

NETWORK

THE NEWSLETTER OF THE INTERNATIONAL NETWORK FOR CANCER TREATMENT AND RESEARCH

INCTR

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THE PRESIDENT'S MESSAGE

LANGUAGE AND CANCER

Part 2. Reading the Signs
by Ian Magrath

Philosophy is written in this grand book - the Universe... but it cannot be understood unless one first learns to comprehend the language and interpret the characters in which it is written.
Galileo Galilei.

Galileo Galilei, one of the giants upon whose shoulders Isaac Newton metaphorically stood, referred to the universe as a continuously open book. Close observation of the celestial bodies was all that was needed to reveal its secrets - but only to those able to understand its language. In the last ten thousand years or so - a mere moment in life's four and a half billion years of evolution - human beings, living on a small planet orbiting an average star in an average galaxy, finally learned, or perhaps were taught by the *cosmos* itself, the syntax of this universal language. To use it to the full required the development of instruments able to bring the sounds and sights of the universe



The alphabet we use today is derived from a set of simple pictograms depicting objects and animals familiar to early agricultural communities. Modified symbols that we refer to as letters are named after the Phoenician pictograms (e.g., aleph: ox, beth: house, gimel: camel) and came to represent the first phoneme of each noun. The full set of letters, or alphabet (after the first two letters in the Greek version), allows graphic representation of the sounds of human speech.

into the limited range of human sense organs, but once accomplished, messages that had started their journeys long before the emergence of life itself arrived magically from the universe. The shifts in the spectra of electromagnetic radiation reaching us after billions of years of travel from the atoms in distant galaxies, and the cosmic

microwave background (CMB), a relic of the universe from a time before the galaxies of stars began to form, speak eloquently of a dynamic (evolving) universe and of the beginning of time. Miraculously, lessons learned from painstaking observation and experiment on one small planet amongst the trillions of celestial bodies has allowed

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a plausible reconstruction of the events that took place in the first few minutes of the existence of the universe - at a time, in the absence of a solar system, when a minute had no meaning. It might seem that the empiricists were correct - that all human knowledge derives from experience of the world (in its broadest sense) in which we find ourselves. Even theories involving imperceptible or unimaginable phenomena, such as the existence of more than four dimensions, or of multiple universes, which at first sight might appear to be the fruits of pure (*a priori*) reason are, in truth, mere extensions of the perceptible. More tenuously linked to experience are discoveries that spring unsought from mathematical equations, such as the patterns inherent in the *Mandelbrot set* (Figure 1), or the indication in Dirac's equation, developed to describe the characteristics of the electron, that

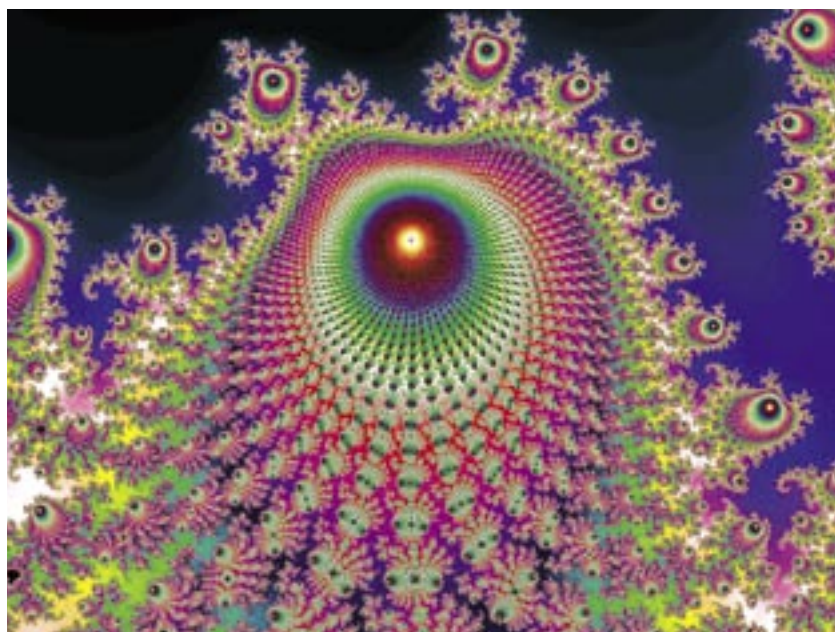


Figure 1. The Mandelbrot set is a family of complex numbers, each consisting of a real plus an imaginary number (a multiple of $\sqrt{-1}$) with a magnitude less than two (see <http://www.olympus.net/personal/dewey/mandelbrot.html>). The set derives from reiterations of a simple polynomial equation ($Z = Z^2 + C$) where Z is a complex number and C a constant. The resultant pattern on the complex number plane can be endlessly explored simply by “zooming in.” This example, *Budding Turbines*, is by David R. Ingham. Mathematical relationships of this kind do not originate in either our sensory world or the mind, but are linked to both through the invention of mathematical symbols and the rules that allow them to be meaningfully manipulated.

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anti-matter must exist. Such phenomena derive neither from experience nor from classical *a priori* reasoning. Instead, they seem to emerge from the archetypical *Forms* that Plato believed must underlie reality. The *Forms* were silent until sufficient competence was achieved in mathematics (the language to which Galileo referred) to understand their messages. For long used to describe the patterns of cancer in populations, mathematical interpretation has now also become an essential tool for decoding the patterns of gene expression in cancer cells, providing information that is fueling advances in diagnosis and treatment.

SONIC MAPS

Human speech can be thought of as a medium to which events experienced in the external world can be mapped and the resultant sound patterns communicated to others. Accurate reception of the informational content requires the recipient to have had a similar world experience; verbal descriptions, for example, cannot convey images to the minds of persons blind from birth and abstract ideas must be communicated through metaphors referring to actual experience. The origins of the elementary particles of speech, phonemes, remain unknown, but at least some may have been inspired by the natural

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sounds that our ancestors heard around them, including birdsong, the gurgling of water, animal noises and the sounds they themselves could make by rubbing or pounding objects together. Rhythm, a critical element of language, is inherent in all that exists (as expressed in the Hindu Shiva Natarajan). Each language has its characteristic music, which sculpts the sound patterns in distinctive ways, helping to define the parts of speech while simultaneously expressing feeling - imbuing the language with a sense of vitality. The music is lost when words are frozen into graphic or electronic symbols, although it can be recreated from them. Perhaps not surprisingly, writing was initially always read aloud. By elevating the importance of pitch and rhythm to that of words, or eliminating words entirely, for example, by the use of musical instruments, emotion can be made the dominant or exclusive element in the resultant sound patterns. Music can excite or inspire, soothe or console, and even encompasses a dispassionate form of wordless communication. It provides, like language, a sense of communal identity and is a critically important component of culture.

A COMMUNAL CREATION

While words and their usage may originate in individual minds, effective communication requires the use of identical (or nearly so) syntax and semantics throughout a community. Language is, then, a communal creation. Coupled to reliable memory, language allows information to be shared by some or all of the community, the survival value of which might reasonably be compared to the evolution of photosynthesis and

aerobic respiration, for all three have had a profound impact on life on this planet. The ability to transmit verbal information both horizontally and vertically (i.e., to succeeding generations), created the potential for extremely rapid adaptation to quite different environments and allowed ever-expanding kinships to define and redefine their community's culture - its creation myth, its political structure, its way of life and its ethical and moral foundations. Much of the flexibility inherent in verbal communication was lost when communal stories were finally written down and fixed, sometimes for all time, by one or a small number of authors. Homer's *Iliad* and *Odyssey*, for example, have remained unchanged since first recorded almost three thousand years ago. Writing, however, gave wide access to the rich cultural heritage of individual peoples. Herodotus was one of the first historians, ethnographers and anthropologists to record such information, and we can still read his works today.

Retrospectively, the foundational stories that inspired our ancestors are strongly equated with religion. The word *religion* implies linkage of the human mind to its foundations, and in this sense, the communal stories of the prehistoric era were religious. They provided an all-embracing matrix for everyday activities and conferred meaning on the people's lives. But prehistoric peoples had vast lacunae in their understanding, and the awe in which they held natural phenomena such as mountains, rivers and storms led to their transformation into mental images of magical forces, or *numina*. To them, the animals and plants upon which their lives depended were

sacred. Through a process of collective confabulation, these supernatural powers, conjured from the world around them, were woven into stories reflecting their own fantasies and frailties (and hence, increasingly conceptualized in human form) - stories that, repeated over the generations, took on the cloak of truth while retaining their dreamlike aura. Ancestor worship was also frequent. It was natural in tribal societies in which the long experience of the elders could save lives, to revere those who had molded society into its present form.

