*Special Communication*

# BASIC SCIENCE EDUCATION IN PAKISTANI MEDICAL CURRICULA: ROLE OF BIOCHEMISTRY AND MOLECULAR BIOLOGY

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**ABSTRACT**

In Pakistan, the traditional science-oriented MBBS curriculum pertaining to basic sciences up to early seventies was loaded with the teaching of anatomy and physiology with less emphasis on biochemistry and molecular biology. Although, there has been a significant change since then, yet the role of cell and molecular biology in the curriculum has remained less than desirable. With the introduction of problem-based learning approach in some of the medical institutions of the country (the Aga Khan University and Ziauddin Medical University), the basic sciences faculty would like to ensure that the medical students are going to get sufficient exposure to cell and molecular biology, which forms the basis of the understanding of mechanisms of disease processes.

The objective of this paper is to emphasize on the need to develop some common scientific learning objectives which constitute the basic concepts within the disciplines of cell and molecular biology and provide the medical students a foundation for clinical reasoning. The aim is to equip medical student with sufficient basic knowledge that is useful in any future career.

**KEY WORDS:** Biochemistry, molecular biology, medical curriculum, education, Pakistan.

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## INTRODUCTION

Basic science education in the MBBS curriculum in Pakistan has undergone a significant change over the past 25 years. The traditional science-oriented medical curriculum up to the early eighties was over loaded with the teaching of anatomy and physiology.

A syllabus recommended by the Pakistan Medical and Dental Council (PM&DC) for MBBS program showed a teaching of 800 hours of anatomy, 600 hours of physiology and 200 hours of biochemistry during the first 2 years. Biochemistry at that time was a less significant discipline and was taught in many medical colleges (especially in Punjab) as physiological chemistry by the Department of Physiology with main focus on metabolic pathways and not much on Molecular Biology.

Khyber Medical College, Peshawar, Dow Medical College and Sindh Medical College, Karachi, were the first to have their own Departments of Biochemistry in the early seventies with some more focus on the teaching of biochemistry in the MBBS program.

In 1983, the first private university in Pakistan, The Aga Khan University (AKU), came

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on the national horizon with the main objective of imparting quality medical education in Pakistan. Its medical curriculum showed a significant departure from the norm in those days in Pakistan. It was the first time in Pakistan that basic sciences, such as anatomy, biochemistry, physiology were accorded almost equal time in the curriculum. Community Health Sciences was assigned 20% of the total curriculum time. The teaching of these disciplines was system-based and integrated to provide a holistic approach to the understanding of structure and functions of the human body.

In 1996, Ziauddin Medical University started its medical school with the Problem-Based Learning (PBL) approach[1]. It was quite a revolutionary step in an environment where traditional subject-based curriculum reigned supreme. Yet, cell and molecular biology still did not achieve any prominence in the curriculum compared to anatomy and physiology. The AKU also has started its curriculum renewal and has shifted to PBL since 2002. However, the basic sciences faculty remains a bit apprehensive whether or not the medical students are going to get sufficient exposure to cell and molecular biology, which forms the basis of the understanding of mechanisms of disease processes.

The objective of this paper is not to enter into the debate of "traditional subject-based curriculum vs the PBL curriculum", but to emphasize that some common scientific learning objectives which constitute the basic concepts within the disciplines of cell and molecular biology can be developed which form the foundation for clinical reasoning in a third world country like Pakistan.

## *Core Biochemistry & Molecular Biology for Medical Students*

Although enthusiastic about the idea of reducing factual overload, many biochemists and cell biologists find themselves facing the daunting task of how to define "what is core medical biochemistry and cell biology? What should be included and why?"

For medical students, most modern curricula are designed with the following objectives[2]:

I. to aim at a knowledge level appropriate for understanding the basis of health and disease (core-concepts).
II. to provide students sufficient background knowledge to allow them to evaluate biomedical literature.
III. To facilitate understanding of the scientific basis for new medical techniques.
IV. To equip students to find out the role of new scientific knowledge in clinical practice.

*I. Core concepts*

There is an overload of factual knowledge in the field of cell and molecular biology. On the other hand the total time, in number of years, for undergraduate degree in medicine has remained unchanged. In Pakistan, it is five years after twelve years of school education. Therefore, it becomes imperative to focus only on the "core curriculum" - a curriculum in biochemistry and cell biology which lays the foundations for better understanding of the molecular basis of health and disease.

This has placed biochemists all around the world in a dilemma.

> "What to leave out without detriment to the biochemical training of a physician in a medical school".

