N E T W O R K

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INCTR

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THE PRESIDENT'S MESSAGE

THE CELL

Part 3. "Simple" Cells

by Ian Magrath

Stromatolites (from the Greek, *stroma*, mattress and *litho*, stone) are layered structures that form in shallow water. Some of the layers are biofilms that consist of colonies of prokaryotic cells (like modern stromatolites) that trap and bind sedimentary grains of rock and precipitate carbonate mineral which form intervening layers. The most ancient stromatolites were formed in the Achean period, which began 3.8 billion years ago. Picture from Wikipedia Commons taken by C. Eeckhout.

The ancient Greek philosopher, Anaximander (610-546 BCE), was one of the first of the "rational" thinkers. A member of the school of philosophy founded by Thales (624-546 BCE) in Miletus in Ionian Greece, he believed that "laws of nature" rather than anthropomorphic gods governed natural phenomena. Anaximander postulated (doubtless based on earlier mythology) the existence of an unobserved, undefined first principle that was limitless in time and space (*apeiron*), and which gave rise to the "elements" recognized by the ancient Greeks - water, air, fire and earth. These elements, he proposed, in various harmonious mixtures, account for all that exists. Thales himself had favored water as the primeval element, and Anaximenes, Anaximander's student, suggested that apeiron was simply the subtle, invisible air. There was, of course, no scientific evidence that could support or refute the ideas of these early natural philosophers; the ancient Greeks were, in any event, theorists rather than experimentalists, but the idea that everything was composed of mixtures of the four basic elements was not, in many ways, a bad guess. As we know today, water, without which Life as we know it could not exist, is composed of two highly

reactive chemical elements that are gaseous at ambient temperatures and pressures. Hydrogen is highly combustible, while oxygen supports combustion and combines with (*oxidizes*) almost all other chemical elements. Oxidation releases energy, whether explosively, for example, when hydrogen is ignited in its presence, or slowly, as in, for example, the controlled oxidation processes of (some) living cells that produce the energy that can be stored in the chemical bonds of adenosine triphosphate (ATP) and released as needed to drive chemical reactions. It is difficult to imagine how water, the seemingly bland constituent that provides the internal milieu in which all cellular reactions take place, can be composed of two such highly reactive elements, but the answer lies in the fact that the formation of water releases energy, such that water molecules are in a highly stable, low-energy state with the result that an input of energy is required to break them into their constituent elements. In effect, it represents a "harmonious" mixture, quite close to Anaximander's ancient idea, although Anaximander, of course, had no knowledge of the chemical elements we now recognize.

INCTR

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A UNIVERSE PREGNANT WITH LIFE?

Today, we recognize the critically important roles played by the 92 naturally occurring chemical elements in our world – they provide both the substrate on which life evolved and persists, as well as the stuff of Life itself, for the elements forged in the stars are essential to the creation of the mineral-rich terrestrial planets on which Life has emerged (at least once). It is possible, of course, that the chemical elements, like the stars themselves, are merely an inevitable consequence of the values of the fundamental physical constants that happen to exist in our universe, but the human mind has difficulty in conceiving of such a high degree of self-organization as purposeless. Prior to the formation of stars (the latest estimates from studies of the microwave background by NASA's WMAP satellite indicate that stars began to form 400 million years after the *Big Bang* that initiated spacetime), hydrogen, deuterium, helium and lithium were the only elements that existed. Because of this, astronomers refer to all other elements, whose concentrations in galaxies are indicative of prior stellar synthesis, as *heavy elements* or *metals*. Today, some 13.7 billion years after the Big Bang (a figure, again, based on data derived from WMAP), hydrogen still accounts for 74% of all ordinary matter in the universe, and helium 24%. Of the remaining 2%, oxygen and carbon are the third and fourth most abundant elements, and nitrogen the seventh. These elements, along with hydrogen, are also the predominant elements of Life, although many others, particularly phosphorus, play vital roles and are "concentrated" in all life-forms. From the human vantage point, it is the emergence of Life, and ultimately, after billions of years of evolution, intelligent Life, that seems to give meaning to the stellar synthesis of elements. Put slightly differently, it could be said that the values of the fundamental physical constants of the universe, and its age, are *constrained* by the fact that intelligent life ("observers") has emerged; for Life requires the existence of certain conditions in at least some locations in the universe. This idea was formulated originally in 1974 by Brandon Carter and referred to as the weak version of the *anthropic principle*. He also formulated a strong version, which states that the fundamental parameters on which the universe depends and lead to its evolution *must* have values that permit the emergence of "observers" at some point in its history. While readily dismissible as a tautology, the anthropic principle is something of a philosophical conundrum, since unless the universe can be observed it cannot be known to exist. The degree of intelligence required of the observer can be debated but the universe certainly ceases to exist for

the individual observer at the time of death (or even unconsciousness), assuming that "intelligent observation" also ceases with death. This troubling idea can be overcome by postulating an afterlife or rebirth, thereby ensuring that the miraculous beauty of the universe neither disappears, nor exists unobserved.

Also arising, at least in part, from the anthropic principle, is the possibility that other universes exist where the fundamental physical constants are not consistent with Life. In a *multiverse* (a term coined in 1895 by the American psychologist and philosopher, William James), consisting of a series of parallel universes with different physical constants, life would emerge in only those (or possibly in one of them) with physical constants consistent with the ultimate emergence of life. The existence of a multiverse is unverifiable, and therefore on a par with the speculations of Anaximander and his fellow naturalist philosophers in Miletus who also, incidentally, conceived of the existence of many worlds. This need concern us no longer. The complexities of the emergence of Life on Earth provide more than enough fertile ground for speculation.

BUILDING MACROMOLECULES

A number of hypotheses – too numerous to be discussed in detail here – have been proposed to account for the linking of the individual elements (*monomers*) into the key polymers or *macromolecules* of Life, i.e., *DNA, RNA* and *proteins*, in the prebiotic era. Such hypotheses must take into account the fact that the conditions required for monomer synthesis are very different from those required to join monomers together in chains, or to permit them to remain intact. Even if synthesized in different locations, relatively high concentrations of monomers would have to accumulate at a site suitable for or conducive to polymer assembly, using energy available from the environment (e.g., heat, or chemical energy). Only in recent years has it become known that the sea contains very high concentrations of bacteria and bacteriophages (viruses that attack bacteria) – in surface waters bacteria are present in concentrations of 10^6 to 10^7 per milliliter, and bacteriophages typically an order of magnitude higher. Bacteria and their viruses also occur at even higher concentrations in deep ocean sediment and make up perhaps 90% of total biological carbon in the world's oceans, playing a critical role in global ecosystems. Although this situation could well have existed since the emergence of highly efficient replicating molecules encased in cells, it seems unlikely that key polymeric molecules evolved in surface waters since they are readily broken into their component parts, e.g., by ultraviolet light which, in the absence of an atmospheric ozone layer in the primeval atmosphere, would have been more intense. In fact, water itself inhibits the formation of peptide bonds between amino acids (a molecule of water is released during peptide bond formation), and breaks down existing bonds by hydrolysis (the water molecule is "added back"), although this is a slow process. Similar considerations apply to RNA and DNA, in which the long chains of nucleotide bases are held together by the sugar phosphate backbone, in which the phosphodiester bonds that bind the sugars (ribose or deoxyribose) together are also subject to hydrolysis, particularly at high temperatures. Few insights have been gained regarding the formation of the sugar-phosphate backbone of nucleic acids – indeed, only recently have laboratory experiments suggested possible pathways to nucleoside (nucleotide bases coupled to a pentose sugar) synthesis. Polymerisation of monomers (phosphorylated nucleosides, i.e., nucleotides) would be one such pathway, but it has also been suggested that RNA evolved from pre-RNA molecules - assuming that RNA was the first nucleic acid to be synthesized, as in the *RNA world hypothesis* previously described. In such hypothetical pre-RNA molecules, the backbone holding the polymer together would be different from the sugar-phosphate backbone of modern RNA; for example it might be a chain of amino acids. Molecules of this type have been synthesized in the laboratory, but how such molecules could serve as an intermediate step is unclear. One theoretical possibility is that they held nucleotide bases in fixed position, creating a template on which a second RNA chain with a sugar-phosphate backbone could more readily form.

CATALYSTS AND SCAFFOLDS

One problem that must be addressed in understanding the origins of macromolecules is the observation that catalysts are invariably required in the laboratory to synthesize polypeptides or nucleic acids. Another way of looking at this is that such

reactions occur extremely rarely in the absence of other molecules that are able to dramatically reduce the energy required for the reaction, e.g., by fixing and helping to define the shape of the reactants, or by binding them together in such a way that reactive sites are adjacent to each other, thus enormously increasing the likelihood of a specific reaction taking place. However, even if hundreds or thousands of years are required (such that human scientists are highly unlikely to be able to reproduce the reaction in the laboratory), the fact that a reaction can take place rapidly (sometimes millions of times faster) when influenced by an efficient catalyst suggests that it could also take place spontaneously, or under the influence of an inefficient catalyst, if given a sufficiently long period of time. Prior to the evolution of RNA and protein catalysts, minerals may have provided sufficient catalytic activity to create polymers as well as a protective environment that would increase their lifespan. Interestingly, a large number of modern enzymes, including those of the citric acid cycle responsible for energy production in all modern cells, are associated with minerals, such as iron, iron-sulphur complexes or other metals, suggesting that the minerals themselves might once have been the sole catalysts.

