GENOMICS AND SOCIETY
Ethical, Legal, Cultural and Socioeconomic Implications

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CHAPTER 14

Genomics and Traditional Indian Ayurvedic Medicine

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INTRODUCTION

With rapid advances and new developments in genomics and related ‘omics’ fields, the medical and healthcare practices globally are under pressure to plan and implement effective changes in the current modern and traditional medical practices. This is not only to meet the challenges in diagnosis and treatment of rare and common
chronic and complex medical diseases but also to address the variability in therapeutic outcomes and develop effective and efficient public and population health strategies.

The advent of genomics has provided a tremendous impetus to bring much needed changes in the current medical and health care practices. However, there are a number of challenges before this could be implemented. A number of countries notably China (see Chapter 15) and India are leaders in this endeavour. Ayurveda, the ancient traditional Indian system of Medicine is probably best suited for this paradigm shift. Its concepts and approaches closely matches to the contemporary predictive and personalized medicine practice and fulfills the core principles (P4)—predictive, preventive, personalized, and participatory—medicine and probably also has a promotive component.

The Ayurveda has documented proven methods for maintenance of health and personalized management of chronic diseases. It is also widely practiced in most Indian communities despite sociocultural variations and many aspects for preventive health are also integrated into Indian traditional living. Despite this a large number of challenges exists in getting this system to mainstream and for its global acceptability. This chapter highlights some of these aspects in the genomics context and proposes a novel ‘omics’ field, the Ayurgenomics as a new paradigm for modernizing the current medical and health practices with global applications.

**NEED FOR A PARADIGM SHIFT IN MODERN HEALTH CARE PRACTICE**

The western medicine system, the allopathy, forms the mainstream of global health care system. Discovery of antibiotics and a number of vaccines in the twentieth century, have led to successful eradication of huge number of microbial diseases. In addition, technological advancements in imaging, surgical, and diagnostic as well as life support devices have led to a substantial reduction in morbidity and mortality. These have been the primary reasons for its wide global acceptance as it has hugely reduced perinatal. Infant, maternal and adult mortality as is evident from average increased life expectancy. Perhaps a good example would be the early detection of chromosomal anomalies and inborn errors of metabolism in genetic programs for carrier and prenatal screening reducing the burden of common inherited, for example Down syndrome, cystic fibrosis, sickle cell anemia, hemophilia, beta-thalassemia, Tay Sachs disease and other metabolic diseases. In addition, detection of late onset monogenic disorders and syndromes such as cardiomyopathies, muscular dystrophies, etc. is now possible and adopted in many public health programmes.

In the recent times, with the capability to sequence an individual’s complete genome at a very affordable cost, the catalog of human genetic variations associated with Mendelian diseases has seen a steep rise [1–5]. The most exciting potential has been realized in the area of pharmacogenomics where now in many cases it has been become possible to predict responsiveness/nonresponsiveness to therapy using genetic markers [6,7].
This has been useful in predicting the outcome of different cancer therapies, use of warfarin, clopidogrel, etc. or managing the dosage of drugs that are used in chronic ailments and have frequent side effects [8–12]. However, management of common and chronic diseases still remain a challenge especially in the contemporary times as there is a threat of a global epidemic of lifestyle disorders. Compounded with an increase in number of aging population this now threatens the economics of health care management systems even in the developed countries. A major focus besides reducing the burden of disease is now on maintenance of quality of life both in health and disease through preventive interventions. There are also a number of other challenges that has highlighted the need for a paradigm shift in the current practice of modern medicine [13,14].

**Challenges in Diagnosis and Treatment**

In the allopathic system, classification and treatment of the disease is primarily on the basis of the principal organ or body system that exhibits major signs and symptoms of the disease. The disease is established by measuring gross anatomical pathology, histopathology, or a biochemical test. Diseases are given a nomenclature either based on the organ system or into syndromes if it encompasses a defined set of clinical features. Syndromic classification restricts the clinical phenotypes within a set boundary and also creates artificial boundaries between two diseases which might share the same origin and have overlapping sets of clinical features [13–17]. Also this is ascribed as a cause of ineffectiveness of drugs in a large spectrum of affected individuals since during clinical trials the recruitment of subjects are based on the primary set of features that are used to describe the syndrome. A patient on the basis of the overt symptoms most often approaches a doctor who specializes in the treatment of a specific organ system. Since the treatment and success of treatment is also causative and feature centric this approach not only limits treatment options but also does not heal the system holistically. It is being increasingly acknowledged by practitioners that most of the diseases exhibit clinical and population level heterogeneity and there is a need for methods that would enable delineating the phenotypic variation within a disease.