It was probably the agricultural revolution that gave birth to a sense of control over nature. Initially minor - the intervention of the gods was still sought to ensure good harvests and fertile animals - the sense of separation and superiority increased dramatically during the industrial revolution when many ill-advised and irreversible large-scale schemes to clear forests, drain swamps, divert rivers and build dams were undertaken. Technological progress, derived from the cumulative wisdom of the ages, provided a launching pad from which to soar, at last, far beyond the confines of the sensual world. Such wisdom could not have been preserved without the development of writing - a powerful intellectual tool harvested from their surroundings by the genetically prepared minds (see picture) of the first farming communities, whose new way of life had led to the need for accounting systems and calendars. These pioneers could have had no idea of the eventual uses to which their graphic symbols would be put. Written numerical systems developed simultaneously and the letters of the alphabet, sometimes in their

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Greek form, eventually provided a convenient means of representing generalized numbers and physical constants - both of which were central to the development of mathematical descriptions of natural laws.

ABSTRACTING THE ALPHABET

The "aide-memoirs" used by early agriculturalists to keep records of their commodities were an important element in the creation of the alphabet. Notches on sticks initially sufficed, but their lack of specificity led to pictorial representations of specific items (*pictograms*). In some cultures, pictograms gave way to *logograms*, which are graphic symbols, often composite, that are able to represent a broader range of words or morphemes and have a utility considerably beyond simple record keeping. Egyptian and Mayan hieroglyphics were comprised of logograms, but Chinese is the sole remaining language in which logograms are used to represent words. Chinese characters provide glimpses of the recombination of ideas that allow the creation of new graphic symbols, e.g., *cancer*, as depicted in Figure 2. Pure logograms do not indicate how to pronounce the word they represent and can thus be used to write quite different languages (Mandarin, Cantonese and many Japanese words in the case of Chinese characters). Numbers, too, are logograms. The graphic form, 2, for example, is expressed by different words in different languages. Logograms can also be used for their phoneme content to represent sounds (similar to using the picture of an eye to indicate "I") either individual phonemes or syllables, the combination of which creates morphemes or words.



Figure 2. The Chinese character for cancer, comprised of three other characters; 疾 signifies a type of disease, 品 refers to the characteristic growth of a cancer - and 山 (mountain), represents the potential for rapid progression into a large mass. Information kindly provided by Professor Yao-Ping Wang.

Between three and four thousand years ago, archeological evidence suggests that Semitic peoples in the Sinai peninsula used 22 Egyptian syllabic pictograms of common animals, objects or parts of the body to represent the consonants in their language and created the proto-alphabet, i.e., a set of symbols encoding phonemes, which gave rise, through its Phoenician derivative, to most of the alphabets used today. Later, vowels were indicated by diacritical marks or modifications of the basic consonants, but the ancient Greeks, who adopted and adapted the Phoenician alphabet to their own phonemes, used seven modified consonant symbols from Semitic scripts to represent vowels. With the advent of the computer, various codes, the most widely used being Unicode, have been developed to allow a broad variety of scripts to be encoded for use in

computers. *Om*, for example, in the Devanagari script (used for Sanskrit and Hindi) is written as U+0950 in Unicode.

Writing allowed much more effective storage of information. Multiple written reiterations of important information can do much to guard against its loss while aiding dissemination. Errors did occur with manual copying, but writing allowed volumes of complex information - events, experiences, ideas and knowledge - to be stored and transmitted without the need for a phenomenal memory. Although reading and writing were originally confined to an elite or to trained scribes, literacy has expanded dramatically (although it lags still in poor countries), allowing much broader access to information. Nonetheless, a great deal of written knowledge has been lost or intentionally destroyed over the millennia, usually to suppress ideas that could lead to changes in the power structure of societies. Electronic dissemination of verbal or graphically encoded information (whether via writing or images) by radio, television and the Internet represents a further giant step forward in the ability to inform an ever larger fraction of the world's population. While the possibility for serious abuse exists (the use of modern media enormously accelerated the tobacco epidemic, for example), and socioeconomic factors influence access to information in any form, the use of electronic media for communication, consultation and education represents a potent tool which, if effectively deployed, will enormously enhance the impact of a broad range of cancer control activities.

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THE MEANING OF MEANING

The transmission of meaning via language requires that any given word or collection of words invokes a series of memories in the recipient brain - of sensory impressions, of specific actions, of events, or of concepts - including archetypical notions such as the idea of a face, but not a particular face. Through a process of association, multiple recalled elements from various parts of the brain are linked to a particular pattern of sound or symbols and synthesized into a coherent "meaning." The set of associated elements may be quite different in different contexts such that the meaning of words (or ideas) cannot be precisely pinpointed; rather they possess what might be called a *field* of meaning which is comparable to the wave function of fundamental particles, expressed by Schrödinger's famous equation. Here the position of a particle is defined in terms of the probability of its existence at particular spacial coordinates. It exists in a specific location only when measured. While this concept is difficult to grasp in the context of fundamental particles since the macroscopic objects we perceive have a precise position, it is not difficult to see that nouns (e.g., chair) are really concepts and have specific meaning only when a particular object is designated (the wave function, in quantum mechanical terms, collapses). Fields, whether in the context of words or elementary particles, allow change, i.e., a dynamic world rather one frozen in time as implied by Zeno's paradoxes - but also one governed by probability rather than certainty. The concept of "fields" could be

extended to cancer risk (and treatment outcome) - a particular individual's likelihood of developing a particular cancer varies according to lifestyle and exposure to environmental factors. The probability field collapses if cancer develops.

At a deeper level meaning is plucked from chaos by the laws of nature. Combinations of protons, neutrons and electrons, for example, are bound together according to specific laws, which permit a finite set of configurations that result in the chemical elements. At different levels, other laws govern the assembly of atoms into molecules, and the formation of cells, organisms, ecosystems and communities. Each successive level is permissive of a broader range of meaningful possibilities because the number of component parts successively increases; and each component, in higher systems at least, is itself a system. Meaning can also be seen to relate to symmetry and harmony (the sides of a mathematical equation must balance), which permits derivation of the laws which govern the symmetry, including the syntactical laws of language, by meticulous observation, experiment, and often intuition. Once formulated, a natural law can be used to predict properties or events in novel circumstances - a powerful test of its validity.

At a psychological level, our lives are given meaning (fulfilled) when we feel ourselves to be a significant part of a pattern beyond ourselves - such as the community to which we belong, or to a higher order of being. A finite life span may be essential to meaningful existence. Freedom and free will, however, is maximally enjoyed in the context of an equitably structured community; the dis-

ruption of which destroys the possibility of fulfillment. Serious diseases, such as cancer, impair the ability to participate in family or community life for many reasons, including fear, particularly the fear of premature death. Such concerns are sometimes enhanced by social exclusion, but recovery from cancer can lead to an enhanced sense of meaning in life, because what was thought irretrievably lost has been found.

**Recipients of information
must have sufficient
experience to decipher
its meaning.**

THE LANGUAGE OF GENES

Human language is a higher order language than that used to encode genetic information, since it is dependent upon the latter for its syntax although not its semantics. Yet language and the creation of an alphabet were essential to the understanding of the structure of *deoxyribonucleic acid* (DNA), the molecule which comprises the matrix into which genetic information is "written." It is the sequential arrangement of four chemical *bases* within the molecule - adenine, cytosine, guanine and thymine (represented as A,C,G and T) - that determines the sequential arrangement of amino acids in proteins. Each amino acid is represented in the gene by a "triplet" (a sequence of three bases) and is assembled into a polypeptide chain, and hence a protein, through the mediation of *ribonucleic acid* (RNA). First, an RNA copy of the gene, known as *messag-*

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er RNA (mRNA) is produced, obeying punctuation marks (specific base sequences) in the DNA that indicate the start and stop points of the several modular elements in the gene (which are separated by intervening DNA sequences). The mRNA is used as a template on which the polypeptide chain can be assembled through the binding of a row of *transfer RNAs*, each of which contains a triplet of bases which "matches" the corresponding triplet in the mRNA, and which carries with it the amino acid coded for by the original DNA triplet.