But minerals may have provided more than catalytic activity. In particular, the structure of clays is such that they might also have provided a scaffold on which polymers could be built (in itself a form of catalysis). Clays are composed of layers of crystallized silicates that are separated by potential spaces (Figure 1). Such spaces can be filled with water (unless the clay is dried out or baked) and are known to bind organic molecules by electrostatic forces. The silicate sheets are linked with various metals, such as magnesium and iron, which may have provided both a modest catalytic effect and even the energy needed to drive the reaction (some modern bacteria, *Acidothiobacillus* species, for example, use iron pyrite as an energy source). Clays clearly have many of the required attributes to function as artificial cells – and also provide an enormous surface area within their multi-layered structure that creates a huge experimental platform on which billions of reactions could have taken place - vastly out-competing modern researchers seeking to demonstrate chemical reactions relevant to the emergence of Life. The uniformity of their crystalline structure could also be relevant to the alignment of monomers prior to joining them into polymers. The possible role of clays as a scaffold on which to create polymers is not entirely speculative. Both polypeptides and nucleic acid polymers (when monomers are provided along with any other necessary raw materials and energy) have been made in clays (e.g., montmorillonite) under laboratory conditions. Although such polymers are tightly bound to the clay, when mixed with lipid and sufficiently agitated, lipid vesicles are formed which contain small fragments of clay to which nucleic acid or polypeptides (or both) are bound – in effect, protocells. At this stage in the emergence of Life, it is possible that the synthesis of vast numbers of different RNA molecules in the course of millions of years led to molecules with different potential survival times – whether because of their sequence, or their immediate environment, including the presence of other molecules. Those molecules with longer survival times, or in an environment that provided sufficient monomers and energy to allow them to replicate, would be "selected" by a process similar to Darwinian evolution, although they could not yet be called living. Indeed, key molecules unable to persist or replicate would decompose into their component parts, potentially to be recreated in more sustainable form.

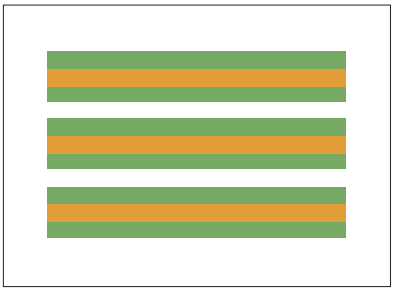

Figure 1. Clay. This diagram depicts the layered nature of clay — in this case montmorillonite. Green layers represent tetrahedral silicate crystals between which are sandwiched octahedral silicate layers. The layers are joined together by sodium, calcium, magnesium and aluminum and sometimes other elements, e.g., iron and potassium. Particles are, on average, a micrometer in size. The spaces between sandwiches are filled with water, which can contain a variety of molecules, some of which may adhere to the sandwich layers via strong electrostatic forces. Some have argued that such tight links could prevent further chemical reactions in large polymers, but there may be ways of overcoming this, including physical disruption of the clay.

Manfred Eigen, winner of the Nobel prize in chemistry in 1967, showed, in 1986, that the viral protein Qβ replicase, that normally catalyzes the formation of RNA in the presence of an RNA template (as it does when Qβ enters its bacterial host), can also create an RNA molecule in the absence of a template. This observation supports the idea that that RNA synthesis requires only nucleotides and a suitable catalyst, and once created, an RNA strand could serve as a template on which to create complementary strands – catalyzed by the same enzyme, and separated from each other, and thus providing double the number of templates, by natural changes in temperature, either locally or through displacement of molecules to other locations. The chance creation of a polypeptide like Qβ replicase, for example, in a location conducive to polypeptide formation (such as clay), could have led to the formation of RNA molecules of various kinds, the creation of self-replicating systems and even an RNA-based translational mechanism which, over time, may have become independent of the original "facilitator" molecule by mutation or the creation of a new RNA molecule that, by chance, encoded an RNA replicase.

COUPLING INFORMATION-CONTAINING MOLECULES TO PROTEIN: THE GENETIC CODE

While these hypothetical situations, even if inaccurate, provide models for the emergence of self-replicating molecules on Earth, there have been few insights into how the information contained in an RNA or DNA sequence became linked to the synthesis of particular proteins, i.e., the evolution of the *genetic code*. Somehow, transfer RNAs able to bind specific amino acids emerged, presumably by chance. In the course of the few hundred million years of the prebiotic era, the entire genetic code – i.e., the correspondence of particular nucleotide triplets to particular amino acids, evolved via the process described in Part II. There are 64 triplets in total – most amino acids are coded for more than one triplet (Figure 2). Some triplets code for punctuation marks, such as critically important "start" or "stop" signals (defining the so-called *reading frame*), so that the same protein is repeatedly translated from a given stretch of nucleotides. Of great import is the universality of the code in all life-forms. This suggests that Life evolved just once, or at least from a single cell. Competitors, if they existed, must have failed to survive. This hypothesis is supported by the molecular relationships that exist among the key molecules in all modern cells.

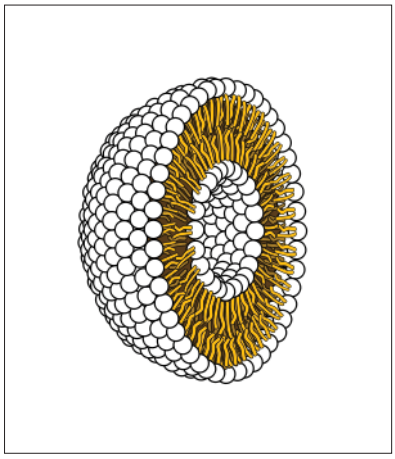

Figure 2. Lipid Bilayer. This diagram depicts a liposome in cross section (it would normally be spherical) comprised of phospholipids arranged in two layers. The hydrophilic "heads" are represented by spheres and the hydrophilic "tails" by brownish lines. The central cavity could contain a broad range of water-soluble molecules. This self-organizing system, used today for a variety of purposes, including drug delivery, suggests how the cell membranes of protocells may have formed.

Initially the genetic code is likely to have been much simpler than it is today – possibly only two nucleotides were needed to specify a particular amino acid, which may account for the fact that multiple triplets that code for the same amino acid differ most often at the third nucleotide base. Initially, it is likely that very few amino acids were defined by the primitive code, and a correspondingly small number of proteins, but the repertoire would have increased over time to encompass all 20 amino acids and a huge range of possible proteins.

Although replicating molecules and metabolic systems (such as the essentially universal citric acid cycle) may have emerged separately - there has been much debate over which came first - it is difficult to imagine how a genetic code could evolve in such a way that it encoded a whole set of proteins that already existed, particularly since such proteins, if not coded for by specific genes, would have a limited lifespan – posing a major problem for the creation of an evolving community of interacting molecules. More likely, (with the possible exception of the transiently required RNA replicase mentioned above), weak protein

Ala/A GCU, GCC, GCA, GCG	**Lys/K** AAA, AAG
Arg/R CGU, CGC, CGA, CGG, AGA, AGG	**Lys/L** UUA, UUG, CUU, CUA, CUG
Asn/N AAU, AAC	**Met/M** AUG
Asp/D GAU, GAC	**Phe/F** UUU, UUC
Cys/C UGU, UGC	**Pro/P** CCU, CCC, CCA, CCG
Gln/Q CAA, CAG	**Ser/S** UCU, UCC, UCA, UCG, AGU, AGC
Glu/E GAA, GAG	**Thr/T** ACU, ACC, ACA, ACG
Gly/G GGU, GGC, GGA, GGG	**Trp/W** UGG
His/H CAU, CAC	**Tyr/Y** UAU, UAC
Ile/I AUU, AUC, AUA	**Val/V** GUU, GUC, GUA, GUG
START AUG	**STOP** UAA, UGA, UAG

Table 1. Genetic Code. Letters in bold indicate the three letter or one letter abbreviation for each amino acid (e.g., Ala or A = alanine); letters in normal font are the nucleotide base triplets (guanine, cytosine, uridine and adenine) that code for the respective amino acid.

(or RNA) catalysts were the chance fruits of encoded information in nucleic acids, i.e., they evolved after the genetic code was defined and ribosomal translation became possible. This would set in motion the process of adaptive evolution, whereby beneficial mutations that resulted in improved survival or replicative advantage of the nucleic acids would persist at the expense of unmutated molecules.

CELL MEMBRANES AND PROTO-CELLS

Modern cell membranes are comprised of a mixture of lipids, primarily phospholipids, carbohydrates and proteins. The lipids form a liquid crystal "lake," to which are attached (both externally and internally) a variety of molecules, some of which completely penetrate the membrane (and essentially float in the lipid lake). The lipid component is in the form of a bilayer, each molecule being composed of a "head" bearing a phosphate group, and a fatty acid "tail," usually containing 16 or 18 carbon atoms. This semi-permeable barrier (small, electrically neutral molecules can pass through freely) regulates the passage of a variety of molecules and ions into or out of the cell generally via "gateways" or "pumps" comprised of penetrating proteins that form "channels" that can be opened or closed. Protein *receptors*, able to bind to specific molecules, also confer some limited "awareness" of the cellular environment and provide a means of interacting with it. If evolution based on mutations began through selection of the most stable informational molecules in the prebiotic era (protected, perhaps by the proteins or RNAs they encoded), these molecules, even if in artificial cells, would still have been liable to disruption or displacement by a variety of changes in their environment. At what point in their evolution such molecules and primitive metabolic systems became enclosed in a protective lipid membrane is a matter for speculation, although lipid molecules could well have been present in clays alongside replicating molecular systems, such that the latter could be readily be incorporated into lipid vesicles, the formation of which is known to occur in clays.

One distinction between this third major molecular element of

the cell (after self-replicating molecules and metabolic, or energy packaging processes) is that lipid molecules, in appropriate circumstances, are self-organizing; the tail is *hydrophobic* (water-hating) and the head *hydrophilic* (water-loving). It is this which causes them to associate in large numbers as membranes in aqueous solutions, since the hydrophobic tails more readily associate with each other rather than water, such that the heads form the inner and outer surface of the bilayer (Figure 3), both of which are in direct contact with water. In cells, the external environment can be aqueous, or consist of an adjacent cell, but the intracellular cytoplasm is always aqueous. In bacteria and plants, the outer surface is associated with a more or less rigid cell wall. Protocells presumably comprised a cell membrane enclosing a nucleic acid and some part of the systems required for replicating the nucleic acid. As molecules accumulated in the protocell, it would have enlarged to a certain point, then burst, creating daughter cells. Initially there would have been no guarantee that all of the necessary cellular constituents would have been present in both daughter cells, and perhaps multiple (billions, if not trillions) of false starts at creating a true, self-replicating cell occurred before a mechanism emerged that permitted equal distribution of all essential molecules between daughter cells. Equipped with a genetic code, however primitive (a mechanism enabling the information stored in nucleic acids to be translated into functional RNA and proteins); a means of storing and using energy (derived ultimately from the environment, whether directly, or via a metabolic, i.e., chemical process); a mechanism for ensuring similar if not identical daughter cells; and a lipid membrane, the first true cell emerged.

