REDEFINING IMMUNE STATUS

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Here intention is to draw attention towards complex subject of immunity, immune status and increasingly emerging infections up to level of epidemics where in thoughtful understanding of compromise in immunity is desirable.

The immune system is a defense mechanism against disease. It is an internal biological process structure within organisms to protect from possible diseases. The immune system is able to distinguish between different infective organisms and within an organism able to detect healthy or unhealthy cells or tissues. This detection process is extremely complex and is followed by the development of an adaptation mechanism.

Immune system varies from unicellular organisms like bacteria; having an enzyme system that tackles infections; to highly advances as for humans and other vertebrates. In humans, the immune structure is composed of a variety of components, such as organs (bone marrow, lymph nodes, tonsils, thymus, and spleen), tissues, cells (White blood cells, phagocytes and lymphocytes) and proteins that act synergistically to create a forceful defense network. The system at the end adapts to some pathogens through ‘acquired immunity or adaptive immunity’ - actually an immunological memory, which makes the body more responsive in case of a second encounter.

Historically, “Immunity” derives from the Latin immunis, meaning exemption from military service, tax payments or other public services. The first written descriptions of the concept of immunity may have been made by the Athenian Thucydides who, in 430 BC, described that when the plague hit Athens “the sick and the dying were tended by the pitying care of those who had recovered, because they knew the course of the disease and were themselves free from apprehensions. For no one was ever attacked a second time, or not with a fatal result”. The term “immunes”, is also found in the epic poem “Pharsalia” written around 60 B.C. by the poet Marcus Annaeus Lucanus to describe a North African tribe’s resistance to snake venom. Attacks over immune defense have been disastrous and represented by the Cholera epidemic of the 19th century, Influenza in early and HIV in late 20th Century and H1N1 in 21st Century.
Infections remain a significant issue in the care of immunocompromised patients, classically including those with malignancies, HIV infection, rheumatologic disorders, or those who undergo solid organ or stem cell transplantation.

Last decades world over a shift in pattern of infections is emerged as alarming. Marked change in pathogen, presentation, outcome and mortality has alarmed epidemiologists as epidemic data has been suggesting paradigm shift. Infections classified typically limited to immune compromised hosts have emerged in otherwise “immune stable” persons.

To list a few, Cryptosporidiosis (protozoan) Diphtheria (bacterium), Malaria (protozoan), Meningitis, necrotizing fasciitis (flesh-eating disease), toxic-shock syndrome, and other diseases Group A Streptococcus (bacterium) and Pertussis (whooping cough) (bacterium). Emergence of zoonotic diseases like Cryptococcosis - Cryptococcus neoformans, Bartonella henselae (agent of cat scratch disease) and B. quintana, Mycobacterium marinum (Nontuberculous aquatic mycobacteria - Fish Tank Granuloma) have also re-emerged. Repeated epidemics of unusual pathogen, breakdown of public health measures, changes in microbiological adaptation leading to altered pattern of antimicrobial resistance have raised alarm to ignite thought process over need to redefine status of immunity or expand spectrum of immune compromised status.

Typically, immune deficiency is a state in which the immune system’s ability to fight infectious disease is compromised or entirely absent. Most cases of immunodeficiency are acquired (“secondary”) but some people are born with defects in their immune system, or primary immunodeficiency. A person who has an immunodeficiency of any kind is said to be immunocompromised. An immunocompromised person may be particularly vulnerable to opportunistic infections, (in addition to normal infections that could affect everyone). For simple understanding, presence of opportunistic infection is the mark of “Immune Deficiency”. Such as

- Candida albicans
- Staphylococcus aureus
- Streptococcus pyogenes
- Pseudomonas aeruginosa
- Polyomavirus JC polyomavirus, the virus that causes Progressive multifocal leukoencephalopathy.
- Acinetobacter baumannii
- Toxoplasma gondii
- Cytomegalovirus
- Aspergillus sp.
- Kaposi’s Sarcoma caused by Human herpesvirus 8 (HHV8), also called Kaposi’s sarcoma-associated herpesvirus (KSHV)
- Cryptosporidium
- Cryptococcus neoformans
- Histoplasma capsulatum
- Clostridium difficile

Out of these, most are found to be surprising clinicians with unusual presentation in otherwise “Immune competent” hosts. While reviewing overall medical history and co-morbidities, most of these patients are found to have one of the following.
• Malnutrition, Anaemia
• Recurrent infections
• Skin damage
• Antibiotic treatment
• Medical procedures
• Pregnancy
• Chronic Illness – Asthma, COPD, Koch’s, Diabetes
• Aging
• Sleep Deprivation
• Environmental exposure

Incidence of such patients is alarmingly high – up to 25% of hospitalized patients.

Typical response to invasion by pathogen in body is executed through innate response (primarily physical or chemical like Skin, Sweat, Tear, Saliva, Stomach acid, Cilia & mucus – non specific), immediate response (inflammatory response – dolor-calor-rubor through WBC/Phagocytes/interferones – non-specific) and delayed response or immunity (lymphocytes-cell mediated, antibodies – humoral immunity – specific). Delayed response has different expression ranging with repeated exposure that lasts from hours to years due to the formation of immunological memory, reinfection at later time points leads to a rapid increase in antibody production and effector T cell activity thus later infections can be mild or even inapparent. This expression of immune status is detected through levels of antibodies. Immune function score has become an important tool for defining status. Immune function score is detected using four parameters CD4 count, lymphocyte mitogen response, neutrophil phagocytosis and oxidative burst level.

With sepsis, initial response of inflammation if followed by hyper immune response, leads to recovery where as inability to produce hyper immune response i.e. status of hypo-immune status or suppression leads to adverse outcome. This was noted with conditions as mentioned in list of typical immune compromised status but recent past epidemiologists have observed alarming rise in patients out of this typical list. Such patients have been very commonly been deprived of early treatment for the sake of “low index of suspicion” and hence morbidity and mortality still is remaining high. As we understand, in such conditions, out of triad of host, agent and environment e have only host factors that can be modulated. Is it not the time for clinicians, epidemiologists and academicians to revisit basic understanding and fixed ideas of immunity and immune compromised status?

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<tr>
<th>Initial response in Sepsis</th>
<th>Inflammation</th>
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<td>Within 1 - 2 days</td>
<td>Immune suppression</td>
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Recovery  Hyperimmune

Days

Host  Agent

Environment