GENES, PROTEINS AND CANCER

If genes are the lexemes of life, then proteins are the morphemes. Proteins convey the "meaning" inherent in the genome through their association into molecular pathways in cells, each of which contributes to the ability of the cell to fulfill its purpose. But proteins also regulate the expression of other proteins as well as the replication of DNA and of all other cellular elements. Those involved in DNA replication (known as polymerases) include modules that ensure the integrity of the replication process, "reading" the newly replicated DNA chain and correcting errors that may have inadvertently entered - a process referred to as "proof-reading. Defects in the ability to excise and repair errors made during DNA replication are frequently present in cancer cells and contribute to the development of additional genetic (syntactical) abnormalities. The combined and coordinated interactions of cells lead to higher level functions - those of organs or tissues, including the neurological system. Specific parts of the brain

create the phonemes, lexemes and morphemes that allow communication with other brains - and the deciphering of the languages of the cosmos and of the genes.

FOXES AND HEDGEHOGS

In the late 1990s, several members of a family, designated KE, were found to be suffering from a severe speech disorder which included difficulties in pronunciation (associated with impaired coordination of facial muscles), grammar, writing and comprehension. The affected family members were shown to have structural and functional abnormalities in the regions of the brain associated with speech. In 2001, Lai, Fisher and Hurst discovered that affected family members also had a point mutation (a change in a single nucleotide, or "letter") in a gene belonging to a group of closely related DNA binding proteins known as FOX (*forkhead box*) proteins. At least 43 FOX proteins have been described. They bind to DNA via the forkhead domain, (in which the mutation in family KE occurs) and function as regulators of the expression of other genes. The affected gene in the KE family, FOXP2, has been shown to regulate a number of molecular pathways involved in the development of parts of the brain concerned with the ideational generation of language and with the muscular coordination required to produce it. Functional imaging studies in affected family members have shown underactivity in Broca's speech area of the brain during word generation. Of particular interest are the findings that the pattern of FOXP2 expression is similar in the brain cells of humans and songbirds -

animals that exhibit vocal learning. In both, FOXP2 expression differs from the pattern in most animals, including our nearest primate relatives, whose repertoire of sounds is innately generated and fixed. There seems little doubt that the genetic origins of human speech are closely associated with FOXP2 and that this gene is an important regulator of the development of the neuronal connections necessary for the generation of language.

But other FOX proteins are expressed in other cell types and their overexpression has been associated with several types of cancer. While it may seem remarkable that alterations in the function of closely related genes are relevant to a speech disorder on the one hand, and cancer on the other, this is merely a reminder that language is ultimately dependent upon the growth and development of many different cell types, including neurons, and their interactions with each other.

FOX genes are themselves regulated by other genes. One of them, *Sonic Hedgehog*, belongs to the set of human homologues of a gene family discovered in the fruit fly, *Drosophila melanogaster*, and named for the appearance of denticles (spiky projections) on the fly embryo when the gene is mutated. Sonic hedgehog (Shh), named after a video-game character, has been shown to be important to the normal development of the gut and pancreas, as well as the regulation of insulin production in the pancreas and of cell growth in the basal layers of the skin. Overexpression of Shh causes overexpression of another FOX protein, FOXM1, and deregulation of these genes, with consequent malfunction of impor-

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tant molecular pathways, is associated with the development and progression of pancreatic carcinoma and basal cell carcinoma, a type of skin cancer. Other FOX proteins are abnormally expressed in childhood rhabdomyosarcoma and in hematological malignancies. Recently, new techniques have been established that allow representation of the patterns of gene expression in cells as an array of dots, the level of expression of each being represented numerically, or by color. Such techniques allow the identification of the "signatures" of molecular pathways and of the derangements to them that occur in cancer.

THE SIGNS OF CANCER

Cancer cells, once they have accumulated to a sufficient number, create symptoms and signs - either directly, through pressing upon or invading adjacent tissues, or indirectly, through the molecules they secrete, which can cause general symptoms such as weight loss, fever or damage to peripheral nerves or endocrine organs (Table 1). Cancers also have characteristic patterns of spread into adjacent organs or structures and regional lymph nodes (another form of "signature"). Blood stream spread to distant sites occurs when blood vessels are invaded, although leukemias (blood cell malignancies), are disseminated from the outset. The degree of spread greatly influences the likelihood of cure because more widespread tumors are less likely to be eradicated by loco-regional therapy (surgery or radiation) and more likely to be associated with resistance to chemotherapy. Staging systems, using numbers or

- C**hange in bowel or bladder habits
- A** sore that does not heal
- U**nusual bleeding or discharge
- T**hickening or lump in breast or elsewhere
- I**ndigestion or difficulty in swallowing
- O**bvious change in a mole or wart
- N**agging cough or hoarseness

Note: these are not the only signs of cancer, and may be caused by non-malignant conditions. They, like any persistent symptoms or signs, indicate a need for further investigation.

Table 1. Early Warning Signs of Cancer in Adults.

- P**ersistent fatigue
- R**ecurrent fever or infection
- E**asy bruising or blood flecks in skin
- P**ersistent bone or joint pain, abdominal pain, headache
- A**bnormal behavior, movements, or head enlargement
- R**ecognition of an abnormal swelling or lump
- E**ye abnormalities; a white gleam in the pupil, or squint

Note: these are not the only signs of cancer, and may be caused by non-malignant conditions. They, like any persistent symptoms or signs, indicate a need for further investigation.

Table 2. Early Warning Signs of Cancer in Children.

letters or both, have been devised to provide a shorthand notation of the extent of disease, and therefore an indication of the likelihood of response to a particular therapy.

In order to understand and effectively diagnose and manage cancer its signs must be read, recorded and interpreted. Mathematics is vital to descriptions of the cancer patterns that occur in populations and their association with exposure to risk factors. Computerized imaging techniques have become an essential aid to identifying the degree of spread of cancer, which is important in determining optimal therapy, while mathematical analysis of the results of clinical trials is essential to progress. Purely verbal descriptions of cancerous

tissue may eventually be replaced by mathematical analysis of their patterns of gene expression, aiding classification, diagnosis and prognosis. Communication and education about the signs of cancer are essential if existing knowledge is to be used maximally in the control of cancer. Not surprisingly, in each of these areas, information technology has an increasing important role to play. It is easy, amidst the boisterous march of progress, to forget the foundational contributions made by Semitic agriculturalists thousands of years ago. Yet without the seminal invention of writing and the alphabet, Galileo's grand book could never have been read, nor the signs of cancer deciphered. ■

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INCTR'S ANNUAL MEETING

INCTR's Annual Meeting has become an important event which serves to bring together INCTR Associate Members from many different countries to strengthen international collaboration in all aspects of cancer treatment and research, to report progress that has been made in INCTR projects in the last year and to identify focal points for discussion that may lead to the development of

It must be recognized that cancer control, although founded on the same basic principles throughout the world, must contend with even greater obstacles in developing countries than those present in more affluent nations - obstacles that ultimately arise from the economic difficulties faced by the populations susceptible to cancer, and the paucity of resources available to study predisposing factors, prevention, early detection and treatment. For these reasons,

ance of cancer, or its detection at the earliest possible stage of its evolution - even before it has become a true "invasive" cancer. Both are dependent upon knowledge of the symptoms and signs of cancer (by health professionals and the population at large), and in those cases where it is known to be beneficial, screening of asymptomatic populations.

INCTR's annual meeting is unique in having, as its entire focus, the problems encountered in developing countries, and in bringing together experts both from within those countries and from affluent nations to discuss possible approaches, as well as the evaluation of such approaches, to the control of cancer; a problem that is becoming more and more immediate as communicable diseases are overcome, and populations age and adopt the bad habits of affluent societies, particularly smoking.

In addition to the INCTR Award Lectures and oral presentations of participants' own work, this year's meeting featured a series of presentations on cancers that are particularly frequent in Asia, but also in many other countries in less developed world regions, and several discussions pertaining to more general issues of cancer management. A plenary session in which INCTR members presented their own work was held, and posters were viewed in the course of the meeting. Two workshops were held, one on acute lymphoblastic leukemia and another on breast cancer, as well as consensus panel discussion and a multidisciplinary conference.