**Variability in Therapeutic Outcome**

Majority of the treatment procedures are targeted toward curbing the activity of the disease by a drug that either kills the pathogen/curs the activity of the biomolecules that are elevated or by chemotherapy or radiotherapy which restrict the growth of proliferating cells. A last resort is surgery which removes the affected part is acknowledged that there is an enormous variability in success of treatment with respect to disease and individuals. As a result, only a finite set of diseases are entirely cured from the root cause. A majority of chronic diseases require medication throughout the lifetime of an individual and in diseases such as cancer and infectious diseases recurrence or
resistance to drugs respectively are quite common. With the increase in life expectancy in most of the population, the cost of health care especially in chronic diseases is unaffordable for a large fraction of the population. Coupled with this, the quality of life is severely compromised due to the side effects of lifetime medications as well as other therapeutic and surgical interventions. The inability to predict the progression and prognosis of the disease in an individualized manner and also the management of the side effects of the therapeutic interventions are additional challenges.

Preventive Measures in Health and Disease

A third aspect is with respect to the preventive measures that are currently available. Prevention has been mostly successful by vaccination for common infectious diseases as there is increasing emergence and spread of new viruses and emergence of new multiresistance pathogens. The list of vaccinations in children as well as the number of drugs that an individual has to take in a complex disease seems unending. Evolving lifestyle recommendations for disease such as diabetes mellitus and metabolic disorders is still in infancy as the genetic and epigenetic causes of these disorders are not fully established. Moreover the recommendations of lifestyle practices which are deemed important in different diseases are mostly generic and restrictive in nature. For instance, excessive restriction of carbohydrate in a person with diabetes or fat and salt restriction in hypertensive/cardiatic patients is mostly arbitrary as it is generally inferred that the amount of consumption would be proportional to the disease severity. A major caveat of this system is limited applications of individual aspects in terms of predisposition, susceptibility to disease as well as responsiveness to treatment and management.

ADVENT OF GENOMICS IN PERSONALIZED MEDICINE

The primary goal of the human genome project was to provide complete sequence of a reference human that would be a reference genetic blueprint for predictive and personalized medicine [18,19]. It was envisaged that understanding of the human genome would allow discovery of predictive markers that could enable assessment of genetic risk to diseases and identification of actionable points for interventions, prognosis of disease, genetic modifiers, and drug targets as well as markers for assessing the responsiveness to drugs, diet, and lifestyle. This is the primary objective of predictive, preventive, personalized, and participatory (P4) medicine [20,21]. Identification of predictive markers in the area of pharmacogenomics as well as in the discovery of specific gene variants and mutations for many monogenic disorders has helped in preventing and reducing the burden of disease. However, there are a number of challenges and we still have a long way to go. Recently, an ambitious genomics-based project was launched where nearly a million people are anticipated to participate in a prospective study [22]. The dynamics of health as well as deviations from individual participant's baseline would be monitored
through sequencing an individual's genome one time as well as the transcriptome and biochemical markers a couple of times over a period of 2–3 years. It is anticipated that this would allow detection of individualized actionable points for interventions and herald a new era of preventive and precision medicine.

However, as more and more complete genome sequences become available from different populations across the world, the definition of human genome in terms of what would comprise as a reference is becoming elusive. There are now nearly 38 million single nucleotide polymorphisms (SNPs), 1.4 million in-dels, 14,000 deletions and 20,000 structural variations represented in the variation databases [23]. The frequency of these variations differs between populations and among individuals as a consequence of migration, admixture, natural selection, pathogen load, or cultural practices [24–32]. These give rise to enormous combinatorial possibilities whose effects impact the entire system [33–41]. There is a further impact of environmental and epigenetic changes and also the enormous human microbial diversity on the phenotype of an individual [24,27,42–48]. Each individual is thus an ecosystem harboring a unique subset of variations and the phenotype of an individual is the net outcome of the ecosystem. This unanticipated extent of human genome variations has nearly ruled out the possibility of defining or reconstructing a reference healthy human from mere reading of the genomic sequences [23,49,50].

A comprehensive assessment of individuality that encompasses different systems and connects it to outcome in health and disease and their relation with personalized therapeutics is not yet available. A primary challenge remains in first defining a healthy individual as we still use disease state as a reference for defining health and not health as a reference point since there are no comprehensive methods for stratifying healthy individuals. It is well acknowledged that 1–5% of the population is at risk of one or the other complex disorder and also the frequency of any monogenic disorder if we consider all the Mendelian disease genes is also 1%. The hope is that if we were able to identify these predisposed individuals at preclinical stage, prevention and management of disease could become much more tractable and so also the burden of the disease could be reduced substantially in Mendelian disease through early interventions. Most of the genetic markers discovered till date are not useful as predictive markers in preclinical stage.

**AYURVEDA: ANCIENT INDIAN SYSTEM OF MEDICINE**

**Contemporariness of the Practice as P5 Medicine**

Ayurveda is an Indian system of life sciences, documented, and practiced since 1500 BC with personalized approach to predict, prevent, and promote the state of health in healthy and alleviation of disorder in the diseased [51]. Understanding of human individuality through assessment of his/her constitution type forms the fundamental basis for P5 medicine. According to Ayurveda an individual is born with a
specific constitution *Prakriti* that not only determines his overall phenotype but also predicts the susceptibility to diseases and responsiveness to extrinsic and intrinsic [51–54,54a]. Ayurveda describes the subject matter through “TRISUTRA,” meaning the three interconnected axes of causes (*Hetu*), features (*Lingga*), and therapeutics (*Aushadha*) both for healthy and diseased person [51,54]. *Hetu*, the causes of diseases documented are from the lifestyle, dietary regimen, and thought process that affect the behavior of various metabolic pathways. These are noticed as signs and the alteration of disturbed metabolic pathways is done with natural interventions from required adjustments in lifestyle; dietary regimen, detoxification with *panchakarma* therapeutics, use of herbal compounds depending on the nature and state of disease and strength of the diseased compared to the level of baseline health state of the person. It also takes care of particular geo-climatic environmental variations during treatment.

