

Immunology of Modern Society Humans [IMSH]

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ABSTRACT

Humans lives in modern society are subjected to an array of factors that impacts the cellularity and functionality of their immune systems. These IMSH factors were ensemble as; Global changes, liberal spread of mental influencing drugs, war warfare ,terrorism ,environmental mutagens and carcinogens as well as environmental allergens .So they are being at risk for both enhancing or dampening effects on their immune systems. Workers have been documenting four main categories of targeted human immune system living at risk of modern society .The IMSH categories are; intravenous drug users, intensive care patients, tumor patients , war warfare and terrorism. The intravenous drug users have shown increase in their humoral B cell immune responses through the elevation of B cell counts and activities and increase in activation markers of T cell subsets. Intensive care patients were mainly showing functionality of cellular immunity like that of ageing immune cells. Tumor patients, however, were found expressing diversity and compositional heterogeneity of immune cell type reaching 33 subsets and marked functional alterations. Tumor microenvironment have shown at least six dominant pan-cancer-classes of dominant immune cells as compared to normal human subjects immune cellularity. Biological warfare and bioterrorism insults were being accompanied by emergence and re-emergence of unfamiliar agent pathogenicity ,seasonality and marked host susceptibility to the terrorism agent necessary need for individual therapy and management ,as well as for pre and post exposure mass vaccination .Each IMSH category have expressed shared and distinctive features. The unified functional insight to the immune systems of human living in modern society is that formed cellular elements of these immune systems behave to different insults in different ways and different elements reacts differently to the same insult.

Keywords: Care Drug, Intravenous, Intensive, Terrorism ,Tumor, war warfare.

INTRODUCTION

Modern society holds different meaning to different societies and to different social professionals[1,2].So far the present review is concerned modern society collectively means; rise up of science culture, rise up of literary culture, industrialization, family structure change ,changes in social values and facing global changes. Such impacts are associated with host susceptibility to the emerging and re-emerging infectious agents and relative deprivation of immune system functionality [3]. The sorts of Infections of modern society, like IDU ,ICU ,tumors and Bioterrorism have been documented by workers[3,4].The objective of the present review was to deduce the immune features modern society humans

HYPOTHESIS

The immune response of a normal healthy human population harboring an ecologic niche to foreign invaders and tumors have shown three basic responder types as low, moderate and high responders. The distribution of these responder types among population contracting pathogenic insults is either of Gaussian distribution or Skewed distribution plot types[[5,6,7]. In normal healthy human populations both of low and high responders were of low numbers while moderate responders were somewhat high. In clinical laboratory senses these compromise with subnormal, normal and abnormal value findings. Modern society humans might express skewing in their immune herd plots than this balance paradigm to either increase towards subnormal or increase of abnormal. This hypothetical holding remained to be elucidated.

MODERN SOCIETY AND IMMUNE COMPROMISED PATIENTS [IC]

From 1998 till 2016 the frequency of immune compromised subjects were increasing in United State[8]. Likewise the frequencies of immune compromised were increasing as to the annia 2002-2006[9]. Both of USA and Canada are best representatives of Society impacts on human living therein. Immune compromised patients increase is a marker for the targeting impacts of society on human beings. Increase of IC lead to increase of susceptibility of the patient to viral infections[8,9].

MODERN SOCIETY HUMAN INFECTIONS

The nature of modern society human infectious agents are depicted in ,Table-1.

Table -1: Infectious agents dominant in modern society human

Category	Infectious agents	References
IDU	S.aureus ,s.anginosus ,HIV	[4]
Intensive care Unit patient	Pseudomonas,MRSA,klebsiella,Sars-cov-2	[4],[10]
Tumor patients	Coagulase negative Staphylococcus,Aspergillus,Pseudomonas,enterococcus,sars-cov-2	[4],[10]
War warfare, terrorism	B.anthraxis ,Botulism ,plage, Poxvirus ,Tularemia	[4] [11]

IMMUNOLOGY OF INTRAVENEOUS DRUG USERS[IDU]

Concept

The mind influencing intravenous drug users are associated with increased incidence of infectious diseases. Drug use constitutes an important risk factor for HIV and Hepatitis C infections[12,13]

