N E T W O R K

THE NEWSLETTER OF THE INTERNATIONAL NETWORK FOR CANCER TREATMENT AND RESEARCH

INCTR

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THE PRESIDENT'S MESSAGE

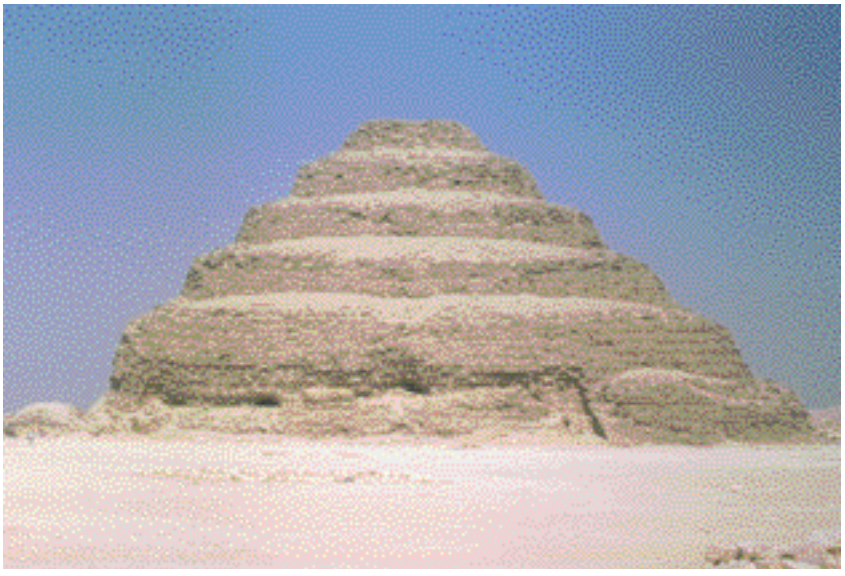
THE MEASURE OF CANCER

Part 1. Quantitation

by Ian Magrath

...all exact science is dominated by the idea of approximation. Bertrand Russell

The silent majesty of the tiny part of the cosmos that is visible on a clear night to the unaided eye has been an inspiration to poets, philosophers and scientists throughout the ages. For long the night sky remained the imagined playground of deities and heroes, but in the last few centuries scientific inquiry has traversed the vast spaces of the unbounded universe, elucidated the natural history of stars, and probed deeply into the nature of energy and matter. In the course of this lengthy and remarkable voyage, a virtual mathematical edifice, providing at once a universal language and a series of powerful analytical tools, has been abstracted, bit by bit, from the worldly and extraterrestrial objects to which its earliest elements had once seemed inextricably bound. Its equations speak lyrically, to those able to hear, of the cosmic harmony that Pythagoras called the *music of the spheres*.



The Step Pyramid of King Djozer, built around 2650 BCE at Saqqara, Egypt, is the first known monumental stone structure. The pyramid and adjacent temple complex were designed by Imhotep, High Priest of Heliopolis and styled "son of Ptah", the sun god. Also astrologer, scribe and physician, he is believed to be the author of the Edwin Smith medical papyrus and was identified by the ancient Greeks with Asclepius, their God of Medicine.

Yet despite their beguiling mystery, it was not the nature of the heavenly bodies themselves that stirred the imagination of the first astronomers, for this was the province of ancient lore, but rather the uncanny association of their movements with time and the seasons. Generations of observation eventually led, when men (or more likely, women) learned the art of agriculture, to the emergence of calender making - an empirical science laced with superstition and jealously guarded by the astronomer-priests

who developed it. Crops were first cultivated in settled hunter-gatherer communities in the Near East, such as the one at Abu Hureyra in the Euphrates valley that took advantage of the routes of migrating gazelle. By 8000 BCE the settlers of Abu Hureyra had domesticated sheep and goats and were growing pulses and other cereals. By 6000 BCE, farming had spread to the Nile and Indus valleys and to other regions of Asia, including China. Crops were also being cultivated in the Andes and parts of central and North America. But farming soon created a need for mathematics that went beyond the priestly skills of calender making. It led to the growth of walled cities (Jericho, in the Jordan valley, was some nine acres in size by 6500 BCE), the bartering of goods, and systematic warfare. Trade required keeping tallies of goods while geometry *(world measurement)* was essential for navigation between the ancient entrepots, and for the construction of new cities and their palaces and temples. The pyramids of Egypt - gigantic tombs of the Pharoahs of the old Kingdom constructed almost 5000 years ago - stand as lasting monuments to the mathematical skills of ancient civilizations.

INCTR

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ARITHMOI

Mathematics began - it still does - with counting. Notched bones dating from 35000 BCE provide evidence of primitive record-keeping well before the agricultural revolution,and such tally "sticks" afforded some of the earliest known aids, beyond parts of the body, to human memory. Cardinal systems of this kind, in which numbers (without requiring a concept of number) are represented by a series of identical units that can be compared, one-on-one, to a collection of objects or animals, were the forerunners of more sophisticated ordinal systems, in which numbers have a specific sequence or order, each with its own symbol. The almost universal sign for the number one, and perhaps other numbers, such as the "handfuls" 5 (V) and 10 (X), probably evolved from notches on bones or sticks. Calculation, however, a natural step beyond tally keeping and the foundation of science and hence material progress, required more dynamic systems. The hand has always been the calculating (and counting) machine *par excellence* but pebbles (*calculi* in Greek),shells or clay tokens have also been extensively used from the earliest times. Counting, i.e, the process of generating arithmetical data, whether for simple record keeping or calculation is, unfortunately, not quite as simple as it might at first appear. The counted units must be "like elements," the definition of which varies according to the context of the counting. Counting apples versus oranges may present few difficulties, but whether heifers should be counted with cows might depend upon the use to which the data is to be put. The notion of defining objects for counting is inherent in the modern mathematical concept of "sets." A set can be defined in any way and may contain zero elements. Examples might be the set of all cancers, or of a particular cancer in the world, or the set of sets of different types of cancers in a defined geographic region. Counting, that is, the quantitation of multitude, is the process of enumerating the elements (or units) in a specified set, i.e, the sequential matching (or mapping) of each of its elements with the next number in a hierarchically ordered series of natural whole numbers *(positive integers)* until all the elements in the set are exhausted.