Dr. Murray Saffran from Medical College, Ohio, suggests doing away with the topics the students are expected to have covered in their premedical years[3]. It might be possible in North America where a vast majority of students entering the medical school already have BA and BS degree covering major portions of biochemistry and cell biology. In Pakistan, where most students entering the medical school have only two years of college with little exposure to biochemistry, this option of "what to leave out" becomes even more difficult. There is another important question! "which topics in biochemistry and cell biology are most relevant to the educational needs of our medical

students?" According to Anthony Turner at University of Leeds, "no clinician will come across a patient from an inherited defect of tricarboxylic acid [TCA] cycle. Why, therefore, is it necessary to teach this topic to medical students?"[4]. The question of whether a doctor needs to know such basic topics in biochemistry was addressed by Arthur Kornberg[5]. He stressed the point that "biochemical sciences, especially molecular biology provide the essential keystone supporting medicine, just as anatomy did a century ago". Therefore, biochemistry is the essential link between morphology, physiology, genetics and chemistry. Without that, it would be difficult to understand the basic principles in pharmacology, microbiology and pathology. Therefore, a prime objective of teaching biochemistry to medical students is to illustrate the biochemical bases of human function and disease.

Going back to the original question, "What are the core concepts?", it is generally accepted that a clinician will rarely come across a patient from an inherited defect of TCA cycle, yet the cycle can be regarded as a "core concept" as it is a major pathway for generation of ATP energy and has a key role in integration of various metabolisms.

As it occurs to the most significant extent in the liver, any damage to hepatic cell (such as, in hepatitis and cirrhosis) will lead to serious metabolic consequences in the human body. For example in hyperammonemia, increased amount of glutamate is used to remove $NH_3$, resulting in depletion of α-ketoglutarate, a key intermediate in TCA cycle and energy production, and ammonia intoxication[6]. Since brain cells mostly derive their energy through TCA cycle, they are most vulnerable when this cycle is impaired. Neurological symptoms in thiamine deficiency (beriberi) as well as in fumarase deficiency 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[7, 8].

There is growing evidence to suggest that the phenomenon of fatigue following cancer chemotherapy also involves subnormal function of mitochondrial proteins involved in TCA cycle. The objective of this whole narration is to emphasize that 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.

Another example will be that of phosphatidylinositol (PI) pathway which is a major signaling cascade for intracellular mobilization of calcium[9,10]. Clinicians have been treating manic depressive illness for scores of years without understanding how it acts at the cellular level. Pollack *et al.* demonstrated that lithium therapy slows down the PI cycle in manic depressive illness by inhibiting the phosphatase that dephosphorylates inositol monophosphate as well as interfering directly with G-protein function, thereby, reducing the overactivity of CNS cells in this disorder[11]. This again shows that something identified exclusively as a biochemical phenomenon facilitates our understanding of the mechanisms of disease processes and the therapy involved. Nitric oxide mediated signaling cascade offers another such example[10]. Angina patients have been treated with nitroglycerine for more than 100 years without an understanding of the molecular mechanism of its action. In fact, Alferd Nobel was among the most famous angina patients who had been prescribed this explosive for his treatment. In a letter to a friend he wrote:

> "It sounds like the fate of irony that I have been prescribed nitroglycerine. They have named it Trinitrin in order not to upset pharmacists and public".

It was in the eighties that Ferid Murad showed that nitric oxide (released from nitroglycerine) interacted with heme containing guanylate cyclase to produce increased quantity of c-GMP, which was responsible for relaxation of smooth muscles in coronary arteries, thereby, relieving angina pain[10]. The question arises, "would it be appropriate to leave out a signaling cascade of this kind from the medical curriculum?"

Before embarking on working out the "core concepts", it is important to bear in mind that there are different roles of medical graduates. Functions of doctors would vary according to the patient care settings, therefore, their needs in terms of basic science knowledge would also vary. For example, some would be working in well-equipped tertiary care hospitals and others working in a district hospital in a remote area. Some others may be planning to go into hard core medical research. It is imperative to cater the needs of all of them in terms of their basic biochemistry and molecular biology.

### *New Curriculum at the Aga Khan University*

As mentioned above, the Aga Khan University has recently introduced a new curriculum for undergraduate medical education that is student-centered, integrated, and contextual and emphasizes active learning[12].

A framework for curricular structure is shown in Figure 1.

- It is evident that initially the curriculum is system-based, multisystem and complex problems will be incrementally introduced. One of the focal instructional strategies is that the students learn through interactive small group discussions – problem-based learning.
- In order to promote the spirit of enquiry and develop the traits of critical thinking there are ample opportunities for research.
- In later years, students learn to apply their basic science knowledge to make scientifically sound decisions in clinical situations.
- The contents of curriculum are based on objectives derived from the AKU list of most common health problems and presentations in the context of national and regional needs.
- Focus is not only on the curative and rehabilitative aspects but also on prevention of disease.
- Ethical and social aspects of health receive attention at all stages of learning.

These lofty objectives could not be obtained without substantial reduction in the current courses in basic sciences. This has become a challenging task for the faculty in the Biochemistry to develop a consensus on the "core" or "basic concepts" in medical biochemistry and cell biology.