PROKARYOTES

The first cells that appeared in the fossil record, some 3.5 to 3.8 million years ago, were *prokaryotes* (Greek: "before a nut"), i.e., cells without a nucleus. Although their molecular characteristics can only be surmised, they formed stromatolites as do some types of modern prokaroytes. In the latter, nucleic acid (DNA) exists as a single strand or *chromosome* containing a linear array of genes and is not surrounded by a nuclear membrane, although it is confined to a region of the cell called the *nucleoid*. The smallest known genome is approximately 160,000 base pairs. Prokaryotes are very small in comparison with the cells of protista, animals and plants (which are comprised of *eukaryotic cells* – i.e., cells with a clearly discernable nucleus). Most are between 1 and 10 microns, but rare species reach 750 microns). Prokaryotes have few intracellular structures or "organelles" but do have a primitive cytoskeleton responsible for maintaining their shape – most are spherical or cylindrical and many bear cilia or flagella that allow them to "swim" in liquid media. They have an enormous range of natural environments and have been found in rock several kilometers below the Earth's surface, in sea-water, soil, fresh-water, air and also in association with many other living organisms, e.g., in the intestines and on the external surfaces of all animals (there are estimated to be 10 times as many bacterial cells in the human body than there are human cells). Some extremophiles can live at temperatures up to 1400C, in highly acidic or basic environments or in high concentrations of salt, a variety of metals and many other substances. Consequently, they have an extremely broad range of metabolic processes and probably comprise the bulk of the global biomass (the totality of Life on Earth). Prokaryotes consist of two very different life-forms, known as *domains* – Bacteria and Archea. Although the Archea superficially resemble bacteria, they are more closely related to *Eukarya* (life-forms comprised of Eukaryotic cells, such as plants and animals) as evidenced by the degree of similarity of the sequences of the proteins involved with transcription (the synthesis of a messenger RNA molecule on a DNA template) and translation (the synthesis of polypeptides, via the ribosomal complex). Classification is based particularly on the sequences of ribosomal RNA genes. Archea also have unique features that are not found in either Bacteria or Eukarya, such as differences in the lipids of the cell membrane. There is considerable debate over the question of when the three main domains of life diverged, although there is little doubt that Bacteria and Archea evolved first. Such "simple" cells have been remarkably successful in evolutionary terms, and, as will be discussed in Part IV, provided the biochemical platform that permitted the evolution of more complex life-forms, including the eukaryotic cell, which came about by a remarkable fusion event, and which was an essential step in the evolution of multicellular organisms. ■

CHALLENGES TO THE PROVISION OF PATHOLOGY'S HIGH QUALITY SERVICES IN CAMEROON

PATHOLOGY LABORATORIES

There are nine pathological services in Cameroon; most of them have a pathological laboratory and a mortuary. The mortuary produces more financial resources for the hospital than the pathology laboratory because the mortality rate is high due to poverty, infectious diseases and cancers. However, postmortems are rarely performed so that the causes of death are often unknown, at least beyond available clinical information.

All of the pathological services appear to be run by one or two pathologists who work at multiple facilities in order to earn an adequate salary. Some work in hospitals as well as medical schools and may have teaching responsibilities in histology, pathology and aspects of oncology. Others work in administration, or spend part of their time in administration. Remarkably, diagnostic services are not overloaded since only 10 percent of cancer patients have a biopsy and/or cytology specimen taken. This has serious implications for cancer registration, treatment and research (which is extremely limited).

PATHOLOGICAL TECHNIQUES AND PROCEDURES

Each laboratory has a microtome and one or a small number of elderly microscopes – for the most part, without digital cameras attached. Technical staff were generally trained many years ago and have not benefited from continuing education or the introduction of newer techniques. Even those few who have attended courses or other educational events pertaining to immunohistochemistry and molecular techniques cannot practice these techniques, and would, therefore, require retraining if they are to be introduced. Even when samples are sent abroad for further testing, generally free of charge, they may make little difference to the treatment given because of the lack of infrastructure, treatment resources (most patients must pay for care, and particularly for drugs, out-of-pocket) and trained oncologists. Paraffin blocks are not kept in most labs as cassettes required for their preparation are recycled due to lack of materials. There are, at present, no tissue banks. The limited funding available via the Ministry of Health and the few NGOs concerned with cancer are generally used for increasing awareness of cancer and attempting to detect cancer earlier. There is a certain sad irony in this, since awareness and early diagnosis cannot improve outcomes in the absence of accurate diagnosis and effective therapy.

The General Hospital, Yaounde.

TRAINING

The number of pathologists being trained is becoming smaller, not greater, since young doctors will not choose this field of practice because of the frustrations relating to the poor work environment. Most practicing pathologists have not received practical training in the field of pathology and are not able to perform postmortems, or understand their value in training and education of pathologists or for research purposes. This also has medico-legal implications since forensic medicine is not taught in universities. Since the more senior pathologists are involved in administration, which has expanded considerably with the creation of new medical faculties in Cameroon, diagnostic services are generally provided by less experienced pathologists. Diagnostic services provided by senior pathologists are likely to be more delayed – by weeks or months – because of their increased administrative work-load.

POTENTIAL SOLUTIONS

Telepathology and telemedicine can now play a major role in developing improved pathology services (although technical training in more modern techniques, and the provision of required reagents will also be necessary) – on the one hand, through its exploitation as a training tool and on the other, to offer consultation or discussion in the context of specific cases. INCTR is already making use of iPath (http://www.ipath-network.

com/inctr/), which requires, only access to the World Wide Web and digital photomicroscopy, in a number of countries, including African countries for these purposes. In the next five years, Cameroon will train more than 500 medical doctors per year, compared to 70 in the past. Involvement in discussion groups and increased communication in general will also enhance the professional experience of pathologists and help attract more trainees to this discipline.

The development of an Institute of Pathology, either focused in one or a few of the new medical faculties, or created as an autonomous institution, would provide advocacy for the discipline in the context of the expansion of medical training, and could lead to standardization of techniques, the introduction of new techniques such as immunophenotyping, the use of modern classification schemes and standardized reporting, all of which would lead to improved pathology training, diagnosis and even the undertaking of essential national research. Unless attention is paid to this critically important discipline, the opportunity to attract pathology trainees from among the 500 medical doctors that will be graduating each year will be lost – and while upgrading and expanding treatment services will also be necessary, improved results will be dependent upon accurate diagnosis. ■

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DEVELOPMENT OF PALLIATIVE CARE SERVICES IN PAKISTAN

INTRODUCTION

Pakistan is a lower middle-income country according to the World Bank classification, with a population of over 160 million and an annual growth rate of 2.03% (WHO, 2005). The population is young, with a median age in males and females of just over 19 years, 39% being less than 14 years. The literacy rate is less than 50% and 32% of the population lives below the poverty line. Nevertheless, cancer, as in countries of similar socioeconomic status, is emerging as a major health care problem. The precise incidence, mortality rates, number of new cancer cases and number of deaths annually for Pakistan are not known, but WHO estimates that there are 61,624 incident cases and 42,624 cancer deaths annually in males and 75,095 incident cases and 43,188 deaths annually in females. Even in children, although malnutrition and communicable diseases are still the major killers, cancer is rapidly becoming an important cause of morbidity and mortality, especially in children above the age of 5 years. Based on the data from the Karachi Cancer Registry, it is estimated that approximately 5 to 6 thousand children get cancer every year in Pakistan with survival rates varying between 20-60%, depending upon both the cancer type and the treatment received.

Pakistan has developed a National Cancer Control Plan using evidence-based strategies for prevention, early detection, treatment and palliation as recommended by WHO. However, implementation of the plan has been poor, particularly with regard to the development of services for early detection and palliative care. Opioid availability is extremely low and falling, rather than increasing. As a result, most patients present with advanced disease whose most urgent need is often palliation. Patients are often abandoned when terminally ill and die an undignified death with poorly or uncontrolled pain and intense psychological discomfort.

PROBLEMS

Barriers to the development of palliative care in Pakistan are no different from those in other developing countries (Figure 1). Palliative care

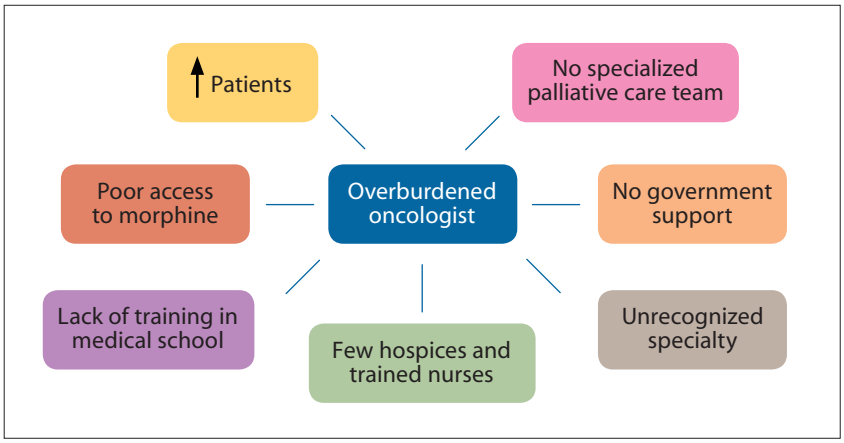

Figure 1. Challenges to the provision of essential palliative care.

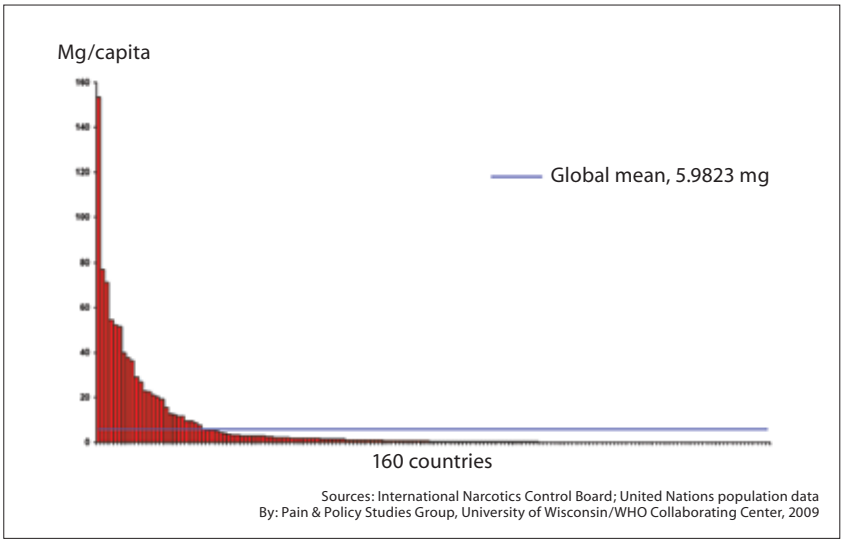

Figure 2. 2007 Global Consumption of Morphine mg/capita.

