EDITORIAL

Hidden spectrum of diseases and "case reporting"

Specific clinical diagnoses may be small visible parts of huge icebergs

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Disease (dis+ ease) is a term denoting to disorder (dis+ order) of function or structure in a living organism. It means feeling of inconvenience.

Well known and specific disorders are human-made classifications for better understanding, teaching, and optimization of management. In most instances classic descriptions of diseases are clear-cut definitions with widely accepted well demarcated margins. From this point of view any one may imagine specific and classic disorders as separate islands apparently apart from each other from a "top-down" view (Figure, top).
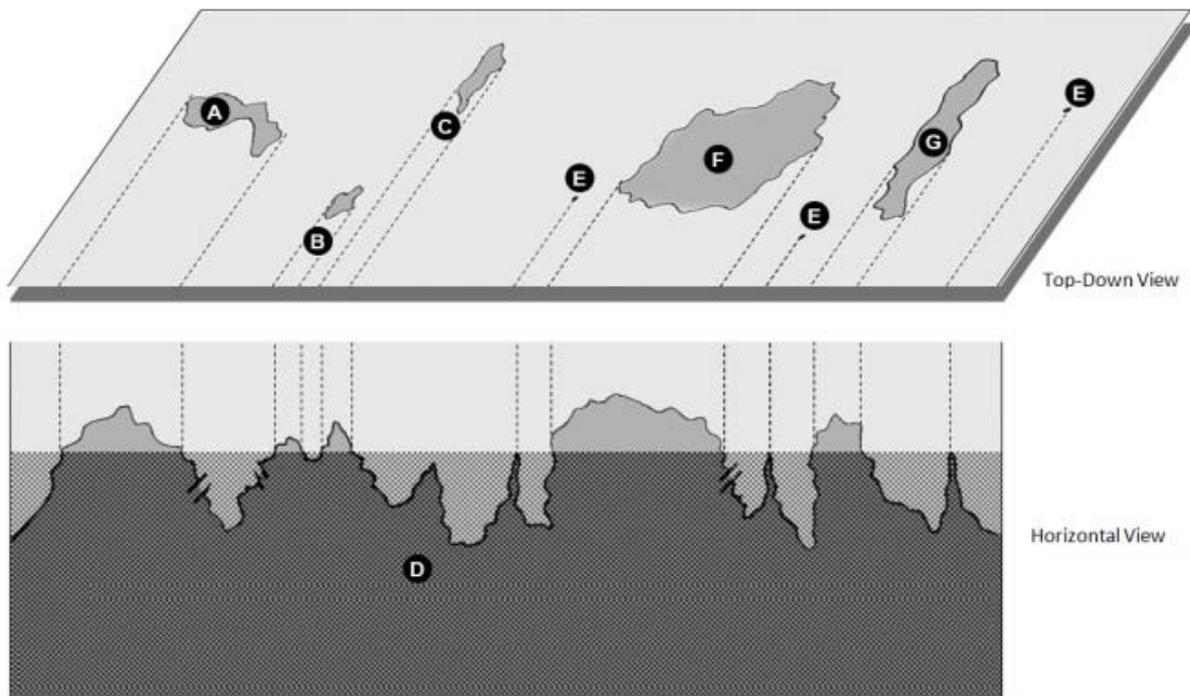

Figure. Proposed "*iceberg theory*" for diseases in rheumatology as an example. In top-down view, well-known diseases are shown as discrete islands (Top). In side view, the depth of realities is better shown, above and below the sea level (bottom). Letter 'E' indicates index cases which merits reporting. 'D' points to any undiscovered diseases. Other capital letters denote specific and well-classified diseases.

The International Classification of Disease (ICD) aims to provide a system of diagnostic codes to classifying diseases. It includes classification of awide variety of signs, symptoms and abnormalities to specific disorders. ICD is designed to map various health conditions to generic categories allowing for some minor variations. ICD evolved over time as medical knowledge advanced. However, the long

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period between revisions and fast advancement in medical knowledge demand for regular updates. This type of classifications are mainly proposed for epidemiologic or research purposes.[1]

There are major categories of disorders that may include developmental, genetic, infectious, traumatic, metabolic, degenerative, neurohormonal, psychological and autoimmune disorders. There may be some overlaps among them. For example, some developmental or metabolic disorders may inhere in genetic basis or some autoimmune disorders may be triggered by some known or unknown infectious organisms but the prominent feature of them are basis for their categorization.