For much of human history, the counting numbers have been conceived as inseparably linked to the objects enumerated. Indian astronomers, in this tradition, gave individual numbers multiple names related to objects imbued with the sense of the number. The number *one*, according to Brahmagupta, writing in the seventh century CE about long-standing practices, was called *adi*, the beginning, or *Tanu*, the body, as well as many other things, each based on an object or event denoting something unique. *Two* was associated with *Ashvin*, the twin gods, *netra*, the eyes and various other "twosomes" or dualities. The ancient Greek word *arithmoi*, often translated as number, in fact meant a number of *things* and did not encompass the modern abstract

concept of a pure number. The idea inherent in arithmoi, which was the ancient norm, resulted in a mental barrier that inhibited the evolution of mathematics, but counting things nevertheless remains a fundamental element of a broad range of human endeavors.

COUNTING CANCERS

Counting the number of cases of a specific type of cancer in a given region or population provides data that can be used to determine the resources required for cancer control in the region. For purposes of comparison with other populations, however, it is necessary to calculate an incidence rate, i.e., the number of new cases occurring for each subset of a specific number of individuals in the population in a defined period of time (most often, the number of cases per 100,000 per year). Differences in incidence rates reflect differences in exposure to environmental risk factors for cancer, tempered, of course, by genetic predisposition. Thus, incidence rates provide a necessary first step towards understanding factors which cause or predispose to cancer, and an assessment, if measured over time, of the success of preventive measures. Their determination is a primary function of cancer *registries*. Mortality rates, in conjunction with incidence rates, provide information on the success of treatment at a public health (i.e., population) level.

Accurate counting of cancer sets or subsets requires accurate definition of the counted elements - in this case, with rare exceptions, a pathological diagnosis. The quality of the diagnosis, however, will vary with the skill and resources available to the pathologist. Many pathologists, particularly those in developing countries, have little or no access to modern diagnostic techniques such as the detection of protein expression patterns or, for some cancers, tumor-specific molecular abnormalities. Cancer subtypes, however defined, may have a different etiology (cause), so that unless cases are diagnosed with a high degree of precision, the strength of the association between risk factors and specific cancers will have a built-in and variable degree of imprecision. Accurate diagnosis is only one element in the calculation of accurate incidence rates. There must also be an active process of case ascertainment that includes all institutions, regardless of location, in which cancers from the population in question may be diagnosed (cases remaining undiagnosed are effectively beyond reach). Cancer registries in single institutions provide information that is largely of value only to the institution itself, although cancer frequencies (i.e., the relative proportions of different cancers) in comprehensive regional centers may approximate population-based data. Accurate incidence rates, of course, also require accurate estimates of the size of the relevant population - whether an entire regional population, or a defined subset based on age, sex, ethnicity, religion or any other desired criterion or set of criteria. There remains a paucity of high-quality incidence data in the world, particularly in poorer countries, which rarely have population-based registries.

For accurate comparison of incidence rates between entire populations rather than between narrow age subsets, it is necessary to correct for differences in the age structure between populations (i.e., the proportion of individuals in different age-groups), since cancer incidence varies markedly with age. Children (age 0-14 years) comprise some 30-50% of the populations of developing countries, but generally no more than 15% of populations in high-income countries (Figures 1 and 2) so that the set of cancers that occur particularly or exclusively in children

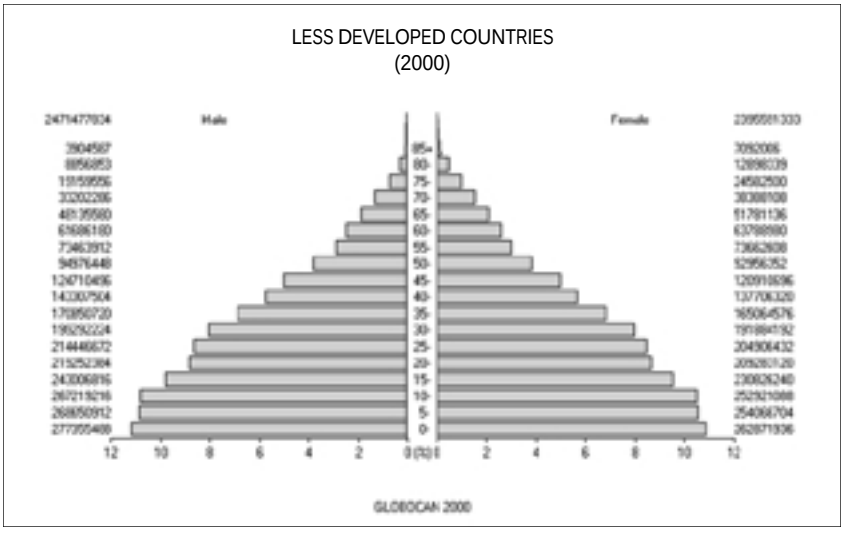

Figure 1. Another kind of pyramid ! This one shows the numbers of individuals in each age group, males and females, in the less developed countries. Data from Globocan 2000, IARC.

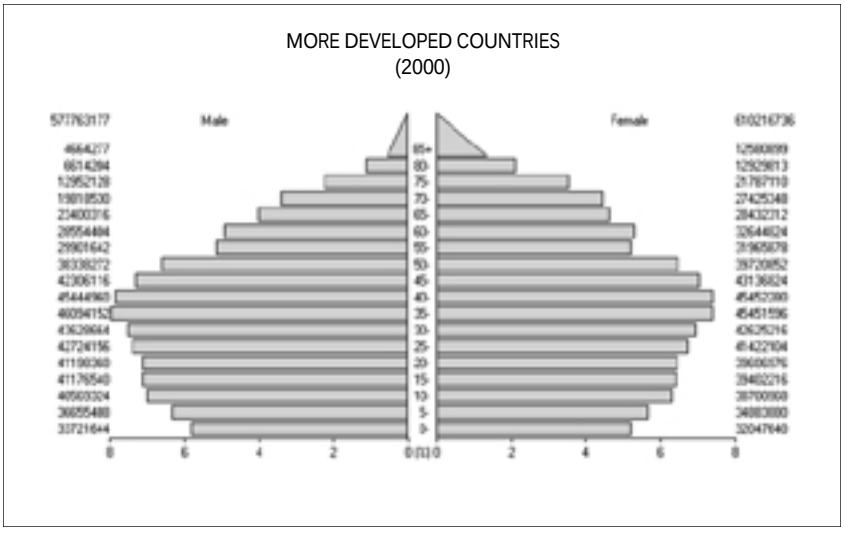

Figure 2. Population pyramid for more developed countries. Data from Globocan 2000, IARC.

account for a higher proportion of all cancers in developing countries even though their incidence rates may be similar to those in affluent countries. Conversely, the fraction of individuals above 65, who have the greatest risk of developing cancer, is much higher in most high-income nations than in developing countries. Thus, while crude (i.e., uncorrected) incidence rates provide an accurate measure of the actual cancer *burden* of a population, regardless of its age structure, *age-standardized rates*, whereby the crude rates are standardized, e.g., to the age structure of the world population, give a better perspective on incidence rate differences that relate to variable exposure to carcinogens. In spite of the many potential sources of error in counting cancer cases and people, the range of differences in cancer incidence in defined populations is generally sufficiently large, compared to the size of the inevitable errors, that cancer registries do, in fact, provide a great deal of valuable information (Table 1), particularly when collected over many years such that time-trends become apparent.