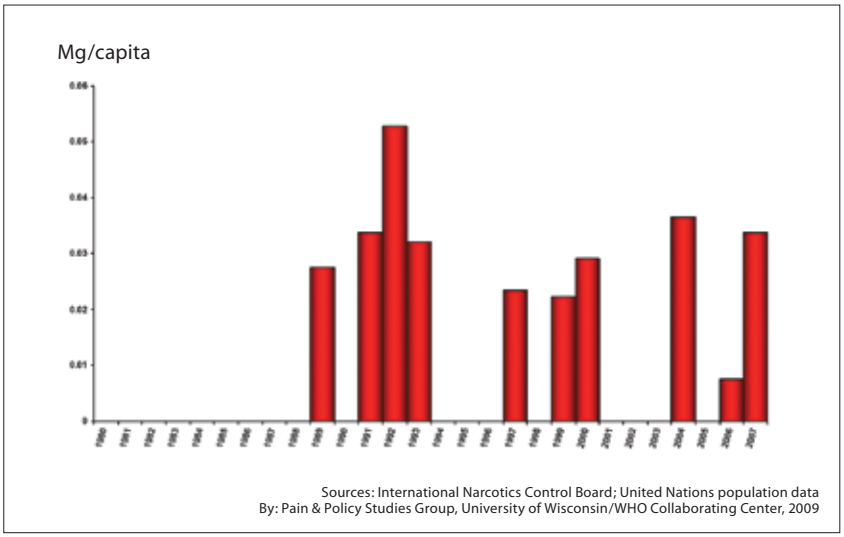

Figure 3. Mg/capita Consumption of Morphine, Pakistan, 1980-2007.

remains sporadic at best and little or no progress has been made in Pakistan over the last 10 years.

MORPHINE AVAILABILITY

Lack of opioid analgesia is one of the biggest problems faced in attempting to implement good pain control, especially for terminally ill patients. Morphine is not freely available, even at the major centers that treat cancer, supply is intermittent and there is no support from the government to improve its availability. As a result, Pakistan lags far behind most other countries in morphine consumption (Fig 2 & 3).

PALLIATIVE CARE SERVICES

Fairly well-developed palliative care services exist at the Shaukat Khanum Memorial Cancer Center (SKMCC) in Lahore, and the Aga Khan University Hospital in Karachi (see below), some private hospitals and a few hospices scattered across the country. Such pain management teams as exist usually consist of anesthesiologists. Even in these centers there is usually minimal home care and poorly developed pediatric palliative care services.

1. Shaukat Khanum Memorial Cancer Center (SKMCC), Lahore

SKMCC has introduced the Liverpool End-of-Life pathway and has a well-developed pain management and palliative care service consisting of a trained palliative care physician and nursing team. Services include in-patient care, out-patient clinics and round-the-clock availability of care providers through a 24-hour telephone support line. Home and hospice care is not well-developed, however, and even here, the supply of morphine is limited. Educational activities include a monthly video conference with St Francis Hospice, UK, where challenging cases are discussed, a monthly palliative care journal club, training courses for physicians and nurses, and international palliative care symposia.

2. Aga Khan University Hospital (AKUH), Karachi

AKUH has a palliative care team consisting of a trained palliative care physician, nurses and a social worker. In-patient and outpatient coverage is available and home care is well developed. Morphine is available for patients along with other pain medications. Educational activities include training seminars conducted locally.

3. Pediatric Palliative Care

Pediatric palliative care is in the early stages of development. The Children's Cancer Hospital, Karachi, and the Children's Hospital, Lahore,

both started small in-patient palliative care units in 2008. The unit at Children's Hospital, Lahore, was established with a grant awarded by the 'My Child Matters' program of sanofi-aventis and UICC in 2008 with mentorship provided by Dr. Aziza Shad. However, the lack of trained personnel and lack of knowledge in palliative care, insufficient supply of morphine and absence of outreach remain major problems.

Role of INCTR in Development of Palliative Care Services in Pakistan:
INCTR is actively involved in the improvement of palliative care services in Pakistan. Some of the initiatives in which it has been involved are described here:

1. In 2008, the 1st Palliative Care Symposium sponsored by INCTR and supported by OIA, NCI, was held in Karachi, Pakistan. Attended by over 100 physicians, nurses and social workers from all over the country, it resulted in a resolution to establish the Palliative Care Society of Pakistan. (Pict 1).
2. INCTR members have been actively involved in subsequent palliative care workshops in Pakistan, and Dr. Shamvil Ashraf from Karachi participated in the MECC/INCTR palliative care workshops in Cyprus.
3. Mentorship for both pediatric palliative care programs is provided by Dr. Aziza Shad. Based on the initial success of the palliative care initiative at the Childrens Hospital, Lahore, the 'My Child Matters' program has been extended by the program steering committee for a second year.
4. In 2008, INCTR officially partnered with APPNA (Association of Physicians of Pakistani Descent in North America) to initiate a program introducing palliative care all over Pakistan. This program is moving ahead and includes future training workshops and introduction of palliative care to the medical and nursing school curricula.

Opening session of the Karachi workshop.

Future Initiatives in Palliative Care in Pakistan:

1. There is an active interest to formally establish a National Palliative Care Association in order to introduce the discipline of palliative care into mainstream medicine in Pakistan. The goal is to increase awareness for palliative care in the community, which will make it easier to lobby the government for provision of support and to increase the availability of morphine.
2. Capacity building in palliative care with the help of organizations such as INCTR and APPNA.
3. Initiation of local training programs in management of pain and end-of-life care.
4. Establishment of a palliative care unit with trained personnel in all centers that treat cancer. Support from NGOs will be needed for this initiative.
5. Introduction of palliative care in medical, nursing, pharmacy and social work school curricula in Pakistan.
6. Focus on research in palliative care. ■

Aziza Shad, INCTR USA,
Muhammad Shamvil Ashraf, Children Cancer Hospital, Karachi, Pakistan
and Haroon Hafeez, SKMCH&RC, Lahore, Pakistan.

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PUBLISH OR PERISH

Scientific and medical research has three critical components: (1) planning the study, (2) conducting the study and recording the results, and (3) publishing the findings. A well-planned, well-conducted study that is not published for the benefit of the wider medical community is useless. It is also a waste of public money. Furthermore, it is on the basis of published reports that medical practice is improved. Medicine would remain static if doctors did not tell others about their observations and innovations.

Faculty and participants outside the INCTR office in Brussels.

Quite apart from the moral imperative of publishing, there is the importance of publishing for one's career. "Publish or perish!" The pressure on academics to publish intensified in the 1950s in universities in the United States and spread rapidly around the world in the following decades. Now, to advance their careers, doctors are obliged to publish regularly and often. Therefore, doctors must publish.

Something was forgotten along the way, however. Whereas the early scientists and doctors writing in the first part of the twentieth century were well-rounded scholars who wrote continually for various reasons, scientific and medical education has become more and more specialized. Thus, doctors today rarely have the practice of writing. They are taught how to design and do studies, but not how to write the articles they have to publish. Many have only a vague idea of how to organize their ideas and present them in a clear, accessible style.

Doctors in the developed world, and especially the United Kingdom and the United States and those at recognized institutions, find that their articles are readily accepted by biomedical journals. Thus, most of the publications in international journals are by authors in Europe and the United States. Good science and good medical practice are, however, being performed all over the world, and it is important that this work be known to the wider scientific and medical community.

In an attempt to correct the balance, three workshops have been conducted for the International Network for Cancer and Research and Treatment (INCTR) by Elisabeth Heseltine, with funding from the Office of International Affairs, National Cancer Institute, USA. To ensure that the workshops were attended by those in a position to benefit, five participants were chosen for each workshop, by an international panel, on the basis of a poster presented at the annual scientific meeting of the INCTR as well as their CVs. Attendees might never have written a scientific paper before, although this was not a prerequisite. It was clearly essential, however, that the scientific basis of the study and its conduct should be sound and that the data be worthy of publication.

After the participants had been selected, they were asked to prepare a draft manuscript and send it to Ama Rohatiner for review, to ensure that the scientific content was valid – scientific writing begins with good science! Shortly before the workshop, they each received the manuscripts of all five participants and a certain number of handouts by e-mail, which they were asked to read carefully before the start of the workshop.

The workshop is designed to help doctors with a good command of English (or for whom English is their native language) to structure their papers — that is, to arrange the necessary material into sections in a logical order so that the reader will be led through the arguments — and their justification — and thus appreciate the relevance of the results.

The workshop starts with a discussion on when to write an article, including literature searching. Participants are then advised to choose the journal to which they wish to submit their article. In that way, they are writing in the style required by a specific jour-

nal, and do not have to adapt their manuscript subsequently. The workshop then addresses the question of deciding on a good title. After a short presentation on the function of manuscript titles, each of the manuscripts is examined to see whether the title fulfills the criteria for a good title: one that attracts attention and reflects the content of the manuscript faithfully. This is important both for the reviewers and in attracting readers. The next step in the workshop is a discussion on deciding who should be authors and the order in which they are listed. The criteria for authorship agreed upon by the editors of the major international journals in the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals* are presented. It is pointed out that it is often a good idea for collaborative groups to develop authorship policies in advance of manuscript preparation to avoid subsequent authorship disputes.

The workshop continues with in-depth discussions of each subsequent section of each manuscript: writing the abstract, deciding on keywords, writing the introduction, writing the materials and methods section, writing the results section, designing clear tables and figures, writing the discussion section, who should be acknowledged and ensuring the accuracy and appropriateness of references. Throughout the workshop, Ama Rohatiner comments on the content of each section and makes suggestions for improvement.

