Plasmodium Falciparum [18].

The reasons behind the resistance to malaria become clear when given an explanation the way in which Plasmodium Falciparum invades its host. This parasite is an obligate intracellular parasite, which must enter the cells of the host it is invading. The band 3 proteins aggregate on the cell membrane at the site of entry, forming a circular orifice that the parasite squeezes through. This band 3 proteins act as receptors for the parasite. Normally a process much like endocytosis occurs, and the parasite is able to isolate itself from the intracellular proteins that are toxic to it while still being inside an erythrocyte. The increased rigidity of the erythrocyte membrane in SAO is thought to reduce the capacity of the band 3 proteins to cluster together, thereby making it more difficult for the malaria parasite to properly attaching to and enter the cell. The reduced free ATP within the cell has been postulated as a further mechanism behind which SAO creates a hostile environment for Plasmodium Falciparum [19-25].

G6pd deficiency proves germ terrain duality theorem

Glucose-6-phosphate dehydrogenate deficiency (G6PD deficiency) a form of which is known as fauvism (after the fava bean), is an X-linked recessive inborn error of metabolism that predisposes to hemolytic (spontaneous destruction of red blood cells) and resultant jaundice in response to a number of triggers, such as certain foods, illness, or medication [26]. It is particularly common in people of Mediterranean and African origin. The condition is characterized by abnormally low levels of glucose-6-phosphate dehydrogenate, an enzyme involved in the pentose phosphate pathway that is especially important in the red blood cell. Carriers of the G6PD allele appear to be partially or fully protected against malaria, with some cases of affected individuals showing complete immunity to the disease [27].

A side effect of this disease is that it confers protection against malaria in particular the form of malaria caused by Plasmodium Falciparum, the most deadly form of malaria. A similar relationship exists between malaria and sickle-cell disease. One theory to explain this is that cells infected with the Plasmodium parasite are cleared more rapidly by the spleen [28]. This phenomenon might give G6PD deficiency carriers an evolutionary advantage by increasing their fitness in malarial endemic environments. In vitro studies have shown that the Plasmodium Falciparum is very sensitive to oxidative damage. This is the basis for another theory that is that the genetic defect confers resistance due to the fact that the G6PD-deficient host has a higher level of oxidative agents that, while generally tolerable by the host are deadly to the parasite [29-33].

Red blood cell deformability and the germ terrain duality theorem

Erythrocyte deformability refers to the ability of erythrocytes (red blood cells, RBC) to change shape under a given level of applied stress, without hemolysing (rupturing). There is very good evidence that various red cell disorders including hemoglobinopathies and hereditary Ovalocytosis decrease the virulence of disease following parasite infection. A number of mechanism (s) [34] are likely responsible for the protective effect of various red cell abnormalities including decreased invasion, impaired intraerythrocytic development of the parasites and altered interaction between exported parasite proteins and the red cell membrane skeleton.

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