

## Redefining the diseases with reincarnation of ‘Germ theory’

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**Abstract:** Chronic diseases or illnesses have a nick name ‘non-communicable disease’, where in spite of best efforts, apparently no microbial agent as cause of disease transmission could have been established till few years back. This confusion stemmed from the gaps in the natural history of those diseases, embedded in a) Absence of cause-effect knowledge, b) Multifactorial theories of morbidity c) Long latent periods, d) Indefinite as well as slow onsets, help damage to hosts long before the overt manifestations that may be irreversible or very difficult to reverse. With these vague ideas of non-communicable diseases we attempted to identify uncountable risk factors. So, primary and primordial prevention remained the mainstay in our armory in the name of ‘First Contact Care’. Recent advancements and innovative wild thoughts (ignited by HIV thanks!) in the fields of microbiology as well as immunology have been able to establish role of microbes as causation of non-communicable diseases.

**Keywords:** Non-communicable diseases, Infection, Immunology.

### Introduction

In 1873 Louis Pasteur advanced the “germ theory” of disease. Earlier theories of disease causation were supplanted. Shedding the dogma and supernatural theories, medical science put the robe of scientific basis. Still after a century of progress, World Health Report 1996 shows that the world stands on the global crisis of infectious diseases, which are costing millions of lives. Theme of World Health Day 1997 ‘Emerging infectious diseases- Global alert: Global response’ had found new milestone in the history of medicine [1].

In last three decades, nearly thirty diseases have emerged to threaten lives on earth. On the top of everything, by the tremendous advances of immunology, evidence of microbial collisions into the non-communicable diseases put us in the crossroad whether this nomenclature still holds ‘certificate of good standing’. So, primary and primordial prevention remains the mainstay in our armory in the name of primary care to fight the slow epidemic of non-communicable diseases [2].

*A soul searching inward journey:* Non-communicable diseases (NCDs) are morbidities those by definition are non-infectious and non-transmissible among people by transfer of any agent. According to James E. Gern, (Associate Professor of Pediatrics, University of Wisconsin Medical School, Madison), the observation that farming environments are associated with lower rates of allergic sensitization and asthma has been replicated in several studies conducted in Europe and North America [3-5].

The mechanism of this association is under intense scrutiny, and so far there is considerable evidence to implicate exposure to microorganisms in the environment. This concept forms the basis of the so-called “hygiene hypothesis”. According to this theory, exposure to microorganisms leads to stimulation of innate immune responses, and this helps the immune system to develop in such a way as to inhibit Th2-type responses (which helps to promote immune tolerance) that lead to allergies and asthma. Additional

evidence is supporting the role of the innate immune response and polymorphisms in genes (for TLR-2 and CD14) in reducing the risk of atopy and modify the effects of environmental exposure to animals and farming environments comes from genetic studies [6-7], These exciting new discoveries of the last few decades provide safe solutions to many common medical problems which were initiated by careful epidemiologic observations by the use of molecular genetics, protein folding, axoplasmic transport, lymphatic system, immunology, a variety of imaging modalities, as well as early psychological assessments [8]. Centers for Disease Control (CDC) has clearly defined Non-communicable disease (NCD) as any Chronic condition that do not result from an (acute) infectious process and hence are “not communicable” and has a prolonged course, that does not resolve spontaneously, and for which a complete cure is rarely achieved [9].

An infectious (communicable) disease (ID) is defined as an illness caused by a specific infectious agent or its toxic products that results from transmission of that agent or its products from an infected person, animal or reservoir to a

susceptible host. This agent can be transmitted either directly or indirectly through an intermediate plant or animal host, vector or inanimate environment [10].

An increasing number of NCDs are being associated with an infectious risk factor. Hence, the distinction between an infectious disease and NCDs is blurring and it is important to bring to the fore their linkages and interactions. This review explores the role of infections in the emergence of NCDs including possible pathogenic mechanisms that need to be explored by the future technologies. Epidemics of communicable diseases follow predictable patterns, spreading across vulnerable population sectors by disease carrying agents or vectors. That leads to the term communicable. But recently many people have challenged the use of the term non-communicable and said that these diseases are also communicable. The mechanisms of how specific strains of an infection cause NCD is related to their ability to release cytotoxic products and also to cause an exaggerated and dysregulated immune response that leads to tissue damage [11].