Each day, the participants revise the parts of their manuscripts that have been discussed, and, on days 4 and 5, the revised manuscripts are examined again, with a short session on how to improve writing style, illustrated by Elisabeth Heseltine editing the participants' manuscripts on screen. The last session is devoted to the publication process, i.e., submitting a manuscript, dealing with reviewers' and editors' comments and correcting proofs.

By the end of the workshop, there are five manuscripts ready to send to the journal of each participant's choice.

The participants in workshops held to date have been from various developing countries. In the first workshop, held at the All-India Institute of Medical Science (AIIMS) in New Delhi, the participants were from Colombia, India and Nigeria. In the second workshop, also held at AIIMS, the participants were from India, Malaysia, Morocco and Nepal. The third workshop was held at the headquarters of the INCTR, in Brussels, and the participants were from Iraq, Nigeria and Pakistan. The institutions at which the participants worked also differed, from a teaching hospital in Zaria, northern Nigeria, and a children's hospital in Bahgdad to a well-equipped cancer hospital and research center in Lahore, Pakistan. Some participants had poor access to international journals, while others had a consistent Internet connection and were able to access publications online.

The outcome has been impressive: of the ten papers discussed at the first two workshops, six have been published, and three of the participants have subsequently written to say that they have published other papers since the workshop. Two of the manuscripts are still being worked on, and contact is being maintained with the authors. One participant can no longer be contacted; and the author of the final manuscript was in a conflictual situation with the first author of the paper and doubts that the differences can be resolved.

The workshops have also had additional benefits. A participant in the second workshop subsequently organized a workshop at her institute in Sarawak, Malaysia, and three out of four papers from that workshop were published. Another participant in the second INCTR workshop is trying to organize a workshop in Kathmandu and has himself run seminars on manuscript writing, using the PowerPoint slides and the handouts from the workshop. The wider dissemination of lessons learned reflects a general principal of INCTR's work — and indeed of the scientific method in general — ensuring that those who benefit from its various approaches to training and education use their new skills and knowledge to encourage others to conduct and disseminate research; and ensuring that research opportunities, which may differ in different developing countries, are capitalized on for the benefit of people in those countries and for the global research effort. ■

Natasha Anwar poses with her poster at the INCTR meeting in Antalya.

Elisabeth Heseltine, Université de Lyon II, Lyon, France and Ama Rohatiner, St Bartholomew's Hospital, London, UK

PEDIATRIC KAPOSI SARCOMA IN SUB-SAHARAN AFRICA: A REVIEW

BACKGROUND

The WHO estimates that 3.5 million children are living with HIV infection in sub-Saharan Africa (SSA), representing over 90% of all children infected with HIV worldwide (1-3). Undoubtedly, the HIV epidemic in SSA has been the greatest health challenge of the last decade and continues to be an ongoing burden in SSA. The consequences of HIV infection are numerous, but immune dysregulation, which gives rise to opportunistic infections and an increased incidence of cancer, is the most prominent consequence. Initial estimates in the US of HIV-related malignancies (HRM) in children suggested an incidence of 2% with NHL being the predominant cancer while Kaposi Sarcoma (KS) was predominately a disease of homosexual men (4). Experience in SSA suggests that KS is different in children in SSA.

This article will discuss the burden of childhood KS in SSA over the last ten years focusing on: the epidemiology of KS and Human Herpes Virus-8 (HHV-8), the patho-physiology and diagnosis of KS, and the treatment of KS in children.

EPIDEMIOLOGY OF HHV-8

The discovery of HHV-8 in 1994 assisted in understanding the pathophysiology of KS (5). The presence of HHV-8, also known as Kaposi Sarcoma Herpes Virus (KSHV), has been found in all cases of pediatric KS (6, 7). Interestingly, HIV-unrelated KS, including the Mediterranean variety, and African Endemic KS are also associated with KSHV, further supporting the essential role of the virus in the development of KS. Given the need for HHV-8 infection, the epidemiology of the virus provides a starting point for understanding the occurrence of KS in SSH, while comparison with the epidemiology of HIV is essential to understanding its relationship to the HIV epidemic. Estimates of the prevalence HHV-8 in SSA (8) show wide variations among the countries in this region (Table 1).

Country	HHV-8 Prevalence (%)
Botswana	87
Cameroon	13
Ghana	36
Uganda	37
Zambia	47
Range in Sub-Saharan Africa	**~ 15 to 90**

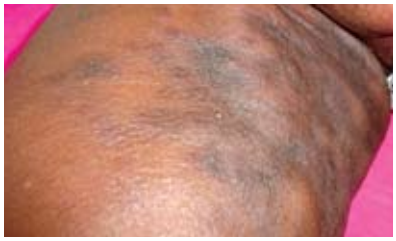
Table 1. Estimates of the prevalence in selected countries in sub-Saharan Africa.

The prevalence of HHV-8 is higher in SSA than in European countries and the USA, and infection occurs at a much earlier age, explaining the occurrence of African Endemic KS in children, whereas KS in children, even with HIV infection, is rare in the West. However, understanding the methods employed to detect the virus is important in interpreting results from HHV-8 prevalence studies. The virus cannot be grown in culture, therefore, there is no "gold standard" that can be used to assess the accuracy of other methods. KSHV can either be detected indirectly, through serology, or by means of PCR technology. (8) Studies using direct measurement of viral loads by PCR are more informative than indirect measurement with serological methods. However, serological methods are frequently employed due to limited resources in SSA.

Similar to HIV, KSHV has different subtypes. In Europe and the USA, subtypes A and C predominate, while subtype B predominates in SSA (8, 9). Subtype B is more oncogenic than the other subtypes (8, 9) such that the higher prevalence of a more oncogenic subtype would appear to explain the higher frequency of KS in SSA.

TRANSMISSION OF KSHV & PATHOPHYSIOLOGY

Despite the evidence that HHV-8 is necessary for KS development, the exact mechanisms of tumorigenesis are not clear. However, it does appear that transmission of KSHV occurs at a young age in SSA, similar to a number of other infections, such as Epstein-Barr virus (EBV). However the modes of transmission are not clear. One study in adults from South Africa did not find evidence for sexual transmission in the population studied (10) although other studies have suggested that sexual transmission is possible (11, 12). Whether or not this is so, the increased incidence in children cannot be explained by sexual transmission. Among the several possibilities,



Classic cutaneous KS with nodular, purplish lesions and associated lymphedema on the proximal thigh of a child.

each of which is supported by some evidence, are peripartum and even in utero transmission of HHV-8 (13), or salivary transmission. The latter is supported by the finding of high viral loads of HHV-8 in saliva with periods of increased viral shedding in mothers (14, 15) as well - documented evidence of mother-to-child salivary transmission via many routes including the common practice of pre-mastication of food (16) during and after weaning. Interestingly, patients with KS appear to have higher levels of HHV-8 shedding in saliva (17) such that the children of HIV +, KS + mothers are more likely to have both HIV and HHV-8 infection. HHV-8 is not present in breast milk, but has been detected in colostrum.

As mentioned earlier, the exact mechanism of KSHV oncogenesis is not understood. However, it is important to note that KSHV has also been associated with Castleman's disease and primary effusion lymphoma (7, 18). Indeed, it has also been demonstrated that children acquire diverse genotypic infections of HHV-8 (9) and that KS lesions are not monoclonal with respect to viral genotype (19).

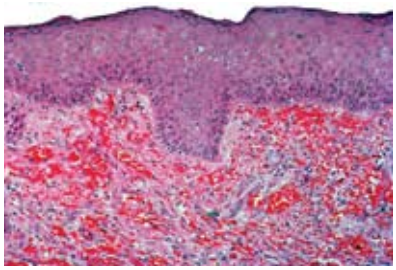
Although HHV-8 is critical to the development of KS, other factors, perhaps related to immune dysregulation from HIV infection, must be present for KS to develop.

EPIDEMIOLOGY OF KS IN RELATIONSHIP TO HIV INFECTION

Although, as mentioned already, KS was known long before the HIV epidemic (it was described in the University of Vienna by Moritz Kaposi in 1872), the presence of HIV infection has markedly modified the age distribution of KS. In SSA, there is a bimodal peak with the first peak in childhood (4-10 years) and the second peak in young adults (30-40 years). Over time, the second peak appears to be shifting to the left, resulting in an overall younger population with KS (20). This may partly be explained by increased mortality in SSA for persons over 40 years of age and the significant drop in longevity throughout SSA as a result of the HIV epidemic (2). However, it is clear that the incidence in children has also increased and there is no doubt that this is due to the HIV epidemic, since various studies from SSA estimate the odds ratio for KS to be 60-100 for children with HIV infection vs. uninfected children (21). Indeed, in one study of adolescents and young adults, 90% of KS was associated with HIV infection (22). Uganda has an HIV prevalence of about 5% (2) and there the incidence of KS in children was 3.6 per 100,000 from 1960-71 and it increased to 39.3 per 100,000 during the years 1991-97 (23). Clearly HIV infection plays a significant, if not fully understood, role in the development of KS.

DIAGNOSING KS

The diagnosis of KS in children depends upon the site of disease. KS can present with either mucocutaneous or lymphadenopathic involvement with or without visceral involvement. There are many approaches to diagnosis and in the settings of SSA, biopsy confirmation of disease is not always feasible. Given the practical aspects of working in resource-limited settings, as well as the frequent presentation of lymphadenopathic KS in children, a balanced approach must be followed. In instances where mucocutaneous disease is clearly present (Figures 1 and 2), a clinical diagnosis can be made. Similarly, in



Kaposarcoma skin biopsy.

the presence of classic skin findings, especially when associated with limb edema, a clinical diagnosis is generally considered sufficient to commence therapy. However, when, as is often the case, pediatric KS is lymphadenopathic, a broader differential diagnosis must be considered, including primary HIV lymphadenopathy (LAD), tuberculosis, and lymphoma, and biopsy will often be necessary to determine the diagnosis. Clearly, a correct diagnosis is critical as was demonstrated by a case study from Malawi (24). Clinical misdiagnosis as lymphoma and no response to therapy led to biopsy and a correction in the diagnosis with subsequent institution of appropriate treatment. Chemotherapy for a cancer diagnosis when tuberculosis is the true disease can prove fatal.

