

1958 : Nobel Prize for Medicine and Physiology was awarded to 32 year old Microbiologist, Joshua Lederberg, USA. His ideas enunciated later are hot topics today. 'Microbiome', then emerged in a collaborative human-microbiome "superorganism" study launched by National Institutes of Health, USA and European MetaHit consortium. What is Microbiome? Lederberg proposed that it was the sum total of all microbes (commensals and pathogenic) residing in human body mostly the gut, outnumbering 100 trillion, weighing approximately 2 Kg. Till recently they were regarded as essentially hostile to human hosts, thought to be perennial enemies, inviting "rampant" antibiotics. Our understanding has undergone a sea-change as we now know human genome contains 30,000 coding proteins-genes. This composite of microbial genome is 100 times larger. Together with 100 trillion microbes, their composite genes and our 30,000 constitute Metagenome. This emerging science has transformed our notions as we now begin to understand this "ecosystem"

within us that profoundly influences our health vis-à-vis disease.

Add to it, dynamic environmental factors and we will appreciate how microbiome can determine predisposition, manifestations of veritable diseases and consequently our treatment strategies.

CAUSE - EFFECT PHENOMENA

To prove, Koch's postulates must be convincingly addressed. A major stumbling block was inability to culture approximately 80% of all bacteria in our microbiome. However, DNA sequencing technology has revolutionized studies in Molecular Biology. Simultaneously, advances in Computational Biology along with Bioformatic tools have enabled us decipher the complexity of such microbial host-environmental interaction within us. (Figure 1)

CLASSIC EXAMPLE: HLA B27 PREDISPOSITION TO ANKYLOSING SPONDYLITIS (AS)

The association of HLA B27 gene and AS is far too well known. In Caucasians the gene is present in about 95%, in Asians about 70 – 75% of AS patients. The organisms most commonly implicated are gram negative, bacilli, eg.. Klebsiella, Shigella, Salmonella. Near identical mirror image cell surface antigenic structures of these bacilli and HLA B27 gene is a fine example of molecular mimicry. This can incite and signal to activate Th and TREGG pathways of the immune system complex signaling, inducing remote sacroiliitis as in AS, or reactive arthritis in HLA B27 patients (Figure 2).

Some subsets of HLA B27 are known to be predisposed to AS eg.27:02, 27:04, 27:05 and other subsets protect the host against AS eg. 27:06, 27:09. The Africans seem protected against AS, the Caucasians seem vulnerable.

TARGETED AND TAILORED P4 MEDICINE

Now many hospitals in India offer genetic profiling in an attempt to predict later disease manifestations. So far our thrust is to diagnose diseases and treat as per their organ involvement. eg. Angioplasty and CABS for episodes of myocardial infarction. About 90% of our investment in medical research and treatments seems towards attacking fully manifested diseases rather as they unfold, or predicted even before. Evidence Based Medicine (EBM) relies on data collection through a variety of studies localized or multicentric in specific, well defined disease subsets of patients with elaborate criteria of inclusion and exclusion. Conclusions if any are then extrapolated

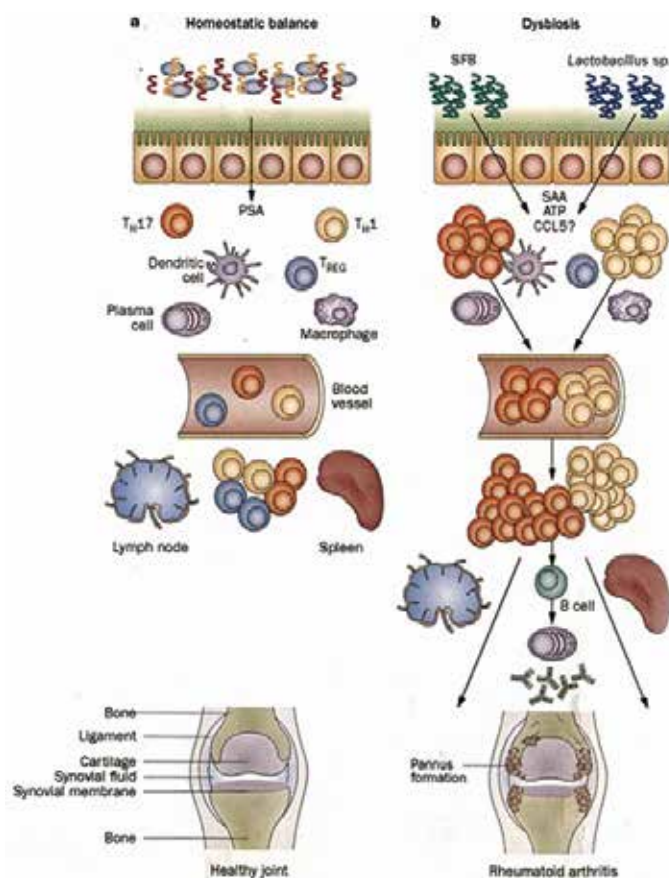


Fig. 1: Diagrammatic representation of microbes - rheumatoid arthritis link



Fig. 2: AS HLA B27 positive patient with marked bilateral sacroiliitis and hip joint narrowing.