AWARDS INFORMATION

Two INCTR awards are presented at the annual meeting to individuals who have made outstanding contributions to cancer treatment or



Opening ceremony of INCTR Annual Meeting in Chennai.

new projects. While it is essential that key figures in cancer treatment and research are involved in these discussions, it is also essential, in the interests of ensuring long-term viability of programs, that young health professionals also participate. Professional education - including continuing education - underlies much of the meeting content, and although primacy is given to an exchange of views among health professionals from a variety of backgrounds, didactic elements are included in order to provide a foundation on which discussion can be based.

essential research relevant to cancer control in developing countries must, in part or in whole, be conducted in those countries themselves, where the pattern of cancer may be regionally unique, where the lifestyles, nutritional status and co-morbidities of potential and actual victims of cancer differ so profoundly, and where the availability or access to treatment may be poor or even absent. It is also critically important to involve the entire family and local community in the process of cancer control - particularly since success to a large degree is dependent upon the avoid-

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research in one or more developing countries. The purpose of these awards is not simply to recognize and honor the recipients, although this is certainly an important element, but also to show, by their example, that much can be accomplished even when resources are limited. It is hoped that their work and philosophy, brought through the award lectures to a broader audience than would otherwise be the case, will inspire others to greater efforts.

The Nazli Gad-el-Mawla Award is made for outstanding contributions to cancer control by an individual from a country with limited resources.

The 2005 Award recipient is Dr. Suresh Advani. Suresh H. Advani is qualified in medicine at the Bombay University in 1966. After training in internal medicine and hematology-oncology at the J.J. Hospital, Grant Medical College in Mumbai, he undertook further training in oncology in the USA. He joined the Oncology Department at the Tata Memorial Hospital (TMH) in 1974 and, in 1985, became the chief of the Department of Medical Oncology. Under his stewardship, the department developed capacities for providing modern medical and pediatric oncology services with laboratories for hematology, cytogenetics and molecular diagnostics, a day care chemotherapy unit, and patient counseling services. He played an important role in establishing the Doctorate of Medicine (DM) in Medical Oncology at TMH (Mumbai University) and trained many successful oncologists. Dr. Advani is recognized as a pioneer in the establishment of bone marrow transplantation in India. He is active in medical and academic research and has over 640 publications. He is the recipient of many

international and national awards including the Padmashri Award, the highest civilian honor, which is granted by the President of India. In 2002, Dr. Advani retired from Tata Memorial Hospital. He is presently the Director of Medical Oncology at Jaslok Hospital & Research Center and the Chief Medical Oncologist at the Asian Institute of Oncology.

The Paul P. Carbone Award in International Oncology is made for outstanding contributions to oncology or cancer research by an individual from a resource-rich country.

THANKS TO SPONSORS

INCTR would like to thank the following sponsors for their support of the Annual Meeting 2005:

AstraZeneca, Agfa, The Susan G. Komen Breast Cancer Foundation, MSD, The Leukemia and Lymphoma Society, the National Cancer Institute, GSK GlaxoSmithKline, the Institut Pasteur Brussels, the Jiv Daya Foundation and a number of Indian corporations.

The 2005 Award recipient is Dr. Dennis Wright. Dennis Wright qualified in medicine at the University of Bristol in 1956. After internships in pediatrics and surgery he began training in clinical pathology. In 1960 he was appointed Lecturer in Pathology at Makerere Medical School in Uganda. He worked with Denis Burkitt, helping to delineate the pathology of Burkitt lymphoma and developing a lifelong interest in the pathology of malignant lymphomas. He was awarded an MD for his thesis on malignant lymphomas in Uganda. In 1968 he was appointed Reader in Pathology at the University of Birmingham and in 1971 acceded



INCTR's Awardees, 2005.



Audience during plenary session.

to the Chair of Pathology at the newly established medical school at the University of Southampton. During his 25 years in Southampton the study of lymphomas was transformed by developments in immunohistochemistry, cytogenetics and molecular biology. The concept of lymphomas of mucosa-associated lymphoid tissues (MALT lymphomas) was developed in Southampton, as also was the specific nature of the lymphoma associated with coeliac disease (enteropathy associated T-cell lymphoma). Professor Wright played an active part in the establishment of the European Association of Hematopathology and was the second person to hold the Presidency of that association. He retired in 1996 but remains active in lymphoma diagnosis and research as an emeritus professor. ■

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INCTR REPORTS

• CLINICAL RESEARCH PROGRAM

The Clinical Trials Office (CTO) coordinates INCTR's Clinical Research Program and has the responsibility for managing the clinical research studies undertaken by disease-specific Strategy Groups and for providing education and training related to clinical trials and data management.

Four studies are in progress. A survey of patients of children with retinoblastoma is on-going in eleven institutions in eight countries - Brazil, Bolivia, Mexico, Nigeria, Zimbabwe, Turkey, India and Pakistan. The objective of this study is to identify factors contributing to delays in diagnosis and obtaining treatment. Over 300 parents have been interviewed. Children from rural areas and older children had higher stages of disease at diagnosis. The fathers' education level was associated with the extent of disease – the less educated the father, the more advanced the stage of the child's disease. The children of fathers with lower education levels experienced longer intervals between the first sign of retinoblastoma and the time of diagnosis.

Four institutions in India are participating in a study of the treatment and characterization of acute lymphoblastic leukemia in children, adolescents and young adults. Patient accrual began in August 2004, and 149 patients have been enrolled in the study. The principal investigators have formed a study committee and meet regularly to discuss protocol progress. Data monitoring has been introduced. A web-based data entry system is used to centralize data collection.

Four institutions in three African countries (Kenya, Nigeria and Tanzania) are participating in a protocol for the treatment and character-

ization of Burkitt's lymphoma. Over 80 patients have been enrolled in the protocol which consists of standard therapy for first-line treatment for newly diagnosed patients and second-line treatment for those who fail first-line treatment. Two secondary objectives are to improve patient follow-up and data collection. Patient loss to follow-up, approximately 11%, has been significantly reduced compared to the era in which a formal protocol was not in use. In November, the CTO provided a training workshop for the study data managers. The workshop included an overview of basic data management and practical exercises in data management procedures relevant to the protocol. Data retrieval for a retrospective survey of the presentation features of breast cancer and risk factors for treatment outcome is underway in Peru, India and Pakistan.

In addition to these clinical research studies, the CTO organized and provided the faculty for a session entitled "Basic Data Management" at the International Chemotherapy Congress held in Manila, Philippines, in June 2005. ■

• EDUCATION PROGRAM 2005

Since its inception, education and training have been central to the ethos of the INCTR. The aim has been to fulfill actual (and not perceived) needs, to focus available resources and to support existing INCTR projects. Emphasis is given to "in-country training", or "south-south" training, conducted in a developing country.

Medical Oncology

In 2005, the Education Program focused on: • Workshop Meetings for doctors and nurses • Proffered papers and poster sessions at the

Annual Meeting • Providing training opportunities for specific individuals • Linking medical schools.

Workshops (where the emphasis is as much on discussion as on the formal presentations):

- A Workshop on Research Methodology* entitled "What you always wanted to know, but were afraid to ask" was held in Lahore in February - in the context of the 7th Annual Meeting of the Shaukat Khanum Memorial Hospital and Research Center, (SKMH&RC). Its aim was to give doctors-in-training practical advice on: writing an abstract, publishing a paper and writing a grant proposal. There were also presentations on the importance of conducting clinical research in developing countries, the role of the individuals who make up the clinical research team, and on study design.

- A Workshop on Lymphoma** was held in collaboration with Dokuz Eylul University (Izmir, Turkey) and the Middle East Cancer Consortium, with an international faculty and 125 medical oncologists and hematologists-in-training from Turkey, the Republic of Cyprus, Jordan, Egypt, Palestine and Israel. The workshop covered both molecular aspects and recent advances in treatment of Hodgkin's and non-Hodgkin's lymphomas. A nurses' workshop was held concurrently.

Proffered papers and poster sessions:

73 abstracts were submitted; 9 were chosen for oral and 34 for poster presentation. On the basis of the data (and their CV), 6 individuals were chosen to participate in a course in scientific writing to be held in New Delhi, in August 2006.

ANNUAL MEETING

Training opportunities and visiting experts:

Afghanistan: Dr. Mirwais Malik* → Tata Memorial Hospital (TMH), Mumbai, for one year, to train in medical oncology - Mr. Hamidulla* → SKMH&RC, Lahore, for three months, to train in pathology technology.