**Table-1: Microbial agents and morbidities with the classified conventional nomenclature of ‘non-communicable diseases (NCDs)’ [12-23]**

Agents	Cancers	Cardiovascular diseases	Neuropsychiatric disorders	Other non-communicable diseases
<b>Virus</b>				
Hepatitis B or C	Hepatocellular carcinoma,	Polyarteritis nodosa		Cirrhosis of liver Mixed cryoglobulinaemia, Nephrotic syndrome/chronic glomerulonephritis
Epstein Barr Virus	Burkitt’s B-cell Lymphoma, Nasopharyngeal cancer including Nasal T cell lymphoma			Rheumatoid arthritis SLE Multiple Sclerosis Chronic fatigue
Human immunodeficiency virus	Non-Hodgkin’s lymphoma, Kaposi’s sarcoma, Squamous cell sarcoma of urogenital tract including cervical cancer Genitourinary malignancy including seminoma & renal cell carcinoma Prostrate	Dilated cardiomyopathy	Dementia	

Agents	Cancers	Cardiovascular diseases	Neuropsychiatric disorders	Other non-communicable diseases
Human Papilloma virus	Cervix cancer, Vaginal cancer Vulvar cancer Anal cancer, Penile cancer Head and neck cancer, Oropharyngeal cancer (middle part of the throat, including the soft palate, the base of the tongue, and tonsils): Laryngeal cancer,			
Human T cell lymphotropic virus type I (HTLV-I)	Adult T cell leukemia/ Lymphoma		Tropical spastic paraparesis	Chronic fatigue
Enteroviruse - B—Coxsackie, Mumps, etc		Idiopathic dilated cardiomyopathy		Type 1 DM
Cytomegalovirus (CMV)		Atherosclerosis, Ischemic heart disease	Congenital mental retardation	
Rubella virus infection			Congenital rubella syndrome	
Adenovirus 36				Obesity
Human Herpes Virus 8	Kaposi's sarcoma, AIDS-related body cavity lymphoma			Castleman's disease
Herpes simplex virus		Atherosclerosis and ischemic heart disease	Bell's palsy Alzheimer's disease	
Parvovirus B19				Anemia, Rheumatoid Arthritis SLE
Measles			Subacute sclerosing panencephalitis (SSPE)	
<b>Bacteria</b>				
Helicobacter pylori	Non-Cardia gastric cancer, Gastric mucosa-associated lymphoid tissue (MALT) lymphoma			Peptic ulcer, Gastritis, Primary biliary cirrhosis, Sjogren's disease
Escherichia Coli 0157				Hemolytic uremic syndrome
Streptococci		Rheumatic heart disease	Sydenham's chorea	Acute rheumatic fever (ARF) Post-streptococcal glomerulonephritis (PSGN)

<b>Agents</b>	<b>Cancers</b>	<b>Cardiovascular diseases</b>	<b>Neuropsychiatric disorders</b>	<b>Other non-communicable diseases</b>
Streptococcus pyogenes			Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS: Childhood onset Obsessive compulsive disorder)	
Group A Streptococcus Agalactiae			Tics, Obsessive compulsive disorder	
Chlamydia		Peripartum cardiac failure (PPCF), Atherosclerosis Ischemic heart disease, Hypertension	Alzheimer's disease	Stroke, Asthma, COPD, Blindness, Reiter's arthritis
Yersinia spp.				Graves Disease, Reactive arthritis
Mycobacterium paratuberculae and tuberculae				Crohn's disease, Nephrotic syndrome, Chronic glomerulonephritis, Sarcoidosis
Salmonella spp.				Reactive arthritis, Nephrotic syndrome/chronic glomerulonephritis
Borrelia spp.			Bell's palsy,	Chronic lyme arthritis
Mycoplasma				Asthma, COPD
Bartonella henselae				Bacillary angiomatosis
<b>Parasites</b>				
Schistosoma haematobium	Bladder cancer (squamous cell carcinoma)			
Campylobacter Jejunia			Gullian Barre Syndrome	Reiter's arthritis
Plasmodium spp	Burkitt's lymphoma			Nephrotic syndrome Chronic glomerulonephritis Malaria nephropathy
Opisthorchis viverrinia	Bile duct cancer			
Chlonorchis sinensis	Bile duct cancer			

Agents	Cancers	Cardiovascular diseases	Neuropsychiatric disorders	Other non-communicable diseases
Toxoplasma		Peripartum cardiac failure, Dilated cardiomyopathy, Endomyocardial fibrosis		
Trichinella		Endomyocardial fibrosis		
<b>Fungi</b>				
Aspergillus	Primary liver cell carcinoma			Asthma, COPD
Dermatophagiodes				Asthma, COPD
<b>Epidemiological link and/or as a possible cause</b>				
Onchocerca volvulus and Simulium fly				Nodding syndrome (NS)
Enteroviruses		Hypertension, Dilated cardiomyopathy, Heart failure		

**Summed up newer concepts**

*Malignancy:* Microbial agents have been identified for Liver cancer, Burkitt’s Lymphoma, Nasal T cell lymphoma, Non-Hodgkin’s lymphoma, Kaposi’s sarcoma, squamous cell sarcoma of urogenital tract including Cervical cancer, Prostrate, Head and neck cancer, Anal cancer, Laryngeal cancer, Penile cancer, Vulval cancer, Adult T cell leukemia/Lymphoma, Kaposi’s sarcoma, AIDS-related body cavity lymphoma, Gastric cancer, Gastric MALT lymphoma, Bladder cancer (squamous cell carcinoma) and Bile duct cancer.