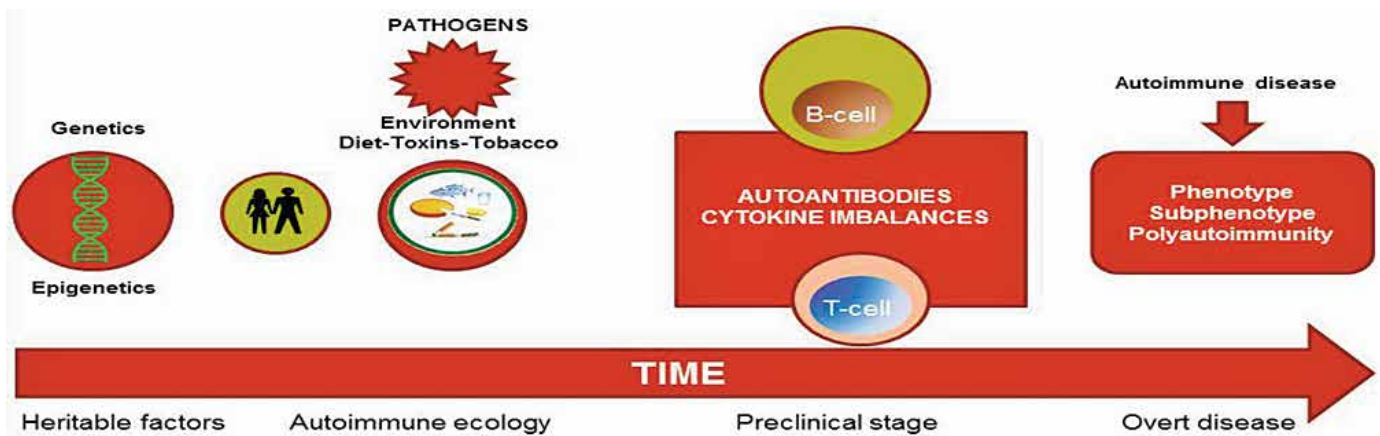


Fig. 3: Genetic, epigenetic, environmental predisposition to disease

into general recommendations presented commonly as ‘guidelines’, or algorithms. Such presumptions and premises are expected to be valid for any patient anywhere by the attending doctor who follows such guidelines to write standardized prescription, that is how most of us are prone to practice medicine daily ... through generalized treatment regimes naturally with highly variable treatment outcome.

A distinguished Immunologist Professor Leroy Hood, who won the prestigious Lasker Award in the U.S. and many more the world over, propagated the concept of P4 Medicine. He advocates that medicine should be Predictive, Preventive, Participative and Personalized. He further writes that new technologies available for studies in microbiome, genetics, metabolomics (metabolic end product of host microbe interaction) and meta-genomics can help predict diseases to come and install strategies to prevent. (Figure 3). He forecasts arrival of ‘Wellness Clinics’ with a thrust on preventive and a holistic approach to individuals with targeted and tailor-made treatments. He believes that this will result in not only high strike rates of treatment outcome but also heavy reduction in treatment budgets minimizing need of high-end, high cost procedures such as organ transplants, bypass or even joint replacement surgeries.

P4 MEDICINE FOR THE MASSES

Computational Biology centres with high capability to collate mass data, dissect and analyze mathematically into reproducible observations, treatment outcome is on the anvil. An individual patient and / or his physician can log in symptoms / signs, investigated reports into a Computational Biology centre to generate and transmit prescriptions. Already 15% of Rheumatoid Arthritis patients in the U.S. have gone a step further and asked for prescribed drug delivery at their doorstep online... sparking a debate on the merits and inherent risks.

MEDICINE AND THE TELECOM REVOLUTION

Taking microbiome, meta-genomics and P4 medicine to the masses allow democratization of Medicine perhaps akin to ‘Obamacare’... via mini gadgets such as smart phones. I have had some patients even from remote villages showing before and after pictures of diseases they or their folks suffer from on their cell-phones. Are not laboratory reports shown to us on ‘WhatsApp’? Don’t increasing number of patients located elsewhere expect “cellular” treatment advice ?

Isn’t telemedicine eroding and cutting down clinic visits of patients? Aren’t ‘Dr. Apple’ and Dr. Google (Figure 4).



Fig. 4: Doctor Apple & Google

'Dr. Google' taking charge of some of our medical practices? Isn't the traditional Holy Grail.

Doctor-patient relationship in peril?

This relentless march of technology is impacting our patients and us doctors every day. This surely facilitates our daily work. eg. scanned reports are transmitted right away on our gadgets from imaging centres. That's good for us; but what when patients expect our prescriptions and advice to be sent on their tools or download direct from internet without having to visit us? Don't we see abuse, misuse, falsehoods and serious errors in medical practice by gullible patients, as we lose our authority to treat our patients ourselves? Is there still room for patients to visit us for that healing touch? In the era of driverless taxis are 'doctorless' clinics in the offing?

Surely for surgical patients this is inevitable despite robotic surgery. As for physicians we have got to adopt, adapt, be adept and accept these new turns and twists of science if we insist that patients must visit us at our clinics in their interest ... and ours.

A MISSING GAP

Today, such new technologies are invented by a new generation of scientists in their laboratories of physics, mathematics, engineering, bioengineering and computer sciences. Are they alive to the needs of our patients? Are we in a position to open a dialogue with them at the start and not at finish? When will our medical conferences, our textbooks and medical curricula incorporate courses of these nascent sciences heavily influencing our ways of medicine and life? Are we ready for this brave new world of relentless march of science? Will we be swept off our feet or ride the change?

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