It is an often asked question as to how a system of medicine which was practiced 5000 years back would be relevant even today since some of the diseases seem to be the effect of modern day living and unlikely to have been observed in the ancient times. It might be worthwhile to mention that population genomics methods that has substantiated the evidence for existence of humans for nearly 100,000 years has also allowed us to trace the origin and spread of diseases across the world and many of the infectious disease have been traced to be old as 8000–10000 years back [55]. So it is not inconceivable that 5000 years which would be substantially recent in evolutionary terms, these diseases would have been nonexistent or not prevalent in India. Some of the founder mutations linked to diseases reported in Indian populations are also shared with African and other world populations [56]. Surprising as it may sound the phenotypic features of most of the diseases that are described contemporarily have descriptions in the ancient texts. The similarity is more at the feature level than at the syndrome level. The practice covers all the aspects of P4 with an additional promotive component (P5).

- Prediction of disease susceptibility and responsiveness to diet, drug, and environment in an individual right from the time of birth
- Prevention through identification of actionable points for early interventions
- Personalized based on an individual’s constitution in health and diseased condition
- Promotive for optimizing the homeostatic and rejuvenating potential of the system
- Participatory through engagement of an individual in his/her own health management through awareness and proactive reporting of the same.

**Potential of Ayurveda in Chronic and Complex Diseases**

Potential of the Ayurveda in the treatment of chronic and complex lifestyle originated disease has been realized world over. There are reports mentioning use of Ayurveda by ~60% of the world populations at some point of time or the other during the treatment of these diseases. Ayurveda describes the methods of deciding the line of
treatment after assessing the prognosis of a disease. All diseases are classified into subtypes based on their being curative or palliative nature which is further decided on the basis of strength and severity of disease as well as that of an individual's strength. Most of the times for chronic and complex diseases a patient approaches an Ayurveda physician with an ongoing allopathic medical treatment. Ayurveda physician treats every individual based on the subtype, stage, and chronicity of the disease, patient's constitution with additional consideration of outcome of the ongoing treatment. In general, it is observed that when an individual adopts Ayurveda there is an improvement in the quality of life with a better control of the disease with ongoing allopathic medicines. Not only this, a fraction of the patients get cured and also a large majority can get better control of disease only with Ayurveda treatment. In a number of instances, for example in case of thyroid problems though the level of thyroid can be reduced by modern medicines sometimes the primary causes for which a thyroid test is conducted such as problems of dryness of skin, constipation, muscular pain, frequent attacks of cough and cold, anxiety are not alleviated. It has been observed that a combination therapy of Ayurveda along with modern medicine can alleviate or totally cure all the problems in 1–3 months. Ayurveda has also been useful in treating asthma, diabetes, diabetic nephropathy, chronic heart failure (CHF), high blood pressure, thyroid, hypercholesterolemia, fatty liver diseases, psoriasis, chronic sinusitis, migraine, rheumatoid arthritis, gout, multiple sclerosis, Parkinson's disease, Alzheimer's disease, prostate enlargement, paralysis, etc.

It might be worthwhile to mention that most of the discoveries of drugs such as levodopa, reserpine, chloroquine, aspirin, codeine, vincristine, vinblastine, bromhexine, digitalis, etc. have their origins in Ayurveda [57–61]. Besides, the same source herbs are used to treat these diseases in Ayurveda. Knowledge of usage of the herbs, their method of preparation, formulation, and routes of administration for different diseases is extensively documented in Ayurveda and is also available in Traditional Knowledge Digital Library developed (http://www.tkdl.res.in/) and maintained by the Indian government. In some cases where it is not possible to cure the disease, food regimen/therapeutic diet/daily usable herbal products can help maintain their healthy state along with the advised lifestyle changes. There are some diseases for which there is hardly any treatment available in modern system of medicine, like inflammatory bowel disease (IBD), ulcerative colitis, NAFLD (Nonalcoholic fatty liver disease), some viral diseases like Hepatitis B, Hepatitis C, etc. where people seek Ayurveda as an option.