There is evidence that fine needle aspiration (FNA) can be used in place of formal biopsy when a skilled cytopathologist is available (25). However, in the absence of adequate diagnostic skill, FNA can frequently result in delaying a biopsy leading to a definitive diagnosis. Furthermore, in that study, ~50% of aspirations showed reactive lymphadenopathy, an inconclusive diagnosis that could be present in HIV or TB infection as well as early KS, such that a biopsy is necessary. However, FNA is certainly appropriate for detection of infectious etiologies, bacterial or myco-

bacterial through smears and culture, and can be performed, in part to decide whether formal biopsy is necessary, as long as there is not inordinate delay in reporting the results.

The true incidence of visceral involvement is not known. In one series of children with pulmonary KS, important clinical observations were made (26) that can be of assistance in the resource-limited setting where pediatric intensive care and bronchoscopy services are rarely available. In the study, 80% of children with pulmonary KS presented with pleural effusion on chest x-ray and all patients had airspace disease along with mediastinal lymphadenopathy on CT scan (26). Also, perihilar and lower lung field involvement predominated (26). While information of this kind cannot be used to make a definitive diagnosis, these findings can certainly assist in guiding the work-up and management of patients where a definitive biopsy or other diagnostics modalities such as bronchoalveolar lavage are not feasible.

PATHOLOGY OF KS

KS is a mesnchymal tumor that is believed to arise from lymphatic channels that fill with blood. There is a progression seen on histological examination from early reactive lymphocytosis (i.e., not true KS) to overt KS containing spindle-shaped cells and dense and irregular blood vessels from which erythrocytes may escape into the tumor stroma and surrounding tissue. There may also be inflammation within the tumor and in adjacent tissue. These characteristics ensure that the tumor has a highly vascular appearance. It is important to note that reactive lymphocytosis must be followed up clinically and a repeat sample sent if there is persistence of disease (e.g. lymphadenopathy) and certainly if there is progression of disease. KS lesions are expected to be positive for VEGF (Vascular Endothelial Growth Factor) the Flt-1 Receptor and LANA-1, (latency associated nuclear protein), which confirms the presence of HHV-8, although these tests are not widely available in Africa. Many histological variants of KS have been described {Grayson, 2008 #68} (Table 2).

TREATMENT OF KS

The treatment of KS in children poses several difficulties in resource-limited settings. There are no results of randomized clinical trials dedicated to pediatric KS treatment. Most data are from adult studies and are extrapolated to childhood KS. The use of anti-retroviral therapy alone has been shown to be effective in patients with limited disease. Liposomal doxorubicin has been shown to be effective in KS, however the high cost of this medication makes it unlikely that it will be widely available. Various centers in SSA rely on combination chemotherapy with either bleomycin-vincristine with or without adriamycin. Historical data suggest a 50-60% response rate to combination therapy (18, 27). However, there are no current published data available. In our institution we employ the three-drug ABV protocol administered every two weeks and have a survival rate of about 65%. (in preparation). There is some evidence that anti-angiogenic agents such as thalidomide may be effective in some patients.

CONCLUSIONS

Pediatric KS presents many challenges to the clinician working in SSA. Studies to date have clearly established the causative agent as HHV-8. The exact mechanism of tumorigenesis is not understood although HIV infection clearly provides a powerful synergistic effect. The diagnosis of KS in children warrants biopsy confirmation when classic skin findings are not present. Unfortunately, treatment strategies in children are not

Histological Type	Characteristics
Patch KS	Newly formed vessels protrude into a larger vascular space
Plaque KS	Diffuse dermal vascular infiltrate with increased cellularity
Nodular KS	Dermal expansion by proliferation spindle cells arranged in fascicles with erythrocytes between spindle cells
Anaplastic KS	Increased mitoses with cellular pleomorhpism with decreased vascularity
Lymphangioma like KS	Dermis replaced by proliferation of channels that do not contain erythrocytes spreading apart dermal collagen
Lymphangiectatic KS	Large intra- and peritumoral dilated lymphatics
Bullous KS	Intra- or subepidermal bullae with underlying KS lesion
Verruocous KS	Epidermis contains verruciform acanthosis and hyperkeratosis with associated fibrosis of the upper dermis

Table 2. Common forms of KS and their key manifestations.

clear, particularly in the HAART era. Studies in this direction would significantly aid the clinician working in SSA and this data clearly must come from SSA where the overwhelming majority of these patients reside. ■

References available on www.inctr.org

Parth Metha, Texas Children's Cancer Center, Baylor International Pediatric AIDS Initiative, USA and Botswana-Baylor Children's Clinical Centre of Excellence, Botswana

INDIAN CANCER SOCIETY – THE PIONEER OF CANCER AWARENESS AND WELFARE IN INDIA

The Indian Cancer Society (ICS), which has been in existence for nearly 60 years, has been a pioneer in cancer care and has many "firsts" to its credit. In 1955 and 1956, the Society established India's first cytology laboratory and first chemotherapy department at the Tata Memorial Hospital. In 1961, the first rehabilitation center for the poor afflicted with cancer was established at Parel, Mumbai. This center was the first of its kind in Asia. In 1963, the Society established the first cancer detection center and the first cancer registry in Mumbai, and also founded the *Indian Journal of Cancer*. ICS launched the first cancer insurance scheme in India in 1985.

To alleviate the economic and mental distress of cancer patients coming to Bombay and living on the streets around the hospital (for want of any other lodging they could afford), ICS started an experimental workshop in 1961 in one small corridor of the Tata Memorial Hospital. The objective was to give patients vocational training and small jobs during their active treatment phase, thus enabling them to sustain themselves during their stay in the city. In 1979, through the considerable efforts of Dr. D.J. Jussawalla, Mr. Naval Tata and Dr. Usha Bhatt, this idea of a single workshop in one small area of the hospital grew into a full-fledged rehabilitation center at Parel, about a kilometer from the Tata Memorial Center. The present Rehabilitation Center has for some time provided comprehensive rehabilitation and welfare services to the poor and needy suffering from cancer, including meals and nutritional supplements, prostheses, social services including counseling, financial aid for treatment costs, and vocational and occupational training.

In 1982, a Prosthetic and Orthotic Workshop was added. The unique aspect of this workshop lies in the fact that all the prostheses and aids and appliances are produced *by* cancer patients *for* other cancer patients and for those who have lost limbs due to reasons other than cancer. Different types of breast and limb prostheses, crutches, calipers, support belts and colostomy bags with irrigation sets are made at this workshop and are sold to patients all over the country at a nominal cost and provided at no cost to the very poor. In addition to the Prosthetic and Orthotic Workshop, the ICS Rehabilitation Center houses additional workshops where patients are given vocational training to suit their individual needs. All patients receive free meals and a daily stipend, which not only helps them financially during their stay in the city, but enables them to complete their treatment. This is vital as most patients are uninsured or underinsured and have no means to complete the treatment. Thus, patient support of this kind can save lives.

In 2007, the ICS in collaboration with another NGO, St. Jude India Child Care Centers, set up accommodations in the form of 14 units at the Rehabilitation Center where the families of children suffering from cancer could stay. Another 16 units were added in 2008. These units are completely free of cost and house the children in a safe and hygienic atmosphere, which is vital for their recovery. The children live here as long as their treatments last, and they are cared for by an extremely competent and dedicated team of staff and volunteers.

Today, the ICS Rehabilitation Center is a hub of activity, providing vocational training and sustenance to about 100 poor cancer patients/survivors every day. Here, they are given the chance to eke out a living while not having to sleep on the streets outside Tata Memorial Hospital, where many of them would otherwise be forced to stay. With increasing survival rates, the quality of survival assumes vital significance. The Rehabilitation Center contributes greatly to the mental and economic well-being of these poor cancer patients.

THE IMPORTANCE OF EARLY DETECTION

Early on, the ICS understood that *when detected early, cancer is treatable and curable*. The Society realized there was an urgent need to establish a service whereby people who otherwise would not opt for regular check-ups could be screened for the various commonly occurring cancers. With this in mind, the ICS started cancer check-ups for the public at various detection centers in Mumbai. However, there was

a need to reach out to those living in the villages and cities where there was no access to such centers. In order to provide this much-needed service, the ICS launched India's first Mobile Cancer Detection Center (MCDC) on March 27, 1982, in Mumbai. By the end of May 2010 a mobile mammography van with digital CR will become operational.

As part of its research activities, the ICS established the Mumbai Cancer Registry in 1963 with the aim of obtaining reliable incidence and mortality trends on cancer from a precisely defined urban population. Data compilation began in 1964. Until then, no continuing activity on registration of cancer cases in a population had been undertaken in India. The registry started in collaboration with the biometry branch of the U.S. National Cancer Institute. Since 1981-82, the registry has become a part of India's National Cancer Registry program.

The Mumbai Cancer Registry's data has been accepted for publication in seven editions of the widely recognized *Cancer Incidence on Five Continents*, two volumes of the *International Incidence of Childhood Cancers* and two volumes of *Cancer Survival in Developing Countries,* all publications of the International Agency for Research on Cancer, part of the World Health Organization.