Nigeria: Dr. K.O. Ajenifuja* → TMH, for one year, for advanced training in gynecological oncology - Mrs. E.T. Aladekomo, Mrs. O.A. Agboola, Mrs. B.O. Adebami, Dr. Anorlu* → TMH, for three months to train in screening for cervical cancer.

Bolivia: Dr. Rocha* → Instituto De Enfermedades Neoplasicas (INEN), Lima, three months, to train in Colposcopy and CIN management - Dr. Ingrid Hurtado* → INEN, one month, to train in colposcopy - Mrs. Franco → INEN, one month, to train in Cancer Registration.

China: A delegation from the Chinese Ministry → to St. Bartholomew's Hospital London, to discuss setting up Ethics Committees.

Pakistan: Ms. Murrell and Ms. Stewart and subsequently Ama Rohatiner → SKMHRC to train nurses and doctors in the delivery of high-dose treatment with autologous peripheral blood progenitor cell support.

Links between Medical Schools:

Dr. V. Shanta will host two final-year medical students from SBH for an elective period - Dr. Trajman (Gama Filho University, Rio de Janeiro, Brazil) spent two weeks at St. Bartholomew's Hospital with Professor Rohatiner and third-year medical students to gain experience with an integrated medical curriculum. ■

* Supported by the Office of International Affairs NCI, USA.

** Supported by the Office of International Affairs NCI, USA and the pharmaceutical companies Roche and Schering AG.

Acknowledgements: Susanne Radtke and Elisabeth Dupont coordinated the "south-south" training programs for Afghani, Nigerian and Bolivian health professionals.

Pediatric Oncology

A number of joint meetings in which INCTR's pediatric sub-committee had a major role were held in the course of 2005. The 1st International Conference on Pediatric Oncology in Karachi, Pakistan, took place in July in collaboration with the Cancer Society of Pakistan and the Pakistan Society of Pediatric Oncology. Pre-conference workshops were held on research methodology and oncology nursing. There were 150 participants from Pakistan and 60 participants from India, Nepal, Afghanistan, Saudi Arabia, Oman, Jordan, Iraq, Europe and the USA.

The Chinese 5th National Congress in Pediatric Oncology was held in Tianjin in September in collaboration with the Chinese Society of Pediatric Oncology and the Children's Oncology Group (COG). INCTR arranged for several faculty members to attend.

A Workshop on Palliative Care for the Cancer Patient was held in Larnaca, Cyprus, in November in collaboration with the Middle East Cancer Consortium. There were 80 participants from Jordan, Israel, Palestine, Turkey, Cyprus, Iraq, Egypt, Pakistan, India, Canada and the USA. In the course of this meeting a Palliative Care Steering Committee was formed which includes Drs. Shad and Brown of INCTR.

A program of continuing education for Iraqi pediatric oncologists was initiated in April 2004 in Amman, Jordan, at the King Hussein Cancer Center (KHCC). Several subsequent

workshops have been held, one during the INCTR Annual Meeting in Cairo, Egypt, in September 2004, one in Karachi, Pakistan, in July 2005 in conjunction with the 1st International Conference on Pediatric Oncology, and another at INCTR's last Annual Meeting in November 2005 in Chennai, India. These workshops have been focused on hematological malignancies, supportive care, transfusion medicine and palliative care.

Three senior fellows from KHCC spent four-month training periods at the Lombardi Cancer Center (LCC) and gained experience in both laboratory and clinical aspects of pediatric oncology. Similar fellowship training is envisaged for fellows from Nepal following Expert Visits undertaken by Dr. Aziza Shad to the Kanti Children's Hospital, Katmandu, in January 2005.

A meeting took place at the LCC in August to explore the possibility of collaboration among a number of organizations involved in pediatric cancer, including the LCC, the Children's Oncology Group, INCTR, NCI, CURE and St. Jude Children's Research Hospital. The group agreed to share resources, to avoid duplication of effort, to apply for joint funding and to undertake joint educational activities.

Funding for these events was obtained from a number of sources, but special thanks are due to the Office of International Affairs, NCI and institutions and organizations participating in the meetings described above. ■



Dr. Aziza Shad, Chairman of the Pediatric Oncology Sub-Committee.

NETWORK

SURESH H. ADVANI
JASLOK HOSPITAL & RESEARCH CENTER, MUMBAI

ACUTE LYMPHOBLASTIC LEUKEMIA PROGRESS IN DEVELOPING WORLD



The tremendous progress in the treatment of childhood acute lymphoblastic leukemia is the true success story of pediatric oncology. From the 1960s when cure rates were a dismal 15-20%, we have come to an era where the five year disease-free survival has reached 75-80%. Advances in all spheres of diagnostics and therapeutics have contributed to this success. The rational use of combination chemotherapy, central nervous system prophylaxis, advances in supportive care, including the availability of safe blood products, use of long-term central venous access devices and potent antibiotics have all played a key role in this achievement. The understanding that ALL is a heterogeneous disease led to risk stratification of therapy. Today, patients with low-risk disease can be treated with minimal therapy with the aim of decreasing late effects, and high-risk patients can be identified upfront and given intensive therapy. Unfortunately India is lag-

ging behind the West in this success story. The MCP841 protocol is a multicenter protocol designed especially for developing countries and was initiated in the mid-1980s in three centers in Mumbai, Delhi and Chennai. It is still being used in many premier institutes in the country. Early results with this protocol showed five year event-free survival of 50%. This gradually improved to 60% by the end of the 1990s. There is still a survival gap of 20% between the West and our country. Several factors have been hypothesized to account for this gap, one of the most important being the difference in the biology of the disease in these two regions. Most Western literature quotes the incidence of T cell ALL to be around 10-15%. In the early eighties, the incidence of T-cell ALL was reported to be as high as 50% in Chennai in Southern India, and 38% and 33% in Delhi and Mumbai, respectively. This high incidence has decreased in the last two decades. By the end of the nineties it was 37% in Chennai and 30% and 20% in Delhi and Mumbai, respectively. Economic development has been proposed as the probable cause of this changing immunophenotypic pattern. With economic growth and better health

care, children are surviving infections early in life to face the subsequent immunologic stimuli of recurrent infections, both clinical and subclinical. This could lead to the emergence of the common ALL clone. Similarly, the presence of a TEL-AML1 translocation, which is a good prognostic marker in ALL, is reported in 35% of patients in the West, but is present in less than 10% of Indian patients. This may be partly responsible for the poorer treatment outcome. Keeping the differences in biology in mind, the next multicenter treatment protocol will be more aggressive and will study the significance of biological characteristics of ALL to outcome, with the aim of stratifying treatment accordingly.



Jaslok Hospital, Mumbai.

DENIS WRIGHT
UNIVERSITY OF SOUTHAMPTON, SOUTHAMPTON

FROM AFRICA TO ZAP-70: A JOURNEY



Our understanding of malignant lymphomas has traveled a long journey in the past half

century. For me the journey started in Africa in 1960 when I began working with Denis Burkitt in Uganda. Denis was not the first to describe the remarkable clinical features of what is now known as endemic Burkitt lymphoma (eBL), but he was the first to systematically study the disease. He subsequently delineated the distribution of the disease in Africa and was the first to use chemotherapy for its treatment. It was my privilege to work alongside Denis recording the pathology of his cases. In those early days our understanding of the immune system and the biology of lymphocytes was primitive and the nature of BL was uncertain. An international meeting of pathologists convened by the UICC and WHO in 1968 concluded that BL should be defined on the basis of its morphology (cytology and histology). Using

this definition, cases of sporadic BL were identified throughout the world. The majority of these cases of sBL differed in their clinical features and relationship to EBV from eBL. Later, AIDS-related BL was recognized; it differs from eBL in its clinical features and relationship to EBV. The common morphology of all types of BL relates to the fact that all show translocations of one of the immunoglobulin genes with the c-myc gene. Consequent c-myc deregulation keeps all BL cells in cycle, resulting in a monomorphic blastic tumor. Our understanding of the immune system underwent a renaissance in the second half of the 20th century and shed new light on the semantic and conceptual confusion that characterized the study of lymphomas. Technical developments in immunohistochemistry, cytogenetics and gene profiling are providing new insights into the biology of malignant lymphomas. Ideally, this

will be matched to more specific therapies for these tumors. Some of these technical advances, such as gene profiling, will not be readily available in the developing world. However they may reveal the expression of genes, the products of which can then be identified by immunohistochemistry - a relatively simple and inexpensive technique. Thus the unexpected ZAP-70 gene expression in poor-prognosis CLL can be detected using immunohistochemistry. Immunohistochemistry, together with modern imaging techniques, has also made it possible to arrive at a precise diagnosis on many needle biopsy specimens. This technique is particularly valuable in the investigation of deep-seated lesions, avoiding the morbidity of invasive surgery.