Principles of Ayurveda in Practice

Human Individuality as a Primary Basis

Understanding of human individuality through assessment of his/her constitution type forms the fundamental basis for P5 medicine. According to Ayurveda an individual is born with a specific constitution Prakriti that not only determines his overall
phenotype but also predicts the susceptibility to diseases and responsiveness to extrinsic and intrinsic environment [53,54]. Prakriti is determined by the relative proportions of three physiological entities Tridoshas in an individual which forms the common organizing principle. The three entities Vata, Pitta, and Kapha govern and determine the kinetic, metabolic, and structural components of the system respectively that are established at the time of birth and remain invariant throughout the lifetime in an individual [51,53,54,54a]. The ethnicity, geography, heritability, age of the transmitting parents, and intrauterine conditions contribute to the relative proportion of Tridoshas in an individual and determines the constitution type of an individual. This can be assessed through a comprehensive analysis of anatomical, physiological, metabolic, and psychological attributes. Individuals of a population can be broadly stratified into seven broad constitution types Vata, Pitta, Kapha, Vata-Pitta, Pitta-Kapha, Vata-Kapha, and Vata-Pitta-Kapha based on the relative proportions of doshas [53,54]. There is a broad continuous spectrum of healthy states in which individuals fall and can be categorized into some groups with three of them described to be at the end of the spectrum. Any perturbation from the baseline state of doshas in a particular constitution type leads to diseases and the purpose of Ayurveda interventions is to bring back the doshas to the homeostatic threshold. Though the proportions of doshas are invariant in an individual, they fluctuate within an allowable range during different times of the day, season, and age of an individual. These are taken into account during Prakriti assessment. Their levels could also be modulated by geo-climatic conditions, food, and drugs as each of these are also described to impact levels of different doshas [54a].

**Maintenance of Health**

Dynamic state of health is maintained through personalized recommendations of diet, exercise, rest, sleep, and other lifestyle practices including yoga with respect to time and amount based on an individual’s Prakriti considering his/her age, place, season, etc. This also includes special care of all body orifices including skin as well as periodic cleansing of entire body during the rhythmic peaks of VPK (Kapha during spring; Pitta during autumn, and Vata during monsoon season) to prevent accumulation of excess toxins and other excretory metabolites. This is carried out following specific protocols which includes a preparatory phase for the system to expel out the toxins, followed by a post procedural care that ensures the proper restoration and rejuvenation. This preemptive approach of Ayurveda toward maintenance of health is aimed at preventing the manifestation of diseases to which an individual is predisposed [51,54a,62].

Ayurveda ad vocates special types of therapy (Rasayana and Vajikanana) for enhancement of regenerative potential and reproductive health of an individual. These therapies are administered only after cleansing the body of toxins, and accumulated Tridoshas. By definition, this therapy is meant to enhance the strength and robustness of the systems by augmenting their cellular functions. It improves the
higher functions of brain and mental faculties like cognition, memory, speech, intelligence, etc. It thus acts as a preventive therapy for aging and age-related disorders, increasing the longevity in an individual. This at times is also administered in the advanced stages of diseases where the recovery from them is expected to come through tapping the regenerative potential of the system rather than through corrective mechanisms of drugs [31,54a,62,63].

**Personalized Management of Diseases**

The descriptions of the diseases are in terms of perturbations of Vata, Pitta, and Kapha and their manifestation in various systems. Classification of diseases is not organ based in Ayurveda, although all the organs are documented in the text and also in the respective diseases pathophysiology. The aim of treatment is alleviation of disorder in the manner that does not provoke the pathogenesis of others or disturb the healthy tissues. Ayurveda describes clinical examination points pertaining to disease and diseased, by physician in order to analyze not only the nature and strength of disease, but also that of the diseased to select the line of treatment and decide if the therapy and the drug as well as dosage advocated for the treatment would at all be tolerated by him. Thus a triad of drug, disease, and diseased is analyzed to arrive at the right combination for an individual [54a].

- Examination of variables related to disease includes clinical presentation with subtypes, severity and stage, strength and multiplicity of triggers, etiological factors of disease—extrinsic and intrinsic
- Affected individual related—baseline—Prakriti, suitability toward therapy and drugs, and age
- Present status of health—physical, psychological, and individual’s present status of metabolism and waste clearance organs, including external environmental factors like geo-climatic and time.

**Indian Traditional Living**

Traditional medicine is very much the part as a domestic remedy in Indian society where locally available herbs are used to treat various diseases and usually this knowledge is acquired with the use in any of the family or community. Some of the modalities of preventive treatment recommendations of Ayurveda have become a part of kitchen in every house of Indian sub-continent as herbs and spices.

These are used in traditional preparations to impart flavor and have led to an extensive diversity of food across the country. Usage of herbs and spices in food ensures maximization of the range of nutrients consumed on a regular basis as well as increased consumption of vegetables through a variety of preparations. Besides, the usages of these herbs have also been demonstrated in decreasing food poisoning as well as protection of the food from early decompositions. Similar to the medicines
described earlier, their usage may differ with the sociocultural and geo-climatic conditions however their usage is universal. The most common herbs are turmeric, cinnamon, cardamom, cumin seeds, dried ginger, pepper, red chilies, curry leaves, and use of rock salt. These herbs and spices have been described for their medicinal properties in Ayurveda [51, 62, 63]. Most of them have been scientifically proven to be effective in prevention of various allergic, metabolic, cognitive, and degenerative disorders all of which are closely associated with increased oxidative processes [58, 64, 65]. Limited clinical trials in humans as well as extensive studies in animal models have revealed the antioxidant as well as anticarcinogenic properties of herbs and spices [65, 66]. For instance, in cancer it has been shown that a pro-inflammatory stimulus leading to increased oxidative stress could result in DNA damage, breaks in chromosome, telomere shortening which ultimately leads to chromosomal instability and increased cancer risk [42]. These pro-inflammatory stimuli also activate mitogen activated protein kinase leading to activation of NFkappa B which in turn increases the expression of cyclooxygenase-2 resulting in cell proliferation and increase cancer risk. Herbs and spices have been shown to inhibit many of these steps of carcinogenesis. Other herbs such as garlic have been found to be useful in atherosclerotic conditions and blood clotting, ginger in alleviating arthritic knee pain and is considered as a nonsteroidal anti-inflammatory alternative to ibuprofen, etc. [58, 67]. Thus herbs and spices which have been used since ancient times not only in India but in other ancient civilizations would be what is considered as a part of functional foods in the contemporary times.