GEOMETRIA

A second major element of mathematics is measurement, i.e., the quantitation of magnitudes, namely mass and dimension. Measurement, like counting, entails comparison, but with a series of units of defined magnitude, such as length (e.g., centimeters, kilometers) or duration (e.g., seconds, hours) rather than the series of counting numbers. The ancient Greeks viewed the numerical expression of measurement, which requires the concept of fractions, as being entirely different from the process of counting. Nevertheless, Pythagoras and the members (called *mathematikoi*) of his secretive philosophical and religious school founded around 518 BCE in Croton, southern Italy (then, Magna Grecia), observed that certain numbers of pebbles could be arranged in specific geometric shapes such as triangles, e.g., 3, 6, 10, or squares, e.g., 4, 9, 16. Pythagoras had lived in both Egypt and Babylon, and doubtless imbibed much of his mathematical knowledge from these more ancient civilizations - including, perhaps, the famous theorem named after him, which was known to the Babylonians and other early agriculturalists at least a thousand years before, and which to this day is a central element in the calculation of space-time coordinates. He believed that the universe is governed by rational numbers, i.e., numbers that can be expressed as a ratio of two other numbers (including all natural numbers and fractions). Consequently, he attempted to suppress the disconcerting fact that the length of the hypotenuse of a right-angled triangle with sides of one unit is a number ($\sqrt{2}$) that cannot be expressed as a ratio of whole numbers, i.e., is *alogon* (irrational, and also unspeakable). Irrational numbers invoke the concept of infinity - anathema to the ancient Greeks. They fit into the infinite number of gaps between the rational numbers arranged along an imaginary "number line" and when expressed as decimal fractions create an infinite expansion of seemingly randomly arranged digits.

Geometria, as rigorously expounded by Euclid of Alexandria in the *Elements*, dating to 300 BCE, dealt with points, lines and circles. Such mental constructs fitted nicely into Plato's concept of "ideal forms" that he believed lay behind all earthly objects, such that ancient geometry, like arithmetic, was a tool that dealt with the tangible - the world of the senses. As with counting, the most immediately available units of measure were parts of the human body - e.g., a hand or foot-length, the distance from outstretched fingers to the elbow (a cubit) or to

the tip of the nose (a yard). Whilst some of these measurements are still used today, the obvious disadvantage of variability in limb size has been eliminated by "standardization" of the chosen unit of length. At first, this was achieved by simply using a particular individual's appendage, e.g., the King's foot, but later, a reference length was used, against which all measuring devices were standardized. Whilst clearly superior, reference lengths do not provide absolute precision. Metal bars, for example, change length according to temperature, and the dimensions and mass of objects would appear to differ when the measuring point and the measured event are in a state of relative motion - a difference that is irrelevant to everyday life, but which becomes important when elementary particles are accelerated to close to the speed of light, as occurs, for example, in radiation therapy. Standards also differ in different countries. After the French Revolution, Talleyrand, while President of the French National Assembly in 1791, stated the principle, subsequently enacted into law, that units of measure must be defined against an agreed upon standard and moreover, that for any standard to be used internationally, it should not be "arbitrary" or contain "anything specific to any people on the globe." Two years later, the meter - defined as a ten millionth part of a quarter of the Earth's meridian - was introduced as the standard unit of length. Sufficiently non-partisan, the Earth's meridian suffered from the problems of accurate measurement and accessibility. In 1799, therefore, a standard meter bar was placed in the archives of the new French Republic, along with a mass of 1000 cubic centimeters of water at a temperature of 4 degrees centigrade (the standard definition of a kilogram). These standards have been subsequently improved upon several times. A meter, for example, was most recently defined in the XVIIth General Conference on Weights and Measures (1983) - *as the distance traveled by light in space in 1/299,792,458 of a second*, a second having been defined at an earlier conference as *the duration of 9,192,631,770 cycles of microwave light absorbed or emitted by the hyperfine transition of cesium-133 atoms in their ground state undisturbed by external fields* - in essence, a measurement based on the wavelength of a highly coherent microwave beam.

MEASURING MASSES

In the context of cancer, measurement is a means of assessing the burden of disease in an individual. This does not require a high degree of accuracy. For many years, comparison of the size of tumor masses with commonplace objects, such as a nutmeg or an orange, was sufficient, since, apart from the possibility of surgical removal in some cases, there was generally little, until the 20th century, that could be done to alter

	LESS DEVELOPED COUNTRIES			MORE DEVELOPED COUNTRIES		
	Cases	Crude rate	ASR	Cases	Crude rate	ASR
Oral cavity	72687	3	3.7	24466	4	2.4
Nasopharynx	16436	0.7	0.8	2387	0.4	0.3
Other Pharynx	16062	0.7	0.8	6005	1	0.6
Oesophagus	117092	4.9	6.2	16253	2.7	1.3
Stomach	192850	8.1	10	125029	20.5	11
Colon/Rectum	154064	6.4	7.9	291897	47.8	25.4
Liver	132298	5.5	6.8	33680	5.5	2.9
Pancreas	39449	1.6	2.1	61230	10	5.1
Larynx	12390	0.5	0.6	6845	1.1	0.7
Lung	161719	6.8	8.4	175392	28.7	15.6
Melanoma of skin	13904	0.6	0.7	53511	8.8	6.1
Breast	471063	19.7	23.1	579285	94.9	63.2
Cervix uteri	379153	15.8	18.7	91451	15	11.3
Corpus uteri	75336	3.1	3.9	113618	18.6	11.3
Ovary etc.	101060	4.2	4.9	91307	15	9.9
Bladder	27895	1.2	1.4	48129	7.9	4.1
Kidney etc.	22882	1	1.1	47936	7.9	4.6
Brain,nervous system	43076	1.8	2	32538	5.3	4.1
Thyroid	53710	2.2	2.5	35635	5.8	4.4
Non-Hodgkin lymphoma	54659	2.3	2.6	66148	10.8	6.6
Hodgkin's disease	11796	0.5	0.5	12142	2	1.8
Multiple myeloma	11754	0.5	0.6	22705	3.7	1.9
Leukaemia	65366	2.7	3	47388	7.8	5.4
All sites but skin	**2561666**	**106.9**	**127.9**	**2175974**	**356.6**	**218.3**