Mulago Hospital Kampala, where Professor Wright worked in Uganda.

NETWORK

Nursing Oncology Report

In most developing countries, nurses undertake relatively menial tasks, and their training generally does not include cancer care. INCTR (and its French branch, AMCC) emphasizes in-country training and training in other developing countries ("south-south" training). Four workshops and training courses were held in 2005:

- In April, 2005 a three-day workshop entitled "Recent Advances in Cancer Nursing" was held in Ismir, Turkey. Eighty nurses from Middle East countries attended.
- In June, a palliative care workshop was carried out in Tanzania in concert with the INCTR Palliative Care Team and the INCTR Tanzanian office; 20 nurses were present.
- In October, a training course on "Prevention and Early Diagnosis of Breast and Cervical Cancer for Health Staff" was held in Niger. For five days, 75 people (surgeons, doctors, midwives, nurses and cancer association's members) discussed the care of women with cancer.
- In November, a palliative care workshop held in Dakar, Senegal, during the 5th Aortic Congress brought French, English and Arabic speaking nurses together from all over Africa. ■

• TRANSLATIONAL RESEARCH PROGRAM

A five-year overview was presented. The Translational Research Program was designed to provide the laboratory component for achieving the overall INCTR mission of improving clinical outcome of cancer patients from developing countries. The main aim is to catalyze bidirectional interactions such that unique clinical observations from the patient setting in developing countries can be translated to a laboratory environment and, simultaneously, rapidly

move key and novel laboratory observations to the patient in developing countries. The strategy is based on interactive and comprehensive organ-site specific programs, using multiple methodological platforms (real-time polymerase chain (PCR) reactions, microarrays, tissue arrays, restriction fragment length polymorphisms (RFLP), cell culture, etc).

The main focus is on acute lymphoblastic leukemia (ALL). There are five main projects: 1) Molecular subclassification, in which a real-time RT-PCR test for the most common chromosomal translocations was developed and validated, and laboratory staff of INCTR centers in India trained in sample collection, storage, usage, techniques and analyses. The distribution of molecular subtypes in India was described and differences with ALL patients in the West (four publications). 2) Gene expression profiling, in which real-time RT-PCR validation of published data was undertaken and a microarray facility started (three publications). 3) Epigenetics, in which the methylation pattern of selected genes in childhood ALL cells was correlated with the molecular subtype. Differences with adult ALL and with AML were observed (four publications). 4) Pharmacogenetics, in which combined PCR-RFLP assays for over 15 genes involved in metabolism of drugs and xenobiotics were established and a population-based study was conducted and published. 5) Proteomics of apoptosis, in which western blot assay for proteins involved in the intrinsic and extrinsic



Participants in the first joint meeting between MECC and INCTR in Larnaca, Cyprus.



Palliative Care team consults on a patient in Nepal.

apoptotic pathways were first measured in cell lines, then validated in clinical samples. These studies provided proof of the principle that apoptotic pathways provide a target for therapy (three publications).

Additional activities for improving the management of ALL patients were also studied, including the development of molecular assays for the identification and quantification of fungal infections, diagnosis of CNS disease and minimal residual disease, and quantification of Epstein Barr virus load. ■

• PALLIATIVE CARE PROGRAM

Nepal: The INCTR care team, with the invaluable help of NNCTR, carried out two visits to Nepal, visiting Kathmandu and Bharatpur in a continuing collaboration to help

develop palliative care in that country. This effort has been focused at Scheer Memorial Hospital, Kanti Children's Hospital, Bhaktapur Cancer Center and Hospice Nepal. Oral morphine is now freely available for the program. Hospice Nepal has developed a very active home-based care program and was helped financially by INCTR in the purchase of a vehicle for this purpose. At Bhaktapur Cancer Center and Kanti Hospital there is continuing improvement in both quality as well as capacity in the care of terminally ill patients. Educational activities designed to reach greater numbers of health professionals are planned for 2006.

Tanzania: A workshop was carried out at the Ocean Road Cancer Institute, in Dar es Salaam in June 2005, and plans were made for the development of a teaching center in palliative care based at that institute.

Cyprus: INCTR team members collaborated with the Middle East Cancer Consortium in a workshop for health professionals from Cyprus, the Palestinian Authority, Jordan, Turkey, Egypt and Israel.

India: A collaboration with Pallium India, the American Cancer Society and INCTR has been initiated to develop palliative care training centres in India starting in 2006.

Clinical Guidelines for Palliative Care have been developed (Dr. Fraser Black, editor) and have been posted on the INCTR portal. ■

Melissa Adde, Clinical Research, Ama Rohatiner, Medical Oncology, Aziza Shad, Pediatric Oncology, Sabine Perrier-Bonnet, Nursing Oncology, Marina Gutiérrez, Translational Research, Stuart Brown, Palliative Care.

A MULTIDISCIPLINARY TEAM (MDT) MEETING ON DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL)

MDT meetings, sometimes known as "Tumor Boards", are occasions when the entire team of health professionals meets to discuss specific patients. They provide learning experiences for all team members and improve overall patient care. INCTR has introduced MDTs into its annual meeting to demonstrate their value to those unfamiliar with the concept.

CASE HISTORY

A 59-year-old man presented with generalized lymphadenopathy and weight loss of six months' duration.

DIAGNOSIS

Several discussants pointed out that in regions where tuberculosis is prevalent, it should be considered in the differential diagnosis. Professor Wright stressed that to establish the histological subtype of lymphoma, an excision (or cutting needle) biopsy is mandatory. Dr. Ngoma and Dr. Nkegoum (from Tanzania and Cameroon, respectively) agreed, but pointed out that for the diagnosis of African Burkitt lymphoma, an F.N.A. would suffice.

PATHOLOGY

Professor Wright demonstrated the importance of immunophenotyping in differentiating B from T cell lymphomas and identifying subtypes. In this case, Bcl-2 was strongly expressed in the cytoplasm, typical of many cases of DLBCL, whilst Bcl-6, surprisingly, was negative. He discussed the morphological variants that comprise DLBCL in the WHO classification: centroblastic, immunoblastic, T-cell/histiocyte-rich and anaplastic,

and mentioned the intravascular large B-cell and mediastinal (thymic) large B-cell subtypes. He also discussed the pathogenesis of DLBCL in light of recent advances in gene expression profiling. Patients in whom the lymphoma cells express a germinal center B-cell signature appear to have a better prognosis than those with an activated B-cell profile when treated with CHOP or similar regimens. Such lymphomas also appear to be the predominant subtype in children.

STAGING INVESTIGATIONS

The bone marrow aspirate and biopsy revealed no lymphoma cells and CT scans showed intra-abdominal lymphadenopathy; thus, the disease stage was IIIB. The group consensus was that CT scanning should be mandatory for all patients with lymphoma. Dr. Khan discussed the role of gallium and MRI scanning, the latter being reserved for lesions involving the brain and spinal cord. PET scanning (where available) is particularly useful in identifying viable tumor in residual mediastinal or abdominal masses after treatment.

TREATMENT

It was agreed that CHOP regimen (Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone) remains the standard regimen (given with Rituximab, if possible) for DLBCL. In the eventuality of recurrence, a second-line regimen, e.g. 'ICE' (Ifosfamide, Cytosine Arabinoside and Etoposide), could be used with a view to high-dose treatment, supported by autologous peripheral progenitor cells, in patients who have a partial response. The session was interactive and generated lively debate.

Anita Chandra and T.G. Sagar, Chennai, Dennis Wright, Southampton, Ali Khan, Manchester and Ama Rohatiner, London.

NETWORK

CARBONE FOUNDATION SUPPORTS LEGACY PROJECT

Paul Carbone's lifetime contributions helped set the standards for clinical oncology and research, as well as for patient care. Upon his death in 2002, family and friends established the Paul P. Carbone Memorial Foundation to memorialize the internationally acclaimed medical oncologist who in 1972 shared the Lasker Prize for Medicine - considered America's Nobel Prize - and who presided over two of the most prestigious cancer research societies in the United States: the American Society of Clinical Oncology and the American Association for Cancer Research.