*Cardiovascular diseases:* Microbial agents have also been identified for Polyarteritis nodosa, Idiopathic dilated cardiomyopathy, Atherosclerosis, Ischemic heart disease, Acute rheumatic fever, Rheumatic heart disease, Peripartum cardiac failure (PPCF).

*Neuropsychiatric Disorders:* Microbial agents have been identified for Congenital mental retardation, Bell’s palsy, Sydenham’s chorea, Tics, Obsessive compulsive disorder, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS: Childhood onset Obsessive compulsive disorder), Stroke, Gullian Barre Syndrome.

*Other non-communicable diseases:* Microbial agents have been identified for Liver diseases like Cirrhosis of liver, Kidney diseases like Hemolytic uremic syndrome, Malaria nephropathy, Post-streptococcal glomerulonephritis, Nephrotic syndrome, Chronic glomerulonephritis, etc. Mixed cryoglobulinaemia, Rheumatoid arthritis, SLE, Type 1 DM, Congenital Rubella Syndrome, Obesity, Castleman’s disease, Anemia, Arthritis, Asthma, COPD, Blindness, Graves Disease, Reactive arthritis, Crohn’s disease, Chronic lyme arthritis, Bacillary angiomatosis,.

**Data abstraction and analysis**

A difficult question and one that should be frequently pondered not least because there is no definitive answer but many and, more importantly, we each have a way of defining it. This has been a challenge for contemporary philosophers. Perhaps it is Antonovsky’s Salutogenic model of health that poses the key questions and tries to explain using “the sense of coherence” framework. More empirical and objective ways of addressing what is health is associated with lack of health when it is lost in the ocean of disease [24-25]. Because a specific etiology usually get unnoticed for most human infections in clinical practice, many times we cannot follow them to the long

term complication to be forerunner of the chronic diseases [26-27]. In fact, certain non-communicable conditions are acute in nature, while certain communicable conditions require chronic, ongoing care. For example, HIV/AIDS clearly has an infectious aetiology but requires long term management by the healthcare system. As such, it has a great deal in common with type 2 Diabetes. Conversely, acute appendicitis is a “non-communicable disease” that requires an urgent health care response quite similar to bacterial meningitis [28]. The convergence of NCD and IDs is neither trivial nor transient; it represents a phase in the epidemiological transition that presents new challenges and new opportunities to enact responsive changes in policy and research. Integrating public health activities for ID and NCD should extend beyond health care services to prevention, which is widely seen as crucial to successful NCD control [29].

Public health responses to IDs and NCDs should be concomitant rather than mutually exclusive. Where IDs and NCDs are endemic, aligning prevention efforts, health education and health promotion could provide important benefits, such as in regions where both TB and diabetes are endemic. Screening and diagnostics should be coordinated by a clinical workforce skilled in preventing and treating both NCD and ID. Many IDs and their sequelae are chronic and like NCDs, demand long-term follow-up, treatment and care. This is certainly true for HIV/AIDS, as it is for chronic HBV, TB and some parasitic diseases. The convergence of NCD and ID in developing countries presents new challenges and new opportunities to enact responsive changes in policy and research. In LMICs, experts, institutions and policies that support prevention and control of these two overarching disease categories have limited interaction and alignment. NCDs and IDs share common features, such as

long-term care needs and overlapping high-risk populations. There are notable direct interactions between NCDs and IDs, such as the association between certain IDs and cancers, as well as evidence of increased susceptibility to IDs in individuals with NCDs. With some low and middle income countries now focused on major health system reforms, a unique opportunity is available to jointly address NCD and ID challenges with newfound urgency and novel approaches [30-31].

### Conclusion

We have extensively searched for the communicable agents of the non-communicable diseases. In the above mentioned table and discussion we have described those as detail as possible. In the light of present research findings we may conclude that many more disease agents will be discovered in the era of explosion of science and technology in this new millennium behind every disease which are today bound in the nomenclature of non-communicable diseases and probable anti-microbial cure as the downstream affect [32]. Someday may come when revival of ‘Germ theory’ of disease will enlighten to find pathogenesis of many more diseases and disorders are likely to provide the basis for new public health strategies.

We advocate a shift away from the “negative” term non-communicable diseases. The term “lifestyle related diseases” is sometimes used. In many ways we feel that the most appropriate advice would be to start widely to use the conventional term ‘Chronic diseases’. Some people prefer to add ‘Transmissible chronic diseases’.

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