Table 1. Cases, crude and age-standardized (to the world population) incidence rates (ASR) per 100,000 per annum (in 2000) of major cancers *in females* in less and more developed countries. Note that some subsets, e.g., Leukemia, include many different types of cancer. Data from Globocan 2000, IARC.

the natural history of the disease. Even today, ultra-precise measurements of the size of an individual tumor are of limited value. More important is the likelihood that the tumor will cause compression, erosion or invasion of adjacent organs or tissues, (which depends upon location and biological properties as well as size), and the ability to define the margins of the tumor, such that local therapy (surgery or radiation therapy) is maximally effective. Reduction in size is, however, the primary measure of the effectiveness of treatment, and is central to the assessment of the efficacy of new drugs. Precise measurement of tumor size is difficult, since tumors tend not to develop as geometric shapes susceptible to the accurate calculation of volume. They are often irregular and sometimes ill-defined, because of the invasion of surrounding tissues. Tumor cells may also float in "serous" fluid in body compartments, such as the pleural or peritoneal cavities. In glandular tissue such as the breast and pancreas, they tend to fill the gland ducts early in their evolution. They may eventually break through the *basement membrane* surrounding the ducts, thereby gaining entrance to the rest of the organ and potentially spreading to other parts of the body. Similarly, leukemias - neoplasms of blood cells and their precursors - diffusely involve the bone marrow and circulate in the bloodstream, making direct assessment of total tumor burden difficult. Here, treatment response is based on the ratio between malignant cells and normal cells (other than red cells) in a bone marrow sample, once circulating cells are eliminated. In all cases, tumor masses contain some - often a great deal - of normal tissue, as well as some dead tumor cells, such that even if precise measurements of a mass were possible, the proportion of contained tumor would remain, at best, an estimate.

Patients with most forms of cancer are assigned to a clinical *stage*, i.e., to one of several hierarchical categories that are designed to indicate progressively more advanced disease.

Counting cancers is the foundation of epidemiology and public health. Measuring cancer is necessary for optimal treatment and clinical research.

The stage of a tumor is a function of both its physical size and the biological properties of the tumor cells that determine the degree of spread in the body. Although size and biological characteristics are, to a degree, related (in part because the greater the number of tumor cells, the more likely are additional molecular changes to arise), the relationship is not precise. Moreover, tumor volume itself depends upon the biological properties of the tumor cells, including their proliferative rate and death rate, as well as the duration of time that has passed from the onset of a cancer to its diagnosis. Tumor cells disseminate to regional lymph nodes or to distant parts of the body by penetrating lymphatics and blood vessels, but only those capable of surviving and growing in one or more tissues or organs that would be hostile environments to the normal counterpart cells are capable of giving rise to new tumor cell colonies at distant sites. Such colonies are referred to as *metastases* - literally, tumor that "stands" or "stops" in a different place. Their constituent cells are able to resist the signals that induce apoptosis (programmed cell death) in displaced cells - a mechanism that normally ensures the integrity of organs and tissues. The ability to avoid apoptosis also renders tumor cells relatively resistant to chemotherapy and frequently to radiation therapy. Consequently, the presence of metastases is nearly always associated with a poor treatment outcome, regardless of the tumor burden when treatment begins. Clinical staging, therefore, provides a guide to treatment, since more advanced stages require more intensive therapy and/or a different blend of local and systemic treatment. In developing countries, patients tend to have higher stage disease at the time of diagnosis than in affluent countries, at least in part because of delay in diagnosis. This must be taken into consideration in determining resources required for treatment and in comparing treatment outcome with that achieved in in more affluent countries. The accuracy of stage assignment, however, is a function of the availability and use of various imaging techniques which must also be taken into account when comparisons are made. Apparent improvements in the survival of patients with localized disease, for example, can result when new techniques that improve the detection of disseminated disease are introduced, eliminating a fraction of patients previously included in this category.

While clinical stage is usually one of the most important determinants of outcome (particularly in tumors where systemic therapy is ineffective) additional predictive value may be provided by histological features (often also categorized into several *grades*), including the degree of invasion of adjacent tissues at a

microscopic level and by the tumor's molecular profile. The concentration of various tumor *markers* in the bloodstream, such as hormones, proteins or molecular abnormalities present in circulating tumor cells or DNA, can also permit the prediction of outcome with a particular treatment, provide a more precise measure of treatment response, or indicate imminent relapse. In normal individuals specific markers may be associated with an increased risk of the development of cancer. Finally, many factors other than those associated with the tumor itself can influence both the therapeutic outcome and the toxicity of treatment. These include age, performance status, coexistent chronic infections and malnutrition, inherited variations in the metabolism of chemotherapeutic drugs and the ability of tumor cells and normal tissues to repair radiation or drug-induced damage.

Clearly, determining associations between tumors and potential etiological factors, predicting outcome with a particular therapy, or comparing the results of clinical trials all require sophisticated mathematical techniques considerably beyond the capabilities of ancient civilizations. Their evolution required the development of new number systems (i.e, ways of writing numbers), which in turn depended upon the discovery of *zero*. These advances permitted the development of an abstract concept of number, i.e., the separation of number from the things they referred to, such that they could be generalized as algebraic expressions. Algebraic *analysis* is of profound significance to progress in all branches of science and technology. Its relevance to cancer control will be discussed in Part 2 of this message. ■

IMPROVEMENT OF CANCER PATIENT FOLLOW-UP

The importance of loss to follow-up (LTFU) in patients with cancer is self-evident. If LTFU occurs before treatment is completed (abandonment of therapy), the result is very likely premature death. Strategies for reducing abandonment of therapy have been reported, e.g., in children in Central America. In some parts of the developing world, Abandonment of Therapy is the most important cause of treatment failure. If LTFU occurs after completion of therapy, recurrence of disease cannot be monitored, late sequelae will not be detected, and treatment outcome cannot be determined. Understanding the causes of LTFU is the first step in developing interventions designed to minimize LTFU and so improve cancer control. This is particularly important in low-income countries where LTFU is most prevalent and programs of cancer control are only now emerging.

At King Faisal Specialist Hospital and Research Centre (KFSHRC) in Riyadh, Saudi Arabia, in collaboration with the INCTR, two projects have been undertaken in adults and children with malignant lymphoma. In a retrospective study involving patients referred to KFSHRC from several institutions, of 144 pediatric and 431 adult patients diagnosed in 1997 and 1998, 30% and 48.5% respectively were LTFU after four years (excluding patients known to have expired). In 2001-2002, 196 pediatric and adult patients were enrolled in a prospective study at KFSHRC in which detailed explanations were obtained for non-attendance at follow-up appointments (no show) during active treatment. Sixteen months after commencement of the study, 49 patients (25%) were "no show" due to patient-based errors—such as the patient forgetting about the appointment, or being mistaken about the appointment date (20), transportation problems (8), patient not contactable (18), and personal reasons (3). In addition, 45 patients (23%) were recorded incorrectly as "no show" because of hospital-based errors (failure to communicate properly with patients). These initial results have been reported [1].