Dr. Carbone began his career at the National Cancer Institute in 1960, as part of the original team working on the development of cancer chemotherapy. He participated in early studies of the treatment of Burkitt lymphoma, one of the first tumors shown to be curable by chemotherapy, in Uganda with Denis Burkitt. In 1971, Dr. Carbone joined the Eastern Cooperative Oncology Group (ECOG), and over the next 20 years built it into a premier national clinical trials organization, pioneering research on a number of fronts and providing sustained leadership at the international level.

But it was in America's heartland - at the University of Wisconsin - where Dr. Carbone's influence was most keenly felt. As director of Wisconsin's comprehensive cancer center for nearly two decades, Dr. Carbone distinguished himself as a scientist, teacher and humanitarian.

"He committed the better part of his life to the fundamental research of cancer," says his eldest son, Paul, a managing partner at Robert W. Baird & Co.

and a trustee of the Carbone Memorial Foundation, "and he was known for his outstanding patient care. He put both together in his work at Wisconsin, and his patients loved him because he had a remarkable bedside manner that touched and comforted people."



Dr. Paul Carbone

The Foundation has focused its fundraising efforts on Wisconsin's Carbone Legacy Campaign, which seeks to raise \$10 million to expand and rename the comprehensive cancer center as a tribute to Dr. Carbone. The University of Wisconsin Paul P. Carbone Comprehensive Cancer Center will be part of a new Interdisciplinary Research Complex within the University of Wisconsin Health Sciences campus.

"This is the centerpiece of what the foundation is trying to accomplish, since my dad spent the last half of his career there," says son David. Over \$9.5 million has been raised in private funds for the comprehensive cancer center expansion so far. The University has secured an additional \$14 million in federal money given in Dr. Carbone's honor.

David Carbone, an oncologist at Vanderbilt University specializing in lung cancer and a Foundation trustee, says different people remember his father for different things.

"He's known objectively as a member of the team that developed some of the first effective chemotherapies for lymphomas at NCI," says David. "Among those in the medical profession, he is most respected for his interest in oncology training and the way he helped guide junior physicians in oncology. After his retirement, he set up fellowship programs in Taiwan and Singapore. He really liked doing that. From talking with other physicians, I believe he made the biggest impact by helping people professionally, and by systemizing and codifying the practice of oncology into a standardized, evidence-based, careful and thoughtful approach. He was quite proud of the fact that he developed the oncology certification exam."

The foundation of modern oncology is still very much relevant. When David was diagnosed with large cell lymphoma in 2000, he was treated with virtually the same four-course regimen that his father had developed at NCI.

"One of these drugs has a numbing/tingling side effect," David says. "When I asked him about it, my dad pulled out the original paper he had authored 40 years earlier, discussing the safety of the drug. When investigators at NCI found that certain cancers could be cured, it was a major leap forward and became a founding principle in the field."

A celebration of the renaming of The University of Wisconsin Paul P. Carbone Comprehensive Cancer Center will be held on September 26, 2006, at the Overture for the Arts Center in Madison. For additional information, or to make a contribution, contact Andrea Engebretson at 608-263-0852 or andrea.engebretson@uwfoundation.wisc.edu. ■

Marcia Landskroener for INCTR

1ST INTERNATIONAL CONGRESS ON CANCER CONTROL (ICCC)

The first ICCC meeting took place in Vancouver, Canada, from 23rd to 26th October. The 325 delegates came from 65 countries to attend educational sessions and to participate in a broad range of workshops, including one on Cancer Control in Developing countries. The main message of the congress was the importance of sharing knowledge and working together if the growth of the world-wide cancer epidemic is to be slowed. INCTR participated in the steering committee responsible for planning the meeting. ■

TRAINING COURSE FOR DATA MANAGERS

Four African data managers attended a training course in Brussels from 7th to 10th November. The course covered basic skills and use of the data base that will be used for INCTR's clinical trial in African Burkitt lymphoma. ■

5TH AORTIC CONFERENCE


The African Organization for Research and Treatment of Cancer took place in Dakar, Senegal, from 14th to 16th November. Four hundred persons participated from many African countries and several societies were represented, including the International Psycho-Oncology Society, INCTR and AMCC, INCTR's French branch. Conclusions of the meeting were that the participating organizations should work together as closely as possible and that palliative care should be given more emphasis in Africa. ■

ESO ADVANCED COURSE IN MALIGNANT LYMPHOMAS, CERVICAL CANCER AND GASTRIC CANCER

A course organized by the Latin American chapter of the European School of Oncology was held in Lima, Peru, at the Instituto Nacional de Enfermedades Neoplasicas on 24th to 25th November. The course chairmen were Dr. Santiago Pavlovsky and Carlos Vallejos and participants attended from many Latin American countries. INCTR participation included discussions of the evolution of the control of cervical cancer and the epidemiology of lymphomas. INEN serves as an INCTR regional training school in cervical cancer detection. ■


INCTR USA BOARD MEETING

The US Branch Board of Directors met in Washington DC on 7th December. In view of the resignation of the President, Dr. Elmer Huerta who has become President-Elect of the American Cancer Society (he will remain a member of the Board), a new President, Dr. Richard Pestell (formerly Vice-President) was elected. Dr. Aziza Shad was appointed to a newly created post of Director, and two new Board Members were also elected – Fred Rooney and Dr. Vinay Jain. The branch will continue to play a major role in pediatric oncology education, but Board Members plan to identify other priority areas for the Branch in the coming months. ■



SAO PAULO, BRAZIL
March 1st - 4th, 2007
Blue Tree Hotel Ibirapuera,
São Paulo, Brazil

**7TH INCTR ANNUAL MEETING
2007**




Annual Meeting Highlights

INCTR's 7th Annual Meeting will be held in Brazil, the largest country in Latin America. The meeting will retain its standard components, including keynote lectures, reports from INCTR programs, educational/scientific sessions, workshops, and "Meet the Expert" sessions. The meeting will begin with INCTR award lectures.

INCTR members will have the opportunity to present their own work either as an oral presentation or poster based on submitted abstracts.

The educational/scientific sessions will deal with important cancers in Latin America, including breast and cervical cancer, AIDS-associated malignancies, pediatric cancers and lymphoma. General aspects of cancer control and palliative care will be included in the program.

There will be ample opportunities for discussion and exchange of ideas.

Conference Hotel

The 2007 INCTR Annual Meeting will take place at the:
Blue Tree Hotel Ibirapuera
Av. Ibirapuera, 2927
Moema
CEP: 04209-200
São Paulo - SP
Tel: +55 11 5053 2200 - Fax: +55 11 5053 2201
www.bluetree.com.br

Additional Information

For updated program information and registration form, please visit www.inctr.org

or contact:
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NETWORK

KING HUSSEIN CANCER CENTER, AMMAN, JORDAN

As the second major cause of death in Jordan, cancer poses a great challenge to all healthcare institutions to improve cancer education,



King Hussein Cancer Center is the only comprehensive cancer center in the Middle East. In addition to specific treatment, the Center offers psychological counseling, patient support, education of families of cancer patients, and after-therapy care.

prevention, early detection and treatment. In the year 2002, the Jordan National Cancer Registry recorded 3,430 new cases of cancer. The crude incidence rate of all cancers among Jordanians was 64.4 cases per 100,000 people. Among adult males, colorectal cancer was the most common cancer, accounting for 11.5% of all adult male cancers. Other leading cancers in adult males included bladder, lung, leukemia and prostate. Among females, the most common malignancy was breast, accounting for 30% of all adult female cancers. Among children, the most common malignancy reported for both genders was leukemia, accounting for 36% of all cancers, followed by brain/spinal tumors and lymphomas. Currently, the top ten cancers, by site, in the Jordanian popu-

lation, regardless of gender and age are: breast, colorectal, leukemia (including multiple myeloma), lymphoma, lung, urinary bladder, stomach, prostate, thyroid and brain/CNS.

There are two obvious risk factors in Jordan. The first is the prevalence of tobacco use, especially ubiquitous among males and quite common among females. The second is the social shame still associated with cancer within the Jordanian culture, which leads to reluctance to accept the diagnosis and undergo treatment.