Besides, as a part of routine practice, regular breathing exercise and yoga, meditation, social functions, fasting, long walks by way of annual pilgrimage and a routine in sleep and dietary practice during different times of the year have been advocated and practiced in traditional households as cultural practice since centuries.

**Practice of Ayurveda in Most Indian Communities Despite Sociocultural Variation**

Ayurveda is practiced across the Indian sub-continent and nearly 70–80% of rural India uses it as the preferred primary health care system. On the other hand, in urban settings where people have access to modern allopathic medicine avail Ayurveda for cases where there is little or no help from modern medicine is available, for example in chronic and complex diseases as well as terminally ill patients with no relief possible from allopathy. In contrast to modern medicine, the globalization of the Ayurvedic practice entails adjustment for geo-climatic and sociocultural variations for better suitability. Thus, so far as principles of understanding the disease, their diagnosis, and treatment are concerned there is not much difference across communities. Ancient classical texts, Charaka and Shushruta Samhita are followed by physicians across the country. However shorter/easier compiled versions like Ashtanga Samgraha, Ashtangahridaya, Sarangdhara, Madhava, and other about 12 Nighantus and Bhaishajya
Ramavali, Chakradutta, Sahasrayoga, etc. have been developed in different parts of the country to make it easier to understand and practice with the need of time. In clinical practice, in the southern part of India most of Ayurveda institutes including pharmacies use Sahasrayoga as reference text, in western part Ashtanga Hridayam is commonly followed whereas northern part of India Charaka Samhita and Bhaishajya Ratnavali remains main texts of reference. Thus when it comes to delivery of health care and recommendations for healthy life, different communities use Ayurveda with some variations to suit biological requirements of those populations based on geo-climatic conditions and sociocultural practices. The variations are also sometimes noted because the same medicinal preparations are called by different names in different communities. Also the variations are not always done in the choice of medicines rather there are different formulations/dosage forms developed from same combinations. For example, medicated oils and decoctions are more common in south India than in northern or western parts of India, whereas in northern India preferred formulations are easy to take dosage forms like tablets, capsules, etc. It would be worthwhile to mention that Ayurveda’s claim of being a personalized medicine matches with the descriptions of diverse ways in which the same disease can be managed in order to suit the person in a particular place, age, and strength.

In an attempt to make Ayurveda treatments acceptable, modern diagnostic methods are also integrated by Ayurveda physicians in their practice as they provide clinical, biochemical, or radiological markers that are helpful in monitoring the disease as well as effect of treatment. Although this also has its disadvantages as the limits of diagnostics would be limited to the extent measurable or defined in the modern times. A very illustrative example is diabetes which is commonly measured by blood sugar levels. In Ayurveda, diabetes is classified as one of the subgroups of a class of diseases under Prameha and in this class, subtyping of the subject besides clinical evaluation is also carried out by looking at the properties of urine in terms of color, odor as well as the dispersion behavior (specific gravity) of a drop of oil in urine of the subject. In modern language it could well be the outcome of metabolites in the urine which had been used for diagnosis and measurable by metabolomics. In the prevalent practice of Ayurveda, in majority of the clinics the ancient practice of detection has been replaced by blood sugar estimation.

**GETTING AYURVEDA TO MAINSTREAM**

**Perception of the Common Man**

Understanding and awareness about the practice of Ayurveda is not uniform across the cross section of population including common people both from rural and urban background, modern medicine practitioners, academic and research faculty, public health scientists as well as policy makers. A clear demarcation does not exist in the
mind of people of what is herbal, traditional or Ayurvedic and therefore all these are perceived similarly. This has created a collateral damage since the perception has propagated the belief that anyone can practice Ayurveda, any herbal medicine off the shelf is Ayurveda and a recommendation from a neighbor who had a success with some medicine can be taken without consulting a clinician. Since Ayurveda-based herbs are used as spices as well as medicines, when used as latter, the recommendation has to be made under clinical supervision is not very evident to a common man. The most common perception about Ayurveda in western world is that it is a kind of traditional knowledge maintained and passed on as a grandmother’s recipe. This mind set prevails because of the ignorance about the existence of its extensive documentation and scientific literature. Although originally written in Sanskrit, translations in several languages are available today. At times practice of Ayurveda is also equated with the practice of Hindu religion since all ancient Indian literary work including religious texts referred in religious ceremonies of Hindu household are also written in Sanskrit, which was the prevailing language of that time. Over the last 100–150 years, this system of medicine which was once mainstream is now the ‘alternative or complementary system’ of medicine. There are historical, socioeconomic, and political reasons which can be ascribed to these gradual loss of connection of modern Indian community with this system of medicine. Today, most often exposure to Ayurveda in school is through a general knowledge question related to Charaka and Sushruta from ancient India. The prevailing perceptions shrouding Ayurveda also emanates from a lack awareness of its success stories. These are not available in mainstream in a way that a large section of society can understand and acknowledge the practice. At this point recommendations are more by word of mouth, by claims of practitioners or in some cases of prominent personalities who are not qualified Ayurveda practitioners but can influence a large section of society.