The pilot study in Saudi Arabia focuses on a country where adequate therapy and diagnosis are available but there is considerable LTFU: a circumstance where resources are such that corrective action can quickly be taken once the cause of the problem is identified. In countries with severe economic and demographic problems, the limited resources of both institutions and patients must be taken into account as well as the possibility that reasons for LTFU may vary widely from one region to another, necessitating different approaches to the problem.

It is proposed to undertake additional prospective studies and LTFU in other developing countries. The objective is to establish follow-up procedures that can be continued as part of routine cancer care after the prospective study is over and that collaborators can help to implement in other institutions. These "self-replicating" programs are perhaps the best way to improve follow-up. ■

Arthur Levin, Stuart Brown, Ronnie Barr, Julia Challinor, Linda Krebs

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CANCER IN A DEVELOPING COUNTRY: OPPORTUNITIES AND FORMIDABLE CHALLENGES

The developed countries are witnessing a progressive decline in age-adjusted cancer incidence, as well as a leveling in number of cancer deaths. These declines in incidence and mortality can be attributed to a number of factors, including public and professional education, primary prevention, early detection and treatment. These trends, however, are unfortunately not present in developing countries. It is estimated that by 2020, 70% of cancer in the world will be diagnosed in developing countries, causing some nine million annual cancer deaths.

Pakistan is a developing country with a population of 150 million people. Average life expectancy is 62 years. It is estimated that 160,000 new cancer cases are diagnosed annually. The total expenditure in the health sector by the government was 0.7% of GNP for the year 2002-03. Health care services are provided to the public through a vast infrastructure of health care facilities, which include government hospitals, private hospitals, basic health units and dispensaries. Less than 5% of the population is fully or partially covered by health insurance. The major health priorities of the government are communicable diseases and maternal and child health. Thirty percent of the population live below the poverty line (defined as a GNP per capita of less than US$ 480) - earning less than US$140 per annum. Of these, 32% belong to the rural population while 19% live in urban regions. The overall literacy rate (defined by the ability to write one's name!) is 50.5 % (63% males and 38% females). Rural and urban literacy rates are between 30% and 70%. Malnutrition, infectious diseases, poverty, hunger and environmental hazards are some of the major problems faced by the poor. They are locked in a vicious cycle that keeps them poor, backward and deprived of basic rights, both socially and politically.

KCR (1995-1999) (N=3891)		AFIP (1984-1988) (N=5449)		AIMC (1997-2000) (N=1629)	
Site	ASR	Site	%	Site	%
Lung	20.0	Lymph node	10.79	Leukemia	23.6
Oral Cavity	16.6	Leukemia	8.01	NHL	15.1
Larynx	9.4	Bronchus	6.97	Bronchus	7.5
Urinary Bladder	9.4	Prostate	6.93	Colorectal	6.7
Pharynx	7.9	Skin	6.20	Liver	5.8

Table 1. Comparison of the rank order of the five most common tumor sites in males in three registries, one population based, in Pakistan. KCR: Karachi cancer registry for Karachi South, AFIP: Armed Forces Institute of Pathology, Rawalpindi, AIMC: Allama Iqbal Medical College, Lahore. ASR = Age Standardized Rate (see President's message). N = number of cases. % = percentage of all cancer cases.

CANCER EPIDEMIOLOGY IN PAKISTAN

According to WHO, 80% of all cancers in developing countries are due to environmental factors, infectious agents and diet. Smoking has become a major health hazard in developing countries. In Pakistan, a conservative estimate is that 50% of males and 9% of females are habitual smokers. This does not include children, particularly in the lower socio-economic groups, among whom smoking has increased tremendously. Tobacco-related cancers are increasing rapidly in incidence because of the dramatic rise of tobacco smoking in developing countries. Betel-leaf and tobacco chewing is common in South Asia, and contributes to the relatively high incidence of head and neck cancers. The prevalence of Hepatitis B & C ranges from 3.5%-18.6% and 4%-25.6% respectively, such that one of the consequences of infection with these viruses, hepatocellular carcinoma, is relatively common in males. In addition, aflotoxins, derived from a fungus, are commonly found in stored food grains. They are believed, together with malnutrition, to contribute to the increasing incidence of liver cancer. H.pylori infection (a bacterium associated with peptic ulceration, gastric cancer and gastric lymphoma) is common in developing countries, with infection rates ranging from 80-100%. Indiscriminate use of cheap and expired pesticides by farmers in the heavily agricultural province of the Punjab may account for the relatively high prevalence of lymphomas and leukemias, which have been shown, in the USA and elsewhere, to be associated with exposure to herbicides and other chemicals.

There are no population-based cancer registries in Pakistan except the Karachi Cancer Registry (KCR). The true magnitude of the cancer problem is therefore unknown.

In women,breast cancer is the most common cancer throughout Pakistan, and according to KCR, the age-standardized rate is 56.6 per 100,000 women per year. No identifiable risk factors are present, however, in 75% of patients with breast cancer. Gall bladder cancer is the fifth most common cancer in our female population. Contributing factors include gall stones, diet, infections and a sedentary lifestyle in this group of patients.

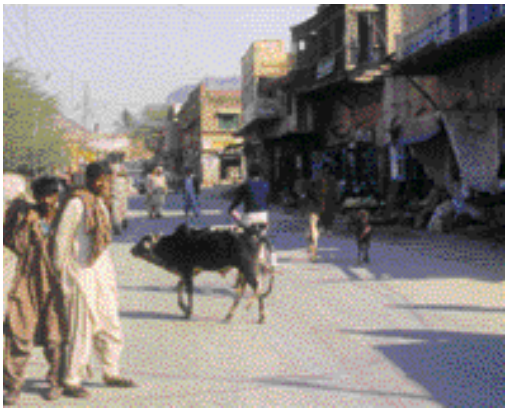
In the developing world, more than 80% of all cancer patients are incurable by the time they are diagnosed. This is particularly true for patients from the less affluent strata (>60%) where multiple factors operate, among which are economic constraints, illiteracy and poor access to health care facilities. Other contributory factors are ignorance of patients and health professionals and disease stigma. The prior use of alternative medicines, hakims (traditional medicine practitioners) and homeopaths also delays appropriate cancer care. This is especially common in the rural areas as such approaches are a cheap alternative to the costly conventional health care systems. Co-morbid conditions like tuberculosis, hepatitis and malnutrition are common in the poorer patients with cancer. Large family size, small living quarters and poor hygiene cause recurrent infections. Our data on breast cancer treatment and survival outcome reveals that 75% of patients from the upper strata have early disease and their outcome is similar to their counterparts in the developed countries. Patients belonging to the lower strata (80%),on the other hand, present with advanced disease and exhibit inferior survival. Similar observations have been made in developed countries in patients belonging to the lower socio-economic strata.