Not content with resting on its laurels, today the ICS's Managing Committee, comprising the best minds from the medical, corporate, financial and legal worlds, is led by Mr. Nihal Kaviratne, Dr. Arun Kurkure, an eminent onco-surgeon, and Mr. Hari Mundra. The Managing Committee leads the full ICS team and strives to promote a movement of compassion and care in the context of the newer, more modern approaches to comprehensive cancer welfare, rehabilitation, awareness and early detection. The aim is to move forward, in tune with today's needs, and to bring about much-needed changes in the way society helps the poor suffering from cancer. ■

Arun Kurkure, Lady Ratan Tata Medical & Research Center, Mumbai, India

AMCC ANNUAL GENERAL MEETING

The AMCC (INCTR's French Branch) Board of Director's meeting and Annual General Assembly took place on 3rd June. ■

VISITS BY DR. BODE TO INCTR AND SUBSEQUENTLY TO TANZANIA

Dr. Bode, former head of the pediatric oncology unit of Bonn University visited INCTR in Brussels on 4th June to discuss his future participation in INCTR's Pediatric Oncology Program. He was accompanied by his wife, Gerlind, who has been very active in national and international associations for the Parent's of children with cancer. Discussions were fruitful and a visit was proposed to Tanzania for the Bode's to see something of INCTR's activities in pediatric cancer at first hand at the Ocean Road Cancer Institute (ORCI) and to provide some education and training of staff members. The visit proved to be extremely valuable. ■

MEETING WITH THE ASSISTANT TO THE IRAQI AMBASSADOR

A meeting took place on June 18th at INCTR's offices to discuss with a representative of the Iraqi Embassy what contributions INCTR could make to cancer control in Iraq. In the past, INCTR has held several workshops for Iraqi pediatric oncologists. The possibility of collaborating in the control of breast cancer in Iraq was also discussed. ■

DISCUSSION ON NON-COMMUNICABLE DISEASES

A telephone conference call was held with Drs Grey and Seffrin of the American Cancer Society (ACS), Mark Lodge of INCTR UK and Ian Magrath, to discuss what might be done by INCTR and ACS to insert a reference to non-communicable diseases into the Millennium Development Goals. It was agreed, as a first step, to write a letter to the British Medical Journal. ■

VISITS TO TANZANIA

Dr. Jay Halbert, a pediatrician in training in London, left on 22nd July to spend a month at the Ocean Road Cancer Institute (ORCI) in Dar es Salaam to work with Dr. Trish Scanlan, INCTR's pediatric cancer representative in Africa, who is in charge of chemotherapy in children's cancer at ORCI. Dr. Harold Robles, of the Medical Knowledge Institute visited ORCI on 6th August to discuss establishing a program whereby patient's mothers could be gainfully employed while in Dar es Salaam, thereby helping to cover the costs of treatment and potentially, loss of income. ■

MEETING IN VANCOUVER TO DISCUSS NURSING CURRICULUM

On 24th Augusts, Virginia LeBaron, PAX's palliative care nurse, met with colleagues to discuss the development of a curriculum for palliative care nursing training in developing countries. ■

Errata; in Part 2 of the President's message, the term nucleotide(s) should have read nucleotide base(s).

THE NATIONAL CANCER INSTITUTE, BRAZIL

BACKGROUND INFORMATION

Brazil is the largest country in South America, with a territory of 8,514,876 km² and 190 million inhabitants. Its

The National Cancer Institute.

population, the fifth biggest population in the world, is very diverse, comprising many races and ethnic groups. In general, Brazilians trace their origins from four major ethnic groups: Amerindians, Europeans, Africans and Asians. Portuguese is the official language.

Brazil's demography is presently undergoing a profound transformation as a result of a reduction in the population growth rate and an increase in lifespan, resulting in a significant increase in the elderly population. These changes have resulted in an altered pattern of diseases and changes in mortality rates in recent years. From 2000 to 2007 the number of deaths caused by cancer in Brazil has increased more than 40% (from 120,517 to 161,491). Cancer has become the second leading cause of death after cardiovascular diseases. During this same period, public health expenditure per capita, has increased from US$110,00 to US$350,00, including federal, state and municipal government expenditure. According to the Cancer Estimates, published every two years by the National Cancer Institute of Brazil, 490,000 new cancer cases and 150,000 deaths caused by cancer are expected to occur in 2010. These data are extrapolated from population-based cancer registries, which have been established in 17 municipalities and cover 20% of the Brazilian population.

The 10 most common cancer types in Brazilian men	Estimated new cancer cases for 2010
1. Prostate	52,350
2. Lung	17,800
3. Stomach	13,820
4. Colon and rectum	13,310
5. Mouth	10,330
6. Esophagus	7,890
7. Leukemia	5,240
8. Skin Melanoma	2,960
9. Other	59,130
Subtotal	**182,830**
10. Skin Non melanoma	53,410
Total	**236,240**

Table 1. Cancer Incidence Rates for Brazil in 2010 - Male.

THE NATIONAL CANCER INSTITUTE OF BRAZIL

The National Cancer Institute – INCA, with headquarters in Rio de Janeiro, is a branch of the Ministry of Health of the Federal Government and has primary responsibility for the design and implementation of cancer control policies in the whole country, covering the entire continuum of cancer control, from prevention through early detection, treatment and palliative care, including education, surveillance and research.

INCA was founded in 1937 (see historical facts below) as a result of a decree by the President of Brazil. Since then it has earned a reputation as the most prestigious public cancer control institution and one

The 10 most common cancer types among Brazilian women	Estimated new cancer cases for 2010
1. Breast	49,240
2. Cervix Uteri	18,430
3. Colon and rectum	14,800
4. Lung	9,830
5. Stomach	7,680
6. Leukemia	4,340
7. Mouth	3,790
8. Esophagus	2,970
9. Other	78,770
Subtotal	**192,590**
10. Skin Non Melanoma	60,440
Total	**253,030**

Table 2. Cancer Incidence Rates for Brazil in 2010 - Female.

of the best health care providers in the country. This is a perception shared by other health care organizations, from government officials and national leaders to the public at large.

In 2005 the Ministry of Health, in view of its determination that cancer is a public health priority, developed a National Cancer Control Policy as recommended by resolution 58.22 of the World Health Assembly. In order to implement the plan, INCA has been developing a Cancer Control Network, where governmental and non-governmental organizations are joining hands to help raise awareness of cancer in order to reduce the cancer burden and to ensure the best possible quality of life in patients undergoing treatment.

Since 1988 Brazil has benefited from one of the most advanced publicly-funded systems of the world: the *Sistema Único de Saúde* (SUS; Portuguese for Unified Health System), which delivers medical care at no cost to more than 80% of the Brazilian population. However, the cost of treatment, in spite of assistance granted by the Ministry of Health, remains high, thus limiting the quality of care available to the majority of patients, including those with cancer. Only 18.5% of the population can pay for private insurance.

CANCER CARE

INCA delivers complete cancer care at no cost to its patients through five national tertiary referral SUS centers located in Rio de Janeiro. Services extend from diagnosis and staging to rehabilitation and palliative care. Bone marrow transplantation is available and clinical research is ongoing in all five centers.

INCA´S REFERRAL CARE UNITS

Cancer Hospital I
INCA´s major cancer care unit and one of the best equipped hospitals of the Ministry of Health. It is able to deliver highly complex cancer care to adult and pediatric patients with various types of cancer.

Cancer Hospital II
Especially designed to provide care to adults with gynaecological cancers.

Cancer Hospital III
This hospital plays an important role in breast cancer diagnosis and treatment.

Cancer Hospital IV
Provides palliative care, including psychosocial support and pain management. It is particularly focused on home care for patients from Rio de Janeiro.

Center for Bone Marrow Transplantation
This unit coordinates and runs multidisciplinary treatment for patients with malignant hematologic and genetic diseases eligible for bone marrow transplantation. It also runs the National Register for Bone Marrow Donors (REDOME) and the National Register of Bone Marrow Recipients.

Treatment outcomes at the five care units are comparable to the best oncology centers in the world, in part due to sophisticated informatics systems which provide online data and help in the monitoring of patients. The analysis of collected data leads to continuous and effective improvement in all aspects of care. All care units have been accredited by the Joint Commission on Accreditation of Healthcare Organizations in the last two years. To meet the needs of the SUS regarding the delivery of equitable cancer care services throughout the country, INCA has a *National Oncology Attention Expansion Program*.

INCA'S MISSION: NATIONWIDE INTEGRATED ACTIONS FOR CANCER PREVENTION AND CONTROL

As a branch of the Brazilian Ministry of Health, INCA faces the challenge to reduce cancer incidence and mortality throughout the country by implementing a comprehensive National Cancer Control Program according to its mission and strategic vision.

VOLUNTEERS

Our Volunteer Program is made possible in large by the philanthropic support of community representatives. Over 700 men and women of all ages and from all walks of life serve as volunteers in all five care units, providing patient support in various ways, including the donation of food, flea market organization and recreational activities.

ORGANIZATION

Along with its five care units, INCA has a center for prevention, early detection, and surveillance programs, a research center, an education unit and other facilities such as a manage-

ment unit, a human resources unit and a TI center, dispersed throughout the city of Rio de Janeiro.

NEW REFERRAL CANCER CENTER BY 2014

The process of coordinating all activities related to cancer control within INCA has become increasingly more complex in the past years. Acknowledging this, the Institute decided to concentrate all its units into a single integrated campus. This new center, which will be completed by 2014, will be built on a 14.5 thousand m^2 property located immediately behind Cancer Hospital I. The building costs, which will be met with federal funds provided by the Ministry of Health, will be around US$150 million. The goal of the new campus is to become the most modern referral cancer care and research center in the country. The building will increase the total number of beds for cancer patients to 400, and permit the treatment of more than 10,000 patients per year in one place. This will permit INCA to be able to include 30% of its patients in clinical trials (as opposed to only 5% at present).

FUNDING AND SUPPORT

INCA's basic funding is provided by the Ministry of Health and the SUS. Additional government resources are provided by the Ministry of Education, the Ministry of Science and Technology and other government funding agencies. Private resources are provided by Brazilian and international companies and institutions.

INCA also receives technical and financial support from the Ary Frauzino Foundation for Research and Cancer Control (Fundação do Câncer), a private, non-profit entity whose goal is to support the full range of INCA activities, permitting the purchase of the latest equipment and the attraction of highly qualified staff members. The Foundation is supported through financial resources of the SUS and donations of companies and individuals.

A surgical procedure underway at INCA.

PREVENTION PROGRAMS

Cervical cancer is one of the most prevalent types of cancer, and potentially one of the easiest to prevent and cure when diagnosed early. Breast cancer is the main cause of death among women, particularly in the age between 40 and 69 years,

due to the advanced stage in which the disease is usually detected. Lung cancer is the second and fourth most prevalent cancer type among men and women respectively.

The goal of the *National Breast and Cervical Cancer Control Program* is to reduce mortality, psychological and social impairment resulting from cancer. It advocates actions towards the early diagnosis of those two types of cancer, respectively, through a Pap smear test and the clinical examination of the breasts, and the proper treatment of the tumor.

Comprehensive practical advice on how to prevent, detect early and treat breast and cervical cancer is provided by INCA to the 26 Brazilian States and the Federal District. Early detection of breast cancer and cervical tumors is also included in the guidelines of the National Cancer Control Policy, launched in 2005.