Frequently we encounter undifferentiated connective tissue diseases (UCTD) supposed to be due to the lack of sufficient data to categorize a condition to a well-knowndisease based on diagnostic or classification criteria. Only small numbers of them evolve into a defined connective tissue disease.[2] Some may think that lack of our knowledge is the essential cause. However, from the point of holistic medicine, disorders from a single category have continuous rather than dichotomous values. From this point of view ("*horizontal view*") specific disorders are just tips of giant icebergs (Fig 1, bottom). Observing undersurface of them may disclose unexpected realities that definitely could not be eminent from "*top-down*" view. In classic approach to "non-classic" features of diseases we usually use the terms "abortive" or "incomplete" such as "incomplete lupus" or "incomplete Behcet's disease" while it could not be the case.

According to our current practice, many patients should be "patient" for months or years (if they last) until most doctors diagnose them while they get completed!

Many unusual or rare clinical manifestations, or single non-specific findings, which are pillar of "case reporting" and belonged to category of undifferentiated diseases. Undifferentiated diseases are debatable issues and matter of challenge among different medical disciplines. For example, unexplained elevated erythrocyte sedimentation rate (ESR) or fever of unknown origin (FUO) may be considered of infectious origin by an expert in infectious diseases or an autoimmune/ inflammatory disease by a rheumatologist or a hidden cancer by an oncologist.[3,4] Similarly, an unexplained pericardial effusion or myocarditis might be labeled as viral or "idiopathic" pericarditis/ myocarditis/ cardiomyopathy by a cardiologist, while a rheumatologist may label it as an atypical or single organ presentation of a connective tissue disease.[5] A similar story is true for weighting of different culprit mechanisms in producing single clinical setting. For example, inflammation versus atherosclerosis/ thrombosis in peripheral arterial diseases (PAD) is a matter of debate in critical organ ischemia.[6]

Diagnosis of vasculitis as a culprit mechanism of acute coronary syndrome (ACS) is seldom made by a cardiologist even in pertinent clinical setting. Almost all ACSs are managed in a rather similar approach in coronary care units. However, coronary artery disease is a known cause of death in some kinds of vasculitides.

Many clinical conditions were believed to be separate entities before rapid development of diagnostic tools and clinical skills in clinical practice. "Idiopathic" thrombocytopenic purpura (ITP) or thrombotic thrombocytopenic purpura (TTP) are discrete diagnoses by a hematologist while clinical spectrum and subtle manifestations of systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome (APS) or systemic autoimmune diseases are overlooked.[7] Another important finding that is subject to underemphasizing is subtle early skeletal manifestations of seronegativespondyloarthropathies (SpA) that seem very similar to Schmorl's node before high resolution MRI devices become available to market and clinical practice.[8]

Another example is the gray zone and disputable borders between osteoarthritis (as a prototype of degenerative condition and inflammatory arthritides) or neurology and psychiatry. Newly emerging specific and rather sensitive markers of inflammation such as anti-cyclic citrullinated peptide antibodies (anti-CCP or ACPA) and discovery of neuromediators clearly differentiated these overlapping conditions.

For years obesity was one of the major cause of mechanical joint diseases i.e. osteoarthritis. However, recent observations revealed obesity is a pro-inflammatory condition.[9,10]

On the other hand, many undiagnosed categories are labeled as psychological problems due to the lack of supervision on all aspects of medicine.[11] For more complexity, depression and inflammation have mutual relationship that may exacerbate each other.[12-15]

Noteworthy, some undifferentiated diseases remain uncategorized forever without any specific diagnosis was made.

With this classic approach we may lose the main body of enfaced problem. Thus a critical role of professors and trainers is to lead trainees to explore beyond the surface in order to see things which have never been seen so far. In this case, *holistic* viewing is the real *supervision*!

Taking together, many (but not all) of case reporting is the product of classic discrete view to the diseases and medicine at all. However, critical

reporting of important case reports is cornerstone of development in medicine when it created correctly.

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