CANCER TREATMENT IN PAKISTAN

Facilities for treatment of cancer patients are available in a few larger cities in both public and private hospitals. There are 18 radiotherapy centers with 65 practicing radiation oncologists; the quality of these centers is extremely variable depending on the expertise of the physician and available equipment. There are only 15 medical oncologists practicing in major cities. State-of-the-art surgical oncology is practiced in only a few hospitals, and as a result, the majority of patients undergo sub-optimal surgery.

KCR (1995-1999) (N=3684)		AFIP (1984-1988) (N=3858)		AIMC (1997-2000) (N=1783)	
Site	ASR	Site	%	Site	%
Breast	56.6	Breast	27.65	Breast	38.5
Oral Cavity	15.4	Skin	6.29	Ovary	13.6
Ovary	9.6	Cervix	4.76	Leukemia	10.3
Cervix	7.4	Leukemia	4.61	NHL	5.7
Oesophagus	7.0	Ovary	4.48	Gall Bladder	4.2

Table 2. Comparison of the rank order of the five most common tumor sites in females in three registries, one population based, in Pakistan. KCR: Karachi cancer registry for Karachi South, AFIP: Armed Forces Institute of Pathology, Rawalpindi, AIMC: Allama Iqbal Medical College, Lahore. ASR = Age Standardized Rate (see President's message). N = number of cases. % = percentage of all cancer cases.



Street scene in a small town in Pakistan.

In Pakistan, profound differences exist with respect to the availability of medical care to different segments of the population. Good quality hospital care is available to the affluent class, either from a small number of excellent public sector hospitals, or from the private sector. The less affluent classes are provided free services in the government hospitals but again, the quality of these services is extremely variable, depending on the available resources and trained personnel. The financial burden of treatment is borne by the patients, which makes it difficult for the poor to receive state-of-the-art treatment. They are supported by monetary donations from individuals as well as government funds and Zakat, a tax that the more wealthy Muslims pay specifically to help the poor. These contributions tend to be insufficient and erratic. Clearly these resources are inadequate to deal with the ever increasing economic burden of cancer patients. It is estimated that fewer than 30% of

YEAR 2000				
	Males		Females	
Age Group.	Age specific rate	Number of new cases	Age specific rate	Number of new cases
0-14	12	4017	7	2277
15-44	41	14910	76	25210
45-54	197	10952	352	17769
55-64	462	14306	518	15662
65+	706	17439	559	14177
All ages	76	61624	99	75095
EXPECTED CANCER BURDEN IN THE YEAR 2025				
0-14	12	4766	7	2707
15-44	41	27100	76	48076
45-54	197	24818	352	40683
55-64	462	42228	518	44902
65+	706	49378	559	41302
All ages	110	148290	137	177731

Data from Globocan.1.

Table 3. Expected increase in cancer cases - all sites but skin - and annual incidence rates per 100,000 in Pakistan for 2025 compared to 2000.

patients receive the minimal recommended treatment for their disease.

WHAT CAN DEVELOPING COUNTRIES DO?

The absence of population-based tumor registries is a major drawback. Information about cancer is largely extrapolated and no formal policies for cancer control have been made. Data from the hospital-based tumor registries are not organized, information is fragmented, and it is likely that regional variations in cancer incidence and types occur. It is essential that governments in developing countries use their meager resources to develop population-based cancer registries, form policies on prevention of preventable cancers, provide optimal training of their personnel, and develop regional sites for cancer treatment with good diagnostic facilities.

EDUCATION

Education is essential to improving the results of cancer treatment as it will result in early detection of cancers and possibly cure in some patients. It has to be done at three levels. Community education,physician education and patient education are all essential to creating cancer awareness and improved treatment options. Education should also focus on smoking hazards, environmental pollution,infectious diseases and use of sub-standard materials in our diet, etc. The younger generation, which comprises the majority of the population, should be targeted. Public education can be achieved through printed matter, television and radio.

CANCER PREVENTION AND EARLY DETECTION

WHO estimates that one-third of cancers can be prevented and one-third could be treated if diagnosed early enough,and if access to knowledge and treatment were widely available. The majority of cancers, which are related to lifestyle and environment, can be prevented or their incidence decreased by such measures as educating people about the dangers of smoking, and vaccinating them against Hepatitis B, etc. These measures should be targeted to schoolchildren and young adults. Early detection of several cancers such as breast, cervix, colon and other sites that can be effectively treated in their early stages would significantly increase survival rates. Breast self-examination and clinical breast examination are important and much less expensive potential alternatives to mammography. Direct visualization of pre-invasive cervical cancers is also a cheap and highly effective means of preventing invasive cancer. For screening programs to be established, we need to allocate resources to the common cancers in our region and to use our resources pragmatically.

TREATMENT OPTIONS

Cancer patients are treated with a variety of protocols developed in developed countries. These protocols may not always be appropriate for patients living in the less developed countries. It is important that indigenous protocols are developed, keeping in mind resources, the biology of the disease and the patients' biology. It is also important that treatment should be provided to the maximum number of patients given the financial constraints. Last but not least, at present the vast majority of patients require palliation for their symptoms and maximum comfort should be provided to them. Herculean efforts are still needed to see the proverbial light at the end of the tunnel. ■

Zeba Aziz, Professor of Oncology, Allama Iqbal Medical College, Lahore

GRUPO MEXICANO DE RETINOBLASTOMA

En México, el retinoblastoma (Rtb) representa un problema importante en el campo de la oncología pediátrica. El Grupo Mexicano de Retinoblastoma (RtbMex) se creó en enero de 2003. Está avalado por la Academia Nacional de Medicina, y cuenta con el apoyo del International Network for Cancer Treatment and Research (INCTR). Actualmente, el grupo está integrado por oncólogos pediatras, oftalmólogos, radioterapeutas y patólogos representantes de más de 16 instituciones del país.

OBJETIVOS

Creación de un Registro Nacional de Retinoblastoma

El Registro Nacional permitirá contar con información de la enfermedad en México, el cuál permitirá la planificación más eficiente del diagnóstico temprano y el tratamiento de la enfermedad.

