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Core concepts in biochemistry and molecular biology in an integrated MBBS curriculum

M P. Iqbal
Aga Khan University, perwaiz.iqbal@aku.edu

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M. P. Iqbal (Department of Biological and Biomedical Sciences, The Aga Khan University, Karachi.)

Introduction

Basic science education in the MBBS curriculum in Pakistan is still based on the traditional subject based model. The Aga Khan University (AKU) when it was established in 1983 introduced, for the first time in Pakistan, the integrated system-based curriculum which provides a holistic approach to the understanding of the structure and functions of the human body. In 1996, Ziauddin Medical University also adopted this model for the first two basic science years.1

The objective of this paper is to define the basic concepts of cell and molecular biology which should be included within an integrated course of basic sciences since they form the foundation for clinical reasoning. There are a number of topics in biochemistry which may appear less relevant to many medical students, however, they constitute the core concepts in this discipline.

The following example of why medical practitioners should have a concept of the Tricarboxylic acid (TCA) cycle will illustrate the need for such concepts within a medical curriculum. TCA cycle is a core concept in cell and molecular biology because it is:

i. a key pathway for integration of various metabolisms;
ii. an amphibolic pathway (plays a role in both oxidative and synthetic pathways);
iii. a major pathway for generation of ATP energy via NADH and FADH2 (cellular respiration).

Although TCA cycle occurs in most tissues of the body, yet it occurs to the most significant extent in the liver. When there is damage to hepatic cell (such as, in hepatitis and cirrhosis) metabolic changes and their consequences can be well appreciated if one has an understanding of TCA and its roles. In hyperammonemia, increased amount of glutamate is used to remove NH_3, resulting into depletion of a-ketoglutarate, a key intermediate in TCA cycle and energy production.2 Brain cells are most vulnerable because they depend on TCA cycle to maintain high rates of energy production. Similarly, neurological symptoms in thiamine deficiency (beriberi) as well as in mercury and arsenic poisoning have been shown to be due to the slowing down of the TCA cycle in neurons which rely essentially on glucose as the only fuel.3 Something which may appear to be dry and a bit irrelevant to medicine constitutes a key concept in understanding of the basis of health and disease. Given below is a list of other 'Core concepts' in biochemistry and cell biology.

Core Concepts

1. Structure - function relationship of biomolecules [Proteins, lipids, nucleic acids and carbohydrates chemistry and metabolism, membrane structure and function].
2. Information transfer from gene to protein [replication, DNA repair, transcription, RNA processing, translation, post-translational modifications, gene expression].
3. Acid-base balance.

4. Regulation of biochemical processes [role of enzymes, coenzymes, cofactors and hormones].
5. Neuro-hormone receptor interactions [cell signaling, mechanisms of action of various hormones].
6. Processes for energy production at the cellular level [glycolysis, TCA cycle, fatty acid oxidation, HMP shunt, electron transport chain and oxidative phosphorylation].
7. Role of molecular genetics in health and disease [genetic engineering and its applications in medicine].
8. Clinical aspects of nutrition [role of vitamins and minerals, balanced diet, obesity].

Cell and Molecular Biology in Problem Based Learning

In AKU where Problem Based Learning (PBL) approach is used in its MBBS curriculum, the strategy adopted for introducing these concepts is primarily through cases or through multidisciplinary, interactive, discussion sessions (interactive large class lectures) with the students. To reinforce certain concepts, laboratory sessions are also given. For example, lab sessions on spectrophotometry, electrophoresis, enzyme kinetics, chromatography, polymerase chain reaction and ligand-binding assay are offered. During the first two years students are also trained to access new information, to evaluate it and then to apply it towards the clinical problems in hand.

In order to facilitate the understanding of the basis of new medical techniques the course also covers the applications of some of the most recent techniques in cell and molecular biology, e.g.,

- Polymerase chain reaction, southern blotting, restriction fragment length polymorphism are routinely used by medical geneticists and oncologists in mutation analysis.
- Immunocytochemistry is used by oncologists in patient management.
- Genetic engineering has provided us with a number of proteins, which have wide application in prevention, and therapeutic management of a number of diseases.

Basic scientific research is now universally accepted as a national investment. When it pertains to some of the medical problems of the country, it contributes to the well being of the population of that country in particular and of the whole region in general.4 Opportunities for elective research during the early years of medical curriculum will train the young minds to be analytical and reflective and at the same time may help them to reinforce certain key concepts. At AKU the medical students especially in first and second years are also given 4 weeks time every year for participating in research activities.

In order to strengthen the linkage between basic sciences and patient care, it is strongly recommended that basic science objectives should be incorporated in clinical modules. The teaching of cell and molecular biology should, therefore not stop after first 2 years of undergraduate medical curriculum, but continue in later years as well. However, the task of integrating basic sciences into clinical curriculum is more daunting than the converse. The AKU basic science faculty has identified topics to be reinforced in the clinical years. As PBL is designed to extend up to Year 4, clinicians have been asked to redesign their clinical clerkships to incorporate these changes.

Conclusion

"Core concepts" in biochemistry and cell and molecular biology through a PBL approach have a critical role in preparing innovative, reflective and competent physicians. Physicians who are well equipped to handle future health problems of this country in

particular and of this region in general.

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