Acceptability of Ayurveda in Health Care

Attitude of the Patient

In most cases, a patient approaches an Ayurveda practitioner in an advanced stage of a disease when the cost of treatment become prohibitive or living with the disease affects the quality of life. The hope and anticipation from the system is for a safe, speedy, and permanent cure.

However, the approach to adopting this system is taken with mixed apprehensions stemming from awareness about the potentials on one hand and the belief created by studies which has demonstrated the presence of heavy metals in Ayurveda products. Another aspect which has also got into our mindset is our faith that a long prescription of drugs can only cure the disease or that an overcrowded medical hospital only demonstrates that people are getting healed. The importance of adopting changes in lifestyle practices, for example in diet and lifestyle routine as well as exercise is
secondary. Since the practice of Ayurveda encompasses a combination of medicine and change in lifestyle practices which is very much closer to our traditional lifestyle, it does not sound contemporary and patients are willing to adopt only the prescription part of the practice. Now with the social media in place where it is possible to do a google search for anything, many are still not able to get a satisfactory answer as to how this medicine can claim to cure cold and cancer and that too by the same practitioner; why would one get treated by such an ancient system when already state-of-the-art systems exist in modern times; how could a system be expected to be successful when it has not worked in big hospitals; why the aid of modern diagnosis for Ayurveda practitioners and more importantly how it could treat diseases which might not have been described in Ayurveda since these are emerging diseases and unlikely to be present 5000 years back. There are no ready references available to connect the modern and Ayurveda sciences. Also even if none of the modern medicines is known to cure a chronic illness for instance diabetes, asthma, Parkinson’s, rheumatoid arthritis and cancer, most patients often do not question the curability of the modern medicine. However, this is the first question that is posed to an Ayurveda physician and there is a need for reassurance for the same from the practitioner about a permanent cure before the patient avails the treatment.

Another aspect often encountered is when an individual patient takes both Ayurvedic and modern drugs, the clinician might not be aware of this since in most cases this information is not shared. Whilst the Ayurvedic practitioner might have some knowledge of the nature of modern drug, in most cases, the modern western style clinician would be unlikely well informed. It is also perceived in general that since Ayurveda is an herbal-based medicine the cost of treatment should be very low whereas sometimes it is observed that is not the case. There could be more than one reason for the same. One, some of the Ayurveda herbs used for treatment of chronic diseases are not readily available and also the methods of preparations of formulations are not trivial. In most chronic and complex disease, for personalized therapeutic interventions it may be required to prepare medicine for the given patient, which might make it more expensive. However if the overall cost of therapy is evaluated against its outcomes in terms of recovery or prevention of complications that might require costly medical care and/or hospitalization, improvement in quality of life, abstinence from work for the patient as well as family attending to the person, etc., it may be found that overall cost of treatment becomes much lesser. This would also be true in case of treatment that aims toward maintenance of health and prevention of disease to which an individual may be predisposed or for better quality of life so as to prevent future therapeutic interventions, frequent hospitalization and loss of work hours. Thus, one needs to consider the higher cost of treatment vis-a-vis the type of health conditions Ayurveda caters to along with the overall outcomes.
When diagnosed with a complex and lifestyle related disease, a substantial fraction of people who are aware of the outcomes of disease and treatment, opt for Ayurvedic treatment. They take this decision with the understanding that Ayurveda treatment will have no or less number of side effects even when taken for long time. Also many of them are ready to adopt lifestyle and dietary changes that could help contain the disease. In fact, some patients in their own words say that in spite of not having much difference in the levels of blood sugar they feel healthier. Some patients are also relieved of the fact that the generalized recommendations that follow after a diagnosis of a disease for instance no exercise on treadmill because of tiredness or avoiding sweets in chronic diabetes can be managed to a large extent by combining treatment with Ayurveda. In some cases after a long usage of Ayurveda drugs along with modern medicine, patients are prevented from progressing to complications of the disease for instance progression to fatty liver diseases due to poorly controlled cholesterol levels even after a long usage of cholesterol lowering drugs. In this category, many people have a family history of disease and therefore seek such ayurvedic medicines as a preventive measure/or at least help in delaying the process of occurrence of that particular disease by adopting a biological required lifestyle and dietary guidelines to minimize the chances of occurrence of diseases guided by Ayurveda physician.