Campaña de Detección Temprana

Ya que el pronóstico y tratamiento de esta enfermedad dependen del estadio al momento del diagnóstico, la detección temprana de este padecimiento puede permitir preservar no solo la vida del niño, sino también la función del ojo. Es por ello que la Campaña de Diagnóstico Temprano ha sido una prioridad para el grupo RtbMex. Actualmente, en el Instituto Nacional de Pediatría (INP) se está realizando un estudio –como parte de un estudio multicéntrico coordinado por el INCTR- para comprender mejor este fenómeno. Los resultados preliminares para el INP han mostrado que de manera general se pueden identificar a) factores relacionados con los padres o cuidadores; b) factores relacionados con los médicos y; c) factores relacionados con los recursos económicos y materiales. Por lo tanto, la campaña está dirigida a diferentes grupos sociales:

Invitados y amigos se reúnen para cenar en la reunión del RtbMex,en noviembre 2003. Attendees and friends meet for dinner on the occasion of the RtbMex meeting in November 2003.

La misión del grupo es desarrollar capacidades para el manejo del retinoblastoma en todo el país, promover el diagnóstico temprano de la enfermedad, ofrecer mejores estándares de tratamiento a todos los pacientes e impulsar la investigación en retinoblastoma.

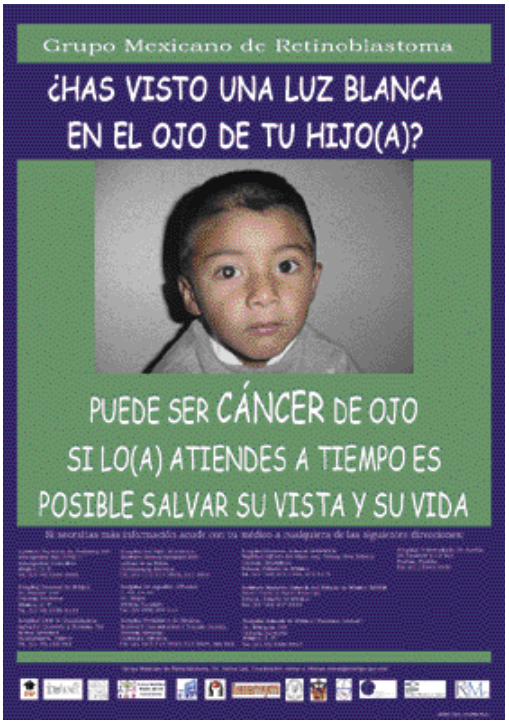
a) Médicos oftalmólogos y pediatras.

Programa dirigido a incrementar el conocimiento de la enfermedad, así como las habilidades necesarias para su diagnóstico involucrando a instituciones relacionadas con la formación y capacitación de médicos especialistas. Hasta el momento se han impartido cursos de actualización para médicos especialistas en Puebla y se planea realizar cursos en Guerrero y Guanajuato.

b) Médicos generales y otros profesionales relacionados con la atención de niños preescolares.

Programa dirigido a incrementar el conocimiento de la enfermedad y capacitar para la detección y referencia oportunas. Como par te de este programa se han diseñado e impartido cursos en la Escuela Nacional de Enfermería UNAM y en la Universidad del Estado de México. Este programa busca involucrar tanto a Universidades como a Centros de Salud, particularmente aquellos que se encuentran en zonas rurales alejadas de los mayores asentamientos urbanos.

N E T W O R K



Una campaña educativa patrocinada por RtbMex alienta a los padres a buscar los signos tempranos que pueden advertir la presencia de un retinoblastoma. An educational campaign sponsored by RtbMex encourages parents to look for the early warning signs of retinoblastoma.

c) Población general.
Programa dirigido a incrementar el conocimiento de la enfermedad en la población general, así como el reconocimiento de los primeros signos de la enfermedad. También se busca proveer información sobre los centros y hospitales en los que es posible dar atención a los niños afectados con Rtb. Como parte del programa,se ha buscado el apoyo de medios masivos de comunicación, logrando hasta el momento algunas entrevistas en dos noticieros de cobertura nacional. Además, se hizo un tríptico con información general de la enfermedad y se diseñó un cartel con información básica sobre Rtb y las instituciones en las que puede ser atendido. El cartel fue producido por el Hospital y Centro de Investigaciones de King Faisal gracias al apoyo del INCTR. El objetivo es distribuir este material en lugares frecuentados por la población general, así como en centros relacionados con la atención de niños preescolares tales como guarderías y centros de salud. Ya se ha iniciado la distribución de estos carteles a través de los diferentes miembros del grupo, logrando involucrar a los ministerios de Salud de algunos estados como Morelos, Jalisco, Sinaloa y Guerrero entre otros, para la distribución de los carteles. Actualmente, el grupo está planeando la distribución en zonas rurales mediante el contacto con las organizaciones no gubernamentales.

PROGRAMA DE REFERENCIA
El Programa de Diagnóstico Temprano debe coordinarse con un programa de referencia que asegure ofrecer a todos los niños un tratamiento de alta calidad. Dicho programa ya está en marcha,las instituciones participantes se han comprometido a proveer atención a los niños afectados y se ha mejorado la comunicación entre los diversos centros.

PROTOCOLO NACIONAL DE TRATAMIENTO
El objetivo del Protocolo Nacional de Tratamiento es asegurar una atención

The Grupo Mexicano de Retinoblastoma (RtbMex) was created in January 2003, and has been supported since its inception by INCTR and the Office of International Affairs of the National Cancer Institute, USA. The mission of RtbMex is to develop the capacity for the treatment of retinoblastoma (Rtb) throughout the country. The objectives of the group are to create a National Register, to develop a national early diagnosis campaign, to ensure that all children with Rtb have access to good medical care, to develop a national multimodality treatment protocol, to collaborate in relevant research related to Rtb treatment and to undertake fund-raising in order to support the activities of the group and to ensure that children with Rtb are assured of high quality treatment throughout Mexico. RtbMex has made progress in the achievement of some of its goals and has carried out a first study on the clinical and demographic characteristics of Mexican children with Rtb. As part of its early diagnosis campaign,it has organized "up-date" courses for general practitioners, pediatricians and ophthalmologists in hospitals and universities. It has also developed an education campaign for the general public which includes the production,supported by INCTR, of a poster that is to be distributed to a wide range of health centers in the country. Another meeting of RtbMex, also supported by INCTR,will be held on August 2004. The main objective of the meeting will be to finalize a national treatment protocol,which will help to standardize treatment while improving the quality of care. INCTR's support and collaboration has allowed RtbMex to participate in international research through developing relationships with international experts and providing opportunities to participate in international collaborations in the multidisciplinary care of patients with Rtb.