Since 1989, INCA has been managing the *National Tobacco Control Program* in Brazil with impressive results. Our Institute coordinates this program, jointly with state and municipal health departments and other social segments, by developing countrywide strategies with a focus on schools, workplaces and health care units.

After 20 years, the prevalence of Brazilian smokers aged over 18 years has been reduced to about 40% due to various measures taken such as the banning of tobacco products advertising, health warnings and images on cigarette packages and most recently the approval of laws (at federal, state and local levels) which forbid smoking in closed environments. Within the SUS, smoking cessation programs are offered to the Brazilian population, including the provision of free nicotine replacement therapy. Other measures taken by the Brazilian Government include:

• The regulation of the manufacture, distribution, sale, and advertising of cigarettes and other tobacco products, on which high taxes are also imposed.

• Public education campaigns, which have contributed to making cigarette smoking unfashionable and unattractive.

Due to the achievements of its Tobacco Control Program, INCA has been recognized, since 1996, as a WHO Collaborating Centre for Tobacco Control for Latin America, including both Portuguese and Spanish-speaking countries. In 2005 Brazil ratified the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC).

TRAINING AND EDUCATION PROGRAMS

Education programs, ranging from technical to post-graduation degrees, are developed, evaluated and improved to meet the needs of the SUS. For professionals with university degrees INCA offers *lato sensu* post-graduate certification in the fields of medicine, nursing, nutrition, physiotherapy, social service, psychology and pharmacology as well as other subjects. Medical and nursing residency programs are offered, with specialization in specific areas of medical oncology.

Specifically designed training programs for technical staff include clinical pathology, cytology, histology, nursing and radiation therapy. The Cytology Program plays an important role in the prevention of cancer in women through training specialists for the analysis of screening tests for cervical cancer.

In 2005 INCA became the second institution in Brazil and the first in Rio de Janeiro to run *stricto sensu* post-graduation programs on masters and Ph.D. degrees.

INCA also offers refresher and re-education programs, fellowship opportunities, and observation visits for interested health professionals from all parts of the country.

RESEARCH PROGRAMS

INCA fosters the production of scientific knowledge to improve diagnostic and therapeutic procedures. Studies within the research program are focused on experimental, translational, clinical and epidemiologic aspects of oncology. The Institute fosters healthy scientific exchange with several similar institutions and research centers in Brazil and abroad. Scientists are strongly encouraged to produce and disseminate scientific knowledge, with a focus on the improvement of diagnostic and therapeutic procedures and on the education of research scientists.

The National Tumor Bank (BNT), located at INCA, is the first in Brazil. Its purpose is to establish a network for the collection and storage of samples of the most relevant tumors in the country. BNT provides the finest conditions for studies focused on diagnostic and therapeutic markers in the most representative cancer samples of the Brazilian population. Using evidence collected as a result of BNT, INCA aims to explore the possibility of individualized treatment based on the tumor genetic profile, in the hope that this will predict the response of tumors to particular drugs. As the BNT network takes form, INCA is simultaneously collaborating with other countries to establish a Latin American Tumor Bank Network.

Research activities focus on four areas: cellular biology, pharmacology, genetics experimental medicine and immunology. Approximately 30 research projects are ongoing.

INTERNATIONAL COOPERATION

Acknowledging that cancer is the second cause of death in the world after cardiovascular diseases combined, and the financial impact as the cost to the health system grows exponentially each year, the Brazilian National Cancer Institute and the Ministry of Health of Brazil have recognized that it is extremely important to reduce the global burden of cancer. Therefore, INCA interacts with several national and international institutions and organizations, getting involved in a network, by seeking global efforts, and focusing regional solutions. Some of the initiatives are listed below:

The *Ibero-American Network of Tobacco Control* was established to coordinate common tobacco control actions among the participating countries regarding their efforts to adopt the initiatives and regulations established by the WHO Framework Convention on Tobacco Control.

A number of Latin American countries with various levels of research and health care delivery capacity have joined with the Office of Latin American Cancer Program Development (OLACPD) to form the *U.S.-Latin America Cancer Research Network*. The Network initially includes Argentina, Brazil, Chile, Mexico and Uruguay, and is responsible for developing a comprehensive understanding of the status of the disease burden, cancer research, and cancer care infrastructures, while building collaborative relationships to support high-quality research and clinical studies. INCA, representing the Brazilain Ministry of Health, is in charge of leading and coordinating the actions in Brazil, which include several other cancer institutions. The current pilot project of the U.S.-Latin America Cancer Research Network is focused on advanced breast cancer and will result in a better understanding of incidence and mortality in the diverse populations that make up Latin America.

In 2007 INCA hosted the *2nd International Cancer Control Congress*, in association with the British Columbia Cancer Agency and the support of the governments of Canada and Brazil. One important result of the Congress was the creation of the *Latin American and Caribbean Alliance for Cancer Control* with the goal of providing a forum for collaboration in cancer control activities in the context of recommendations of the Pan-American Health Organization (PAHO) and the World Health Organization. The Latin American Tumor Bank Network was part of this effort; in addition, meetings involving a number of Latin American countries on breast cancer and cancer registries have been held.

INCA plays another important role as a member of the International Union Against Cancer (UICC), contributing its experience and regional leadership to help strengthen regional and global cancer control efforts. As a signatory of the World Cancer Declaration from 2008, as part of the global cancer community, and responding to the UICC Call to Action, the Institute is committed to provide resources and political backing for the priority actions needed to achieve the declaration's targets. Another UICC initiative is the World Cancer Day, celebrated every February 4th, for which INCA carries out a series of actions to highlight this date. In August 2008, Dr. Luiz Santini, director general of INCA, was elected a member of the UICC Board of Directors.

INCA does not have a formal agreement with INCTR at present. But as a member of the Steering Committee of the 2nd International Cancer Control Congress, held in Rio de Janeiro in 2007 (see information above), Dr. Ian Magrath, President and director of INCTR, contributed significant time and effort to the planning of this event. In addition, INCA has representation on INCTR Brasil's Board of Directors and is discussing the formation of a special relationship with the recently formed INCTR Canada. ■

INSTITUTION´S RESOURCES (2009)

Total number of beds	374
Staff physicians (all dedicated to cancer care)	1,461
Nurses (all dedicated to cancer care and research)	218
Pathologists	10
Oncologists	211
Radiotherapists	30
Pediatric oncologists	12
Surgical oncologists	208
Oncologists in training (postgraduate students, residents)	131
CT Scanners	5
MRI Scanners	2
Cobalt Radiotherapy units	2
Linear Accelerator units	4
Total patients seen at INCA in 2009	58,163
Total inpatients in 2009	15,957
Total outpatients in 2009	42,206
Total adult inpatients in 2009	14,938
Pediatric cancer inpatients (up to 18 years) in 2009	1,019
Adult cancer outpatients in 2009	40,455
Pediatric cancer outpatients (up to 18 years) in 2009	1,751

Luis Santini,
INCA,
Rio de Janeiro, Brazil

PROFILE IN CANCER MEDICINE

RADIATION ONCOLOGY IS NOT ENOUGH !

Dr. Baffour Awuah, a radiation oncologist presently working at Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana, undertook his basic medical education at Kwame Nkrumah University of Science and Technology, Kumasi, from where he graduated in 1989. Although a leader in the cancer field in Ghana, it was more by chance than design that Dr. Baffour became an oncologist. "My oncology career started after attending an introductory course on cancer epidemiology organized by the International Agency for Research on Cancer (IARC) in The Gambia in May 1994. A colleague and I saw a poster about the course and jokingly agreed to apply. We sought funding from friends and used our own savings to raise enough money to attend. The course proved pivotal in my career because it was there that I met well-known epidemiologists like Freddy Sitas and Max Parkin, who were facilitators at the course. I was inspired by them to embark on a career in cancer." Through the award of an IAEA fellowship to study in Johannesburg, Dr. Baffour became a Fellow of the South African College of Radiation Oncology in October 1998.

Returning to Ghana in 2000, Baffour saw that there was much to be done in the field of cancer. "Some of the challenges I recognized were the lack of cancer data, late stage presentation, delayed pathology reporting, and no cancer control program. And this was in the midst of a progressively increasing incidence of cancer coupled to a low level of cancer awareness in the country." In spite of the capital investment

Dr. Baffour Awuah.

that had been made by the government to establish a new radiotherapy center, Dr. Baffour saw that there would be "no meaningful return on the investment because over 80 percent of the patients seen had sufficiently advanced disease for palliation to be their only realistic option."

He wasted no time in trying to change things. "In 2000 I wrote a letter to the Director of IARC and pointed out the need for cancer registration in Ghana. This letter resulted in a visit by Max Parkin, then the Director of Descriptive Epidemiology at IARC, whose recommendations led to the establishment of cancer registries in both Kumasi and Accra." Baffour also recognized the need for early detection, if patients with potentially curable cancers are to be given a chance to survive. He volunteered to participate in periodic radio and TV cancer education programs as well as educating groups in churches and various other organizations. Dr. Baffour is particularly proud of being the first radiation oncologist to work in an oncology center located in northern Ghana, and also of his role in the reestablishment of pathology services at KATH, which had ceased to exist when he went to Kumasi in 2004. At that time," he says, "diagnosis was subject to months of delay at best." With the help of Professor Helga from Norway, and Pathology International, improvements in pathology services have taken place, with diagnoses now being available within two weeks. A well staffed laboratory should become operational at KATH in 2010.

Dr. Baffour is also proud of his role in developing a proposal that resulted in the government receiving an OPEC loan to help expand cancer services infrastructure and delivery. Indeed, realizing that good management is crucial to success, he is currently studying for an Executive Master's degree in Business Administration.

Another of Dr. Baffour's interests is traditional medical practice which, he states, is "ingrained in our society and many other African countries." He believes it essential to develop integrated health services where orthodox and traditional practitioners operate in the same hospital. His first efforts in this direction began in 2009 with a meeting with the Ashanti region herbal practitioners, which attracted close to 100 participants. He hopes to pursue this work in conjunction with INCTR.

Dr. Baffour feels strongly that: "Wherever we are in this world we can do the little we can with the limited resources we have. We should, therefore, begin to talk about solving problems instead of merely talking about problems. The best we can all do is to change ourselves and not try to change others, and to adopt a positive outlook: Yes, we can!" ■