Yet another fraction of individuals adopt this system as a last ray of hope. There are some diseases for which although treatment options are available in modern medicine like surgery or chemotherapy in cancer or switch from oral hypoglycemic drugs to insulin in case of poorly controlled diabetes, dialysis in chronic renal failure or steroid therapy in multiple sclerosis, patients are unwilling to go in for these options and resort to Ayurveda. Among all these conditions there are times when a stage comes, that there is very little survival time left and no hope available from modern medicine side, patient think of Ayurveda for ease of life. Though it may sound a little surprising, there are many instances when people have been living longer than was expected and that too with much more ease. A tag of adopting a Vedic lifestyle in modern era has become a status symbol/matter of boasting about the uses of natural and organic food products along with yoga for a substantial fraction of people all over the world including India especially in upper classes, and this trend is increasing very fast. Though this has gained mass appeal, a suitability of the usage of natural products as well as the amount of exercise as recommended in Ayurveda is not followed.

**Education and Research in Ayurveda**

It is a common perception even among clinical practitioners and researchers that the education and research in Ayurveda is not exhaustive or systematized. Whereas, the undergraduate degree in Ayurveda “BAMS” (Bachelor of Ayurveda Medicine and Surgery) is awarded after five and half years course including 1 year
compulsory internship similar to modern medicine graduation “MBBS.” Almost all subjects, anatomy, physiology, pharmacology, pathology, medicines, etc. that are a part of the undergraduate program of MBBS in India are part of syllabi of Ayurveda degree course in addition to the study of these subjects from Ayurveda point of view. Also the standard of education is regulated and governed by Central Council of Indian Medicine (CCIM), Department of AYUSH, Government of India. Postgraduate course in Ayurveda “MD” is a 3 years training and research program. In India there are more than 250 educational institutes offering Ayurveda graduation/postgraduate courses. There are a large number of MD and PhD research programs in Ayurveda that carry out research toward understanding the principles and practice described in Ayurveda. There are annual conferences and meetings where these are presented and discussed. However, this is mostly restricted to the Ayurveda fraternity and the language of these discussions is mostly based on Sanskrit textual references and also the publications are primarily restricted to University journals and books with few peer reviewed journals in the field. A large fraction of Ayurveda clinicians either get into public health, clinical trials, drug discovery programs as a resource person for providing herbs or in some cases also get into practicing modern medicine. There is a very limited scope for a crosstalk between the two medical fraternities and one can rarely spot either of the practitioners making case presentations in the other audience. Unavailability of a ready reference in modern language has been one of the major reasons for unawareness of the extent of documentation encompassing all areas of P5 medicine.

AYURGENOMICS: APPROACH FOR INTEGRATION OF AYURVEDA INTO CURRENT MEDICAL PRACTICE

As described and highlighted in the earlier sections, both the modern and the Ayurveda system of medicine have merits which can be complemented for mutual benefit and for the society at large. The science of Ayurveda needs to be understood in totality such as a “TRISUTRA” approach in genomics encompassing a broader spectrum for its usage. If this is achieved then there is a potential for development of innovative solutions for finding newer targets and medicines to reverse the chronic complex disorders. This aspect is claimed in Ayurveda Institutes and centers in India but for its globalization, applicability as well as for demonstrating the uniformity in results on the scientific basis as is described in the texts needs to be established by transdisciplinary approaches. Some attempts have been done in this direction in drug discovery programs. However these studies just use the drug enlisted for the treatment of some diseases and it mostly entails identification of the most active molecule in that herb on modern disease models.
Definition of baseline health state with a noninvasive phenotypic assessment as described in Ayurveda if correlated in the molecular terms could be one of the most affordable way of preventive and personalized management of health. The objective measures of anatomical, physiological assessments available in modern medicine could be integrated with the clinical methods of Ayurveda for giving objectivity to the more subjective assessments. There is not only an enormous data generation possibility in genomics but also methods are being evolved for pinpointing precise targets in pathogenesis of disease in modern medicines. The integration of these strength areas of modern day sciences with the documented comprehensive applied aspect of personalized approach in evaluating the state of health and disease and the relation of practical issues not only from diet and nutrition perspective but also, lifestyle, daily-seasonal routines, exposure to sense objects, etc. from Ayurveda can provide holistic health solutions without much untoward effects. However, this would need de-convolution of the intricate and exhaustive literature of language of Ayurveda.

In order to integrate the concepts of Ayurveda into modern health practices, the first step would be to use a shared vocabulary to denote the properties and interrelationships of these concepts (shared ontological descriptions) in the language of system biology or modern network medicine. A primary place to initiate this crosstalk could be integration of Prakriti concepts with Genomics for understanding human individuality. Evidence for this potential has already been provided in the first of its kind genomics study on extreme constitution types of Ayurveda [53]. This Ayurgenomics approach provided the molecular and genomic correlates of Prakriti [53]. It also highlighted that the normal range of biochemical parameter for different constitution types may be different in a population and so also their subclinical ranges. It might well be that what is subclinical might need to be redefined amongst healthy individuals in a population. However, this has to be validated across diverse ethnic populations from different geographical regions for the method to be globally applicable.