Analysis

The IDU patients have shown increase in; Total B cell counts, increase in IgG3,IgG4 and IgM as well as increment in TNF alpha, TGF alpha and IL8[14].The heroin and Methadon IDU patients were showing on stimulation with Mycobacterium tuberculosis, Candida albicans and LPS comparable levels of IL1B,IL6,IL10.IFNalpha,TNF alpha and IFNg among both IDU test groups and controls[12].There were non-significant quantitative differences in CD4+ T cells and CD8+ T cells between IDU and non-IDU HIV patients. Whereas, there were significant differences in

the cellular activation markers CD38,K167,and CD14 in both PBMC and gut mononuclear cells[13],Table- 2 .

Table-2 : The Immunology of IDU patients

Features	[14]	[12]	[13].
Demography	130IDU	82 IDU	HIV INFECTED and Non-HIV infected
Samples	Blood	Blood	Blood and gut mucosal material
Investigations	Flow cytometry	Cell sensitization, Cytokine determination	Immunotyping of CD4+,CD8+ Activation markers CD38,K162,CD14
Immune cells	Two folds increase of total B cell counts, Activated B cell increase	The un-stimulation not differe from control Stimulated showed cytokine production	The difference between IDU and non-IDU HIV patients In CD4,CD8 T cells Increase in activation markers aong IDu Hiv than control
Mediators	Increase in IgG3,IgG4,IgM,SCD40L	IL1B,IL6,IL10,IFN alpha,IFNg and TNF alpha comparable results among test groups	
Others			
Conclusions	Increase humoral immune responses ,increase in systemic inflammation .May impacts optimal responses to vaccination	Apparently stimulation with microbe does not make difference between IDU and Non-IDU	Increase in actvation markers in IDU HIV than non IDU HIV

Immune Features

The immune features of the IDU patients are;

I - Increase in Total B cell counts.

ii- Increased in the activated B cell subsets

iii-increase in IgG 3,IgG4 and IgM.

iv-Increase in the cytokines; TNF alpha, TGF alpha,IL1B,IL6,IL10 and IL8.

v-Heroin and Methadon exhibited no apparent effects onCD4+,CD8+ T cells and increase inT cell activation markers.

Thus the distinctive immune features of IDU are; Susceptibility to infectious agents and activation of both T and B cells

IMMUNOOGY OF CRITICAL CARE PATIENTS

Concept

Monoclonal antibodies ,check point inhibitor and adaptive cellular therapies are the major topics of use in critical care environment[15].Asthma, immune deficiency ,allergy and immune modulation are the daily noted issues in critical care patients[16].Septic patients complex long lasting immune deficiency state involving lymphocytes of both innate and adaptive immune response .Such responses have been associated with mortality and/or infections in critical care patients[17],Table.

Analysis

Intensive care patients have shown increase in; myeloid cells , monocytes, regulatory T cells, regulatory B cells .And decrease in; total T cells, naïve T cells, and thymic emigrant lymphocytes. A state similar to that of physiological ageing effects on immune cells[Duggal et al.2018],Table

Table 3: Immunology of ICU patients

Features	Findings[18]
Demography	20 ICU patients with persistent clinical illness 27-76 years old
Samples	Blood
Investigations	Phentyping of innate and adaptive immune cells
Granulocytes	Elevated mature and immature Neutrophil counts
Mononuclear cells	Increase in CD16 ++ monocytes,increase in CD14+HLADR monocytes
Lymphocyte NK T cells	Lower in counts of each of; Reduced total T cell counts, naïve T cell anPKT7 thymic new immigrant.Reduction in regulatory B cells CD19Cd24+ Increase in CD2+CD4+T cells Rise in neutrophil to Lymphocytes ratios
Conclusions	Change in immune cell phenotypes similar to that of ageing immune cells

Immune features

The major immune features of ICU patients are;

i-Elevation of mature and immature neutrophils.

ii-Increase in CD16++ monocytes.

iii – increase of CD14 HLADR monocytes.

iv-Low counts in each of; NK cell, total T cells , regulatory T cells and naïve T cells

v-increase in CD2+CD4+ T cells.

Thus increase of innate immune cells and decrease of adaptive lymphocyte subsets except CD2+CD4+ T cells increased.

