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Editorial

Infections and pH

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Why do certain infections tend to recur in the same area? For certain at least part of the explanation is opportunity with the infectious agent's location close at hand or an enhancing delivery system. Also certain adaptations by the infectious agent occurs leading to specific locations. But perhaps there is an additional unknown preference that at least on occasion may be involved.

Few are surprised Candida albicans episodically grows on skin, in urine and in the female vagina since these areas are all known to be acidic at times and Candida prefers an acidic environment for growth [1]. But we do not use the same logic for example when an infectious agent grows in the adrenals or bone well away from the original lung location. Tuberculosis was noted to grow best in alkaline conditions as early as 1897 [2]. Reactivation TB is often apical…could this be a more alkaline area of the lung? Miliary TB results from hematogenous spread to other areas. There are probably few areas that cannot be infected with tuberculosis; however there are some areas that appear to be preferred.

Perhaps cellular pumps, channels, transporters and isoenzymes are the way an organism controls pH in an area and adapts. If that is true then perhaps pH varies in organelles and organs in larger life forms under certain conditions. This might explain why there are multiple cellular pumps, channels, transporters and 5-10 or more isoenzymes for many different common enzymes with different optimum pH levels. Obviously that could impact for example bacterial attachment to mucosal surfaces, viruses to their receptors, etc. Often this happens in breaks in the mucosa which could very well be acidic. But perhaps sometimes there is no need for a break if perhaps the pH without a break was near optimum.

If our cellular pumps, channels, and transporters mainly control our pH levels, perhaps one of the reasons we do not understand what causes predisposition to some diseases is because humans could have genetically different combinations of cellular pumps. In addition there could be pH swings as part of normal physiology like we see with the stomach. A pH change would cause some enzymes to become more active while others less active (pH change intracellular could also impact cell membranes).The optimum pH is often a bell curve where small changes like 0.3 can have significant impact. Once certain isoenzymes are activated it might be in some cases to make products to bring the organism back closer to homeostasis. Genetically we probably also have variable levels of the isoenzymes and so returning to homeostasis maybe delayed in certain people with predispositions to certain diseases.

When an infectious agent is in the blood it should grow in multiple locations but often has a few favorite locations…why. Its location probably depends at least in part upon host defenses versus infectious forces. Yes infectious agents have metabolic versatility but there probably is a preference. The preference might be impacted by the energy cost to replicate in a less than optimum environment. Rapid replication is often best done with intracellular alkalinity but that means the cell is possibly expelling protons and developing an extracellular acidity which could impact the host and the host's defenses. However massive replication could eventually cause an overwhelming acidic condition at least locally. Apoptosis is generally acidic [3]. A pH level change could even impact the specific stages of infectious agents for example amebic, viruses, and parasites.

If regions such as organs or areas of infection did have variable pH levels, that might also explain why certain drugs worked under certain conditions. Yes the mechanism of the specific drug against an infectious agent would be key but the environment it had to work within could be an important secondary factor. For example we have known for years nitrofurantoin is more active in an acidic environment while erythromycin is more active in an alkaline environment [4]. Efflux pumps could also be impacted by pH levels (and vice versa).

Possible infectious agents that are also colonizers might spend enough time present in the host so as to adapt. A good example might be H. pylori in the stomach which has a growth optimum in an alkaline environment. As the pH in the stomach becomes more acidic, the bacteria have urea channels that enable movement of urea in order to maintain intracellular pH [5]. Perhaps some H. pylori even get into the duodenal area and thrive where the pH is alkaline making eradication more difficult.

Spread of certain infectious etiologies may be more common in family members not just because of closeness of contact but also because of similarity of isoenzyme proportions, cellular pumps, channels, and transporters. When someone has a genetic predisposition to part of the immune system not being fully functional we are not surprised when they become infected. Perhaps this is just the milder logical deduction.

Some isoenzymes and cellular pumps undergo post transcriptional changes. The infectious agent could even impact the organism by impacting this crucial step (and vice versa). Obviously this could be the dividing line between genetic predisposition and environment influences. Perhaps we are like the early microscope observers centuries ago noting the biconcave red blood cells and wondering why…not knowing this made the cells more flexible and better able to give off oxygen.

Possibly we have overlooked some of our basic science. Botanists

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understand that certain plant life grows best in certain soils… acidic, neutral, or alkaline. One can plant in a less than optimum environment but probably will result in less than optimum growth unless costly adjustments are made.

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