The faculty in consultation with its clinical colleagues has come up with 8 "core concepts" which it believed would equip our medical graduates to effectively undertake any of the previously mentioned roles of a future doctor[13].

### *Core concepts in Biochemistry & Cell Biology*

1. Structure – function relationship of biomolecules
   [Chemistry and metabolism of macromolecules]
2. Information transfer from gene to protein.
3. Acid-base balance
4. Regulation of biochemical processes [role of enzymes, coenzymes and hormones].
5. Neuro-hormone receptor interactions
   [cell signaling, mechanisms of action of various hormones]
6. Processes for energy production at the cellular level
7. Role of molecular genetics in health and disease
8. Clinical aspects of nutrition [role of micronutrients, balanced diet]

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, laboratory sessions on spectrophotometry, electrophoresis, enzyme kinetics, chromatography, polymerase chain reaction and ligand-binding assay are now offered.

### *II. Knowledge to evaluate biomedical literature*

Regarding the second objective in our cell and molecular biology curriculum for medical students, there are thousands of websites through which one can obtain an up to date and in depth knowledge about any topic in cell and molecular biology. Approach to these websites,

is user-friendly, therefore, all one needs is "How to surf through?" Role of the faculty is to arouse the curiosity and rekindle the spirit of enquiry among the students.

### *III. Facilitate understanding of the basis of new medical techniques*

The third objective in our curriculum is to familiarize our students with new medical techniques. With recent advances in the field of cell and molecular biology, newer medical techniques have emerged and are being currently used by clinicians for diagnosis and management of various diseases[2]. For example, DNA and RNA probes are currently employed by pathologists for diagnostic purposes. 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. A better understanding of these techniques will broaden the horizon of medical graduates in terms of their application in clinical medicine.

### *IV. Potential role of new scientific knowledge and basic medical research*

Apart from techniques, new scientific knowledge has immense role in clinical practice. For example, human genome project has opened new vistas in the diagnosis and therapy of a number of genetic diseases. Stem cell replacement and gene therapy are realistic and exciting possibilities for the future. It is important that our curriculum aims at developing our young medical graduates to be innovative and well-trained to address the medical problems.

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[14]. 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. Figure 1 shows that at the Aga Khan University elective research starts in Year-I of the undergraduate medical curriculum. It also facilitates development of reasoning skills and will be useful in any future career[15].

Figure 1: A Framework for Curricular Structure in Years 1 & 2

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YR 1 | Module 1 (8 weeks) | Module 2 (8 weeks) | H | Module 3 (8 weeks) | Module 4 (8 weeks) | H | Module 5 (4 weeks) | Exam & Electives | | | H |
| | Introductory Module: Cell & System | Locomotion & Blood | 1 wk | GIT, Nutrition & Metabolism | Respiration & Circulation | 1 wk | Multisystem | 2 wks Study Leave | 2 wks Exam | 4 wks Research Or Electives | 6 wks Holiday |
| YR 2 | Module 6 | Module 7 | H | Module 8 | Module 9 | H | Module 10 | | | | H |
| | Renal | Endocrine & Reproduction | | Neurosciences | Immunity & Infectious Diseases | | Neoplasia & Multisystem | 2 wks Study Leave | 2 wks Exam | Research or Electives | 6 wks Holiday |
| YR 3 | | | | | | | | | | | |
| YR 4 | | | | | | | | | | | |
| YR 5 Pre Internship | | | | | | | | | | | |

H = Holiday

### *Cell and molecular biology in clinical years*

It should also be emphasized that the teaching of cell and molecular biology in a PBL-based system should not stop after first 2 years of undergraduate medical curriculum, but continue in later years as well. According to a recent study by O'Neill, basic science knowledge is further strengthened in later years of undergraduate medical education by incorporating basic science objectives in clinical modules[16], however, the task of integrating basic sciences into clinical curriculum is more challenging than the converse. AKU basic science faculty have identified the 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 topics.

According to Dr. Peter McCrorie, "Just as basic scientists feel uncomfortable trying to put their teaching into a clinical context because of their lack of clinical knowledge, so do clinicians feel uncomfortable teaching basic science aspects of their clinical cases, partly because they have forgotten much of the basic science they rote-learned before their exams, and partly because of the huge explosion of scientific knowledge that has taken place over the last 20 years" [17].

This issue can be handled by running integrated teaching sessions during the later years. Here cell biologists and clinicians must join hands to have interactive discussion sessions with student on clinical cases. When cell and molecular biology is encountered in context, learning becomes a more enjoyable exercise with better understanding and application. The Aga Khan University has adopted the PBL approach which maximizes the learning opportunities for its undergraduate medical students through out five years.

## CONCLUSION

Certain "basic concepts" in the discipline of cell and molecular biology when imparted to medical students through an innovative, learner-centered approach could prepare competent and caring physicians for the 21st century. The goal is not only to produce competent specialists but also to prepare individuals with the traits of critical thinking and moral reasoning and having an ability to solve future problems of this country.

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