IMMUNOLOGY OF TUMORS

Concept

The growth and spread of tumor cells within the continuum of the affected patient bodies will not be prevented by the potentials of humoral immune responses. Though, the effector T cells, macrophages and natural killer cells have relative tumoricidal effects. Cells bearing tumor specific antigens or tumor associated antigens activate the effector functions of other immune cells through the cytokine action. Even though, this activated effector immune cells may fail to control tumor occurrence or growth[19]. Recent trends in tumor immunology tend to; i- characterize the basic biological mechanisms behind the antitumor immune responses, ii- immune regulate the development and spread of tumors, iii- improve targeting and destruction of cancer cells, iv- understand the molecular basis of haematological malignancies and graft versus host disease[20]. Tumor is a systemic disease that induces several functional and compositional changes in the whole constituents of the immune system. Hence essential to understand the favorable and unfavorable immune mechanisms operable within the tumor micro-environment. Therein, peripheral immune system is required to induce effective natural and therapeutic induced antitumor immune responses rather than re-invigorate the pre-existing immune responses[21].

Analysis

The tumor micro-environment stands as the main contributor to tumor progression and a promising target for treatment. Though there was an evident induced profound variations in their immune micro-environment and be a basis for disease prognosis. The situation necessitate a buildup of comprehensive compendium for tumor immune cells helpful in prediction the immune cell state and their location within the tumor tissues[22,23]. Tumor tissue constitute; Tumor cells, tumor microenvironment[TME], immune cell microenvironment[ICM] and enriched tumor infiltrating lymphoid cells[TILC] co-located in the tumor tissue section. Tumor tissue harbors 25 clusters representing immune cell types. These immune cell types are; 12 T cells, five macrophages/monocytes, three dendritic, three B cells and plasma B cells, one natural killer cells and one mast cell cluster. The finite B cell subclasses were representing; naïve, activated, memory, un-switched memory and proliferative subsets. While CD4 T cells were representing; T reg., T helper, and naïve T cells. CD8 T cells express high levels of granzyme A. Whereas their pro and terminally T cell subtypes are exhausted. All macrophages subsets were abundant in tumor tissues. These findings were finalized by building up a suggested “Pan-Cancer-Immune-Classification” into six major classes[22]

C1 : High proportion of activated and naïve memory T cells.

C2: High amount of cytokines and terminally exhausted CD8 T cells.

C3: High levels of macrophages.

C4: High levels of Plasma B cells

C5: High levels of effector CD4 memory T cells.

C6: High levels of B cells

Table -4 : Immunology of cancer

Features	[22]	[23]
Demography	217 patients ensemble in 13 human cancer type	16 patients of head and neck squamous cell carcinoma
Samples	Tumor tissue type	Head and neck tumor tissues
Investigations	Construction of tumor tissue atlas ,clustering and classification of immune cell composition Spatial transcription analysis	SC RNA analysis Enrichment analysis Deconvolution of bulk tumor
Immune Cells	Patterns and co-location of immune cells, stromal cells and cancer cells in tumor section	B cells, conventional Cd4+ T cells, conventional CD8+ T cells. Tumor infiltrating T cells
Immune classification	-C1-High proportion of activated and naive T cells -C2-High amounts of cytokine and terminally exhausted CD8+ T cells C3- High levels of macrophages C4-high levels of plasma B cells C5-high levels of effector Cd4 memory T cells C6- High levels of B cells	
Other cells	Stromal cells, cancer cells	Macrophages DCs, endothelial cells, malignant cells ,and fibroblasts
Conclusions	Solicit Pan-Cancer- immune cell classification	Tumor infiltrating T reg. cells played a role in regulation of anti-tumor immune-suppressive .This cells are of clinical importance

Immune Features

The immune features of human naturally induced tumors are;

i-Immune cell and their compositional heterogeneity to which six “Pan-Cancer-Immune classification” were buildup for diagnosis and prognosis.

ii-Immune cell in tumor tissue form lymph cell microenvironment

iii-Tumor infiltrating immune cells.

iv- low levels for each of the lymphocytes subsets; NK cells ,trained T cells naïve T cells and regulatory T cells.

v- Increased in CD2+ CD4+ T cells.