It was also hypothesized that an Ayurgenomics approach could help identify axes of variation that can help predict risk for diseases and enable predictive marker discovery. Using this method, we discovered a genetic variation in an oxygen sensor gene EGLN1 that differed between Prakriti types and conferred differences with respect to high altitude adaptation and susceptibility to high altitude pulmonary edema (HAPE) [68]. Further, extension of this study to a cellular model also demonstrated how difference in this axes could be relevant in modulating asthma [69]. This gene is now being reported as a therapeutic target in diseases such as recovery from stroke, cartilage repair, outcome of visceral surgeries or in cancer progression where modulation of hypoxia has been shown to be important [70–77]. Therefore, it seems possible to explore the three axes of cause (Hetu), consequence (Linga), and therapy (Aushadha) in a common molecular language if we are able to integrate both the sciences through a
common genomics framework [77a]. Thus this TRISUTRA framework of (i) generation of data by using the samples selected with Pakriti concept of Ayurveda in understanding the health markers and process, (ii) integration with the functional and disease genomics approach, and (iii) validation in cellular models can provide clinically actionable points.

Understanding of mechanism of therapeutic action of Ayurveda interventions as well as drugs is also essential for the acknowledgment of the scientific basis and its acceptability and adoption at the global scale. In parallel it could also result in the development of genomic signatures that would enable monitoring not only the quality but also the therapeutic outcome. Most often a test result and an assurance for the quality of the drug are the most critical aspects of a treatment. At present, the phenotypic outcome of a treatment of Ayurveda is monitored based on measurement of an outcome that is described in modern medicine. This has caveats. In Ayurveda, similar to modern medicine, diabetes is classified into different subtypes and the prognosis as well as treatment differs between the subtypes. Use of glycated HbA1c which is a sensitive (not specific) measure for assessing chronic glycemia in monitoring a diabetic patient or a therapeutic outcome in Ayurveda system may impact its validation as well as acceptability. Noteworthy, it is now being acknowledged that glycated HbA1c is present in a fraction of individuals who are not diabetic and it is felt that measurement of this would not be useful for assessing diabetes in specific endotypes.

The major emphasis of panchakarma therapy is on detoxification and rebuilding the homeostatic state of the system through dietary as well as therapeutic regimes that are likely to work through restoration of the microbiome. The emerging area of metagenomic studies has revealed altered microbiome dynamics in a large number of clinical conditions such as obesity, arthritis, psoriasis, multiple sclerosis, and inflammatory bowel disease (IBD) etc. [45,46,78]. This has opened up new opportunities in modulating the microbiome through dietary interventions [79–83]. Integration of these well-developed methods with Ayurveda interventions might also allow identification of metagenomic signatures that could be used to monitor the outcome/success of the ayurvedic treatment.

Another important aspect would be to develop a resource that would allow integration of already available large amount of human genomic variation with the practice of Ayurveda for preventive health maintenance. Lack of confidence and trust in routine and traditional dietary practices as a consequence of globalization is now being considered to be a cause of many emerging diseases, like obesity, depression, common cancers and probably some neuro-degenerative diseases. Some recent reports provide compelling evidence of the importance of maintenance of sleep timings, being in synchrony with circadian rhythms, benefits of exercise, and meditation in recovery from diseases as well as importance of fasting in detoxification process.
Evidence for these has been provided in epidemiological as well as model system and molecular studies [87—90].

Whilst there is overwhelming evidence for the revival and reshaping the traditional Ayurvedic medicine, this would need developing medium to long term strategic projects centered around genomics and judicious use of the next generation sequencing methods in developing specific databases for lifestyle, common diseases and response to expensive and life-saving medications. This genomic information resource could then be put together as a package with the Ayurveda in the acceptable format for Ayurgenomics.

**SUMMARY**

To conclude, integration of genomics in Ayurveda could help in:

1. Determination of baselines of health in an individualized manner that would be important in management of health and disease
2. Identification of predictive (genomic biomarkers) markers and noninvasive measures that would be important in assessing health and disease in diverse populations
3. Development of personalized therapeutic (drugs, nutrition and lifestyle related) recommendations for good quality life in health and disease
4. Increase the awareness and participation of individual in his/her own health care.

There are many challenges that need to be overcome. A primary one is to create awareness which would include redefining it in a modern language to remove the perception and biases linked to the Ayurveda practice. This would enable us to develop a critical mass that is needed to embark on a diverse genomic research into this area to validate the scientific basis of Ayurveda and translate the concepts for affordable health care solutions. This would need research to reduce the gap between the two sciences, dissemination and sharing information of success stories in a language that sounds scientific and convincing by the current definition, appreciation of weakness, and strengths of both the modern and Ayurveda clinicians. It is important that genomic scientists, modern medical practitioners and the Ayurveda medical practitioners engage in an effective and positive manner and develop strategically important projects utilizing the next generation sequencing methods, bio-informatic tools and other skills. The future of Ayurgenomics would largely depend on these developments.

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