The Jordanian government is well aware of the impact of cancer on its people, and is taking steps to build public awareness for cancer prevention, early detection and treatment. The National Cancer Registry provides data on the incidence of cancer in Jordan, helping to shape public health policies in general and cancer management in particular. Although several hospitals and clinics in Jordan accept and treat cancer patients, King Hussein Cancer Center is the only specialized cancer center for the treatment of adult and pediatric cancer patients in Jordan and is now considered the primary referral hospital for the government of Jordan. KHCC plays a major role in the shaping of national objectives in the fight against cancer.

INSTITUTIONAL HISTORY

In the early 1990s, Jordanians were offered fragmented cancer treatment and care at a selected number of local hospitals. Patients who were fortunate enough to have a choice elected to seek medical attention abroad because of greater confidence in the standard of care.

The need for a local cancer center offering comprehensive care at an international level became increasingly urgent. In 1991, fundraising was initiated and donations from the citizens of Jordan and other nationals, a grant from the Dutch government, and a loan from the Islamic Bank in Jeddah were key contributions that led to the establishment of Al Amal Center as a non-governmental not-for-profit organization. The Center treated its first patient on January 11, 1997.

King Hussein Cancer Foundation, the legal umbrella for the Center, forged a cooperative agreement in September 2002 with the National Cancer Institute (NCI) in Maryland, USA, for the purpose of enhancing medical sciences and improving cancer patient care in the entire Middle East.

In November 2002, their Royal Majesties King Abdullah II and Queen Rania Al-Abdullah unveiled the Center's new name, King Hussein Cancer Center (KHCC), in recognition of the late King Hussein who fought a courageous battle with the disease. Samir Khleif, MD, an internationally recognized oncologist and senior cancer researcher at NCI, assumed the position of Director General and Chief Executive Officer of KHCC.

Since then, numerous innovative and comprehensive programs have been implemented. The Center serves an increasing number of international patients from the region, and currently treats more than 2,800 new patients each year. With KHCC on target to gain accreditation in 2006 by the Joint Commission for International Accreditation, the Center is reaping the benefits of hospital-wide

PARTNER PROFILE

accreditation orientation and education. The Quality Assurance Department is overseeing policies and procedures for all departments, and active committees, chapter leaders and standard owners are guiding the Center towards greater efficiency.

OUR WORK

Through its collaboration with the National Cancer Registry of Jordan, the KHCC has developed a hospital-based registry to enhance the information collected nationally through a specialized computerized coding system. This has positive implications for epidemiological and clinical research, for understanding the causes of cancer that may be peculiar to the region, and for developing national cancer prevention and control plans.

We have adopted a new team approach to cancer care with the establishment of multimodality clinics, in which a treatment plan is identified for each patient by a group of no fewer than three specialists. Each clinic includes a medical oncologist, a surgical oncologist and a radiation oncologist, in addition to other specialized physicians needed for the particular treatment. The seven established multimodality clinics at KHCC are bone marrow transplantation, breast, gastro-intestinal, lung, head and neck, neurooncology and sarcoma.

Recognizing that prevention is the best medicine, KHCC has established three awareness clinics: the Diet Clinic, the Lifestyle Clinic and the Stop-Smoking Clinic. KHCC runs screening clinics for breast, cervical, prostate, testicular, skin and colorectal cancers.



KHCC collaborates with several international partners including St. Jude Children's Hospital and Johns Hopkins Hospital. The aim is to exchange expertise, counsel and clinical consultations in order to provide a higher standard of care.

KHCC's bone marrow transplantation program offers hope to adult and pediatric patients suffering from

aggressive and recurrent cancers and other catastrophic illnesses. The BMT unit has the facility to collect, process, store and infuse stem cells, as well as the medical knowledge and expertise to offer the specialized after-care that is vital for the success of the transplantation.

The Center offers residency and fellowship programs that apply the latest international clinical care standards. Numerous specialized medical conferences are organized and hosted by KHCC with local, regional and international speakers and participants, thereby merging global knowledge in the field of cancer. With the support of INCTR, KHCC is planning to hold the first regional workshop on clinical trials and data management. ■

Contributed by Faris Madanat, KHCC, and Marcia Landskroener for INCTR

MEDICAL RESOURCES

Total Beds	130
Beds Devoted to Cancer Care	All
Nurses	300
Dedicated Oncology Nurses	230
Pathologists	2
Oncologists	
- Medical oncologists	6
- Radiotherapists	6
- Radiologist	3
- Pediatric oncologists	8
- Specialized surgical oncologists	3
Oncologists in Training	29
General and Specialist Surgeons	8
CT Scanners	1
MRI Scanner	1
Cobalt Radiotherapy units	None
Linear Accelerator units	4

PATIENTS IN 2004

Total patients	2,898
Total outpatients	45,523
Adult cancer patients	2,237
Pediatric cancer patients	377

NETWORK

PROFILES IN CANCER MEDICINE

SAVING THE CHILDREN OF CAMEROON

The art of healing has been a lifelong passion for Dr. Pierre Doumbé, who in the course of his specialization in pediatrics encountered a void in the management of children with cancer in his native Cameroon. "These patients were almost abandoned," recalls Doumbé. "That is what motivates my practice in medicine and, specifically, cancer medicine."

Educated at the University of Limoges in France, with post-graduate training in pediatrics and pediatric oncology at the University of Montreal, Dr. Doumbé now heads the pediatric hematology oncology unit at the Mother and Child Center of the Chantal Biya Foundation. The Center is affiliated with the Yaoundé Central Hospital, a university-related teaching hospital where Dr. Doumbé first began his practice in 1983. He has been a member of the Faculty of Medicine and Biomedical Sciences there for 20 years.

The most prevalent pediatric cancers are Burkitt lymphoma (80%), leukemia, nephroblastoma and germ cell tumors. In addition to treating patients, he is concerned with the training of doctors and nurses, and with seeking international cooperation for assistance in overcoming the many challenges that face healthcare providers in this central African nation.

The incidence of pediatric cancer is increasing but, Dr. Doumbé notes, "the types of pediatric cancer in my country are typically easy to diagnose and easy to treat. Burkitt lymphoma can be diagnosed with fine needle aspiration, and cured with chemotherapy. Our recent successes in the treatment of Burkitt lymphoma have motivated other patients



Dr. Pierre Doumbé

to continue treatment. These successes are also my greatest satisfaction."

From 2001 to 2004, Dr. Doumbé participated in therapeutic trials on Burkitt lymphoma with the GFAOP (Groupe Francophone Africain d'Oncologie Pédiatrique), using a French Society of Pediatric Oncology protocol adapted to the local circumstances. Survival rates improved to 60%. Previous survival rates were never above 20%, he says. A new feasibility study now underway uses a less intensive protocol (FAGOP Cyclo-Burkitt 2005).

In a second therapeutic trial, Dr. Doumbé used the Nephro 2001 protocol (modified from an International Society of Pediatric Oncology protocol) to treat nephroblastoma. Only a few patients were included in this study.

After 25 years in medicine, Dr. Doumbé is beginning to see some improvement in the management of children with cancer. As head of the Pilot Center of GFAOP for projects in pediatric oncology in Africa, Dr. Doumbé is at the forefront of efforts to improve the outcome for children with cancer in

that part of the world. It is a daunting task. "To be successful," he says, "we must increase public education. There must be provision of infrastructure, increased training of personnel, provision of medication, improved facilities, and increased collaboration with international bodies and researchers."

Dr. Doumbé says he sees about 60 children with cancer each year - which represents only about one-tenth of all incident cases. Poverty, the taboo associated with cancer, and the popularity of traditional healers all pose significant obstacles.

"We cannot solve the problem with national resources only; we have no capacity to deal with our cancer problem without the cooperation of the international community. If the international community can give us medication and help us to develop trained personnel - doctors and nurses - we can have better results."

As his government struggles with other issues, local attitudes toward cancer also hamper efforts. "People think that cancer is a malediction," says Dr. Doumbé. "We can overcome this misperception by demonstrating good results of cancer treatment in children. But for those who believe that the cancer is a treatable illness, who have no money to come to us for treatment, a diagnosis of cancer is still devastating. That is the reason we believe in international cooperation."

In addition to his prolific international publications, Dr. Doumbé is active in several national organizations. He is a founding member of the National Committee for the Fight against Cancer in Cameroon and a member of several international societies, including INCTR. ■

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