IMMUNOLOGY OF WARFAIR AND TERRORISM

Concept

The emerging and re-emerging biological warfare and terrorism agents may be directly transmissible or vector born. The interplay between, population pressure, genetic variations ,tourists migration and environmental global changes is in a rather complex way can influence contribute in disease emergence. Due to the threat posed by both biological warfare ,terroric spread of the merging and re-emerging infectious agents. There is a need for urgent identification of the agent in the clinical settings in order to treat the affected individuals and improve public health surveillance and epidemiology. This at risk situation initiate collaboration efforts all over the world to develop identification assay of the terroric agent at the level of individual patients and developing pre and post exposure vaccines or supporting these vaccines from already present commercial makes [24].Three categories of biological agents are prioritized in accordance with their likelihood for bioterrorist use as first[A] ,second[B] and third priority[C].Among which first priority includes; anthrax, botulism ,plague , small pox,tularemia and viral haemorrhagic fever[11].The characteristic features of the bioterroric agents are;i-Easily produced , ii- highly reliable in action , iii- have long shelflife , iv- have aerosol durability, v- high degree of lethality , vi- spread in an un-usual season , vii- affect age groups differs from that usually seen and vector transmitted disease in an area not endemic to that vector[25,26].

Vaccinology

Vaccine for vaccine preventable infectious diseases can be in three versions; the preventive ,the therapeutic version and the vaccine for non-infectious diseases [27,28].Herein , mass spread of bioterroric agents in any geographic niche vaccine needs to be of two other versions as ;pre- and post- exposure vaccines either tempts to develop or order already known commercial makes, Table -5

Table – 5 : Bioterrorism sample type of vaccines features.*

Features	Anthrax	Small pox
Name	Anthrax	Smallpox
Vaccine type	Cell free filtrate of non-capsulated attenuated strain	Live vaccinia virus from calf lymph
Preservative	Bebzelkonium hlorigec	Polymyxin B,Streptomycin ,chlorotetracyclin ,neomycin
Side effects	Local tenderness ,induration, erythema, subcutaneous nodules	Scar formation at the inoculation sits,fever,rash
Contraindications	Anaphylactic reaction to prior dose of vaccine	Anaphylaxis to vaccine components,eczema
Schedule	0,2,4,wk with booster doses at 6,12,18 months	Once by scarification with a booster dose every ten years
Authorization	Authorized	Authorized

***Adapted from [26]**

Immune Features

The main immune features of an incident bioterrorism disease are

- i- An induced immune compromised state.

- ii- Marked susceptibility to the emerging infectious agent
- iii- Treatment and management of individual cases
- iv- Inquiry for pre and post exposure vaccines.

SHARING AND DISTINCTIVE FEATURES OF MODERN SOCIETY HUMANS

Sharing Features

Taken together the sharing features of modern society humans are:

- i-Targeted human immune System function and composition. The immune system reactions intensity depends onto; nature of the insult, exposure time, pre-exposure nature as well as age and sex of personals at risk.
- ii-Immune heterogeneity and immune compromised are of elevated frequencies.
- iii-Aetiology endogenous may genetic or exogenous environmental.
- iv-Inductive in nature
- v-Governed by herd immunity rules and of inductive nature

Distinctive Features

The major distinctive features of the modern society humans are depicted in Table.

Table: The distinctive features of human categories live in modern Society

Category	Distinctive features
IDU	Activate Immune Cellular Elements ,marked susceptibility to microbial infections
ICU	Elevated neutrophils, reduced lymphocytes and being like physiological cell ageing
Tumor	On onset it varies according to the patient health standards. On therapy it of marked immune compromised state
Warfare and Terrorism	Susceptibility to the terroric agent ,need pre and post exposure vaccination

CONCLUSIONS

Modern society impacts human life welfare and targeted their immune systems TIS .Therein ,were found multiple insults of many kinds. TIS responds to these different insults in different ways. Features TIS responses are either of the followings primary or secondary immune compromised[marked susceptibility to the emerging pathogens] ,variable immune cell compositions and marked heterogeneity .It appeared to be that modern human populations mounts immune responses that are governed by herd immunity rules .But the low and high responder fractions might differs from that of non-immune compromised herd immune plots.

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