Una pequeña niña muestra el reflejo de "ojo de gato",un signo temprano de Rtb. A small girl exhibits a "cat's eye" reflex, an early sign of Rtb.

médica uniforme y de vanguardia para cualquier niño mexicano. A lo largo del primer año de vida del grupo, se han realizado algunas reuniones para discutir sobre este punto. En la reunión de trabajo planeada para agosto de este año, se planea terminar un documento con los lineamientos para el tratamiento multidisciplinario del retinoblastoma, que sea aceptado por todos los miembros del grupo. La reunión será patrocinada por el INCTR.

DESARROLLO DE INVESTIGACIÓN

A fin de mejorar el tratamiento y la calidad de vida de los niños con Rtb, el grupo ha considerado necesario el desarrollo de investigación en nuestro país. Antes de desarrollar cualquier protocolo de investigación será necesario consolidar al grupo y desarrollar mejores habilidades para el trabajo coordinado, la comunicación y el intercambio de información. Actualmente, se está planeando un protocolo de tratamiento en coordinación con el INCTR en el que el RtbMex podrá participar.

CAPTACIÓN DE RECURSOS FINANCIEROS

A fin de desarrollar cada una de las actividades planeadas, es necesaria la búsqueda de recursos económicos que permitan dar continuidad al trabajo, así como adquirir equipo y tecnología para las diferentes instituciones que atienden pacientes con Rtb.

Gracias al INCTR hemos podido tener contacto con expertos de otros países, apoyo en nuestras reuniones nacionales y visitas de profesores internacionales que han coadyuvado a la mejor atención de nuestros pacientes. Del mismo modo, estamos colaborando en proyectos de investigación en aspectos de atención oportuna, así como en el desarrollo de un protocolo internacional de tratamiento integral para pacientes con Rtb. ■

Carlos A. Leal, Instituto Nacional de Pediatria,Mexico.

INSTITUCIÓN	ESPECIALISTAS
Centro Estatal de Cancerología Jalapa Ver.	Dra. Lourdes Vega V.
Centro Estatal de Cancerología de Acapulco	Dra. Ana Bertha Rivera
Centro Estatal de Cancerología de Durango	Dr. Francisco Carrete
Centro Médico 20 de Noviembre ISSSTE	Dra. Sandra Páez
Hospital Central de San Luis Potosí	Dra. Cecilia Correa Dr. Francisco Alejo
Hospital Central O'Horan de Mérida	Dr Francisco Pantoja Dra. Gabriela Escamilla A.
Hospital Civil de Guadalajara	Dr. Oscar González R Dra. Consuelo Zepeda
Hospital Civil de Puebla	Dr. Arturo Moreno
Hospital de Pediatría de Hidalgo	Dra. Carolina Soto
Hospital del Niño Morelense	Dr. José de J. Figueroa
Hospital General de México	Dr. Fernando Pérez Dra. Ana E Ayón
Hospital Infantil de México	Dra. Aurora Medina S Dr. Marco Ramírez
Hospital Infantil de Tabasco	Dra. Andrea Ellis Dra. Olivia Yepes
Hospital Miguel Hidalgo	Dr. Ricardo González PM.
Hospital Pediátrico de Sinaloa	Dr. Eduardo Altamirano Dra. Sonia Corvera
Hospital del Niño Oaxaqueño	Dr. Armando Quero
IMSS Centro Médico de Occidente Jalisco	Dr. Ricardo Gómez M Dr. Víctor del Villar
IMSS Centro Médico La Raza	Dra. Sandra Sánchez Dra.Laura Campos
IMSS Centro Médico Nacional Siglo XXI	Dr. Fernando Cerecedo
Instituto Materno Infantil de Estado de México	Dr Isidoro Tejocote Dr. Roberto Cervantes
Instituto Nacional de Pediatría	Dr. Carlos A. Leal Psic. Martha Flores R Dr. Juan C Juárez E. Dr Jorge Amador Z. Dra. Cecilia Ridaura S.
ISSEMYM	Dra. Araceli López F.

Table 1. Instituciones participantes.

NETWORK

CANCER SURVIVOR SCALES WORLD'S HIGHEST PEAKS

Sean Swarner is lucky to be alive, and not just because he lives dangerously, scaling the world's highest peaks. The 29-year-old mountaineer is a two-time cancer survivor who defied doctor's predictions that he would succumb to his disease.

When Swarner was 13, he was diagnosed with Hodgkin's disease, a lymphoma that uncommonly affects anyone under the age of 20. He was given three months to live. Two years later, he was diagnosed with Askin's sarcoma, a pediatric tumor affecting the chest wall and ribs. The prognosis for this disease, with a survival rate of 30%, was even worse; the doctors gave him only two weeks to live! Again, Swarner survived. By the time he was 18, Swarner was cancer-free and fit, winning his high school's track meet in the 800-meter race.

Swarner is living proof that despite the worst prognosis, there is hope for cancer patients and their families.

"Frankly I don't know why I'm alive," Swarner says. " But I'm incredibly grateful for the life I have. Somehow I found the inner will to get up and out of that hospital bed. My message is that people should really enjoy every moment they've been given. You have one chance—make the most of it."

As an undergraduate at Westminster College in Pennsylvania, Swarner pursued his interest in molecular biology and immunology, endeavoring to understand how his body might have combated his cancers. It was a psychology class, however, that affected him most." I did a study looking at the relationship between optimism and the quality of life of cancer patients," he says. He earned a master's degree in psychology in Florida, and was accepted to a doctoral program for psycho-oncology in Chicago.

Sean Swarner equates the extreme physical challenges of mountaineering with the battle against cancer.

"I knew I wanted to help people cope with cancer, but I decided to take a sabbatical from my studies and find another way to touch cancer patients," Swarner says. "When I was going through all that stuff as a teenager, hugging the toilet and finding hunks of hair on the floor of the shower, my friends were collecting baseball cards and chasing girls. They all had heroes and role models, but I didn't know anyone who had been where I was. I decided that if I could climb Mount Everest, I could provide some inspiration to other young people going through those dark times."

On May 16, 2002, at 9:32 a.m., Swarner became the first (and still only) cancer survivor to climb Mt. Everest. Since then, he has reached the summits of Kilimanjaro and Elbrus, the highest peaks in Africa and Europe, respectively. His goal is to climb the highest mountain on each continent, and then trek to both the North and South Poles. If he is successful, he will join an elite group of 100 mountaineers worldwide.

On each of his climbs, Swarner has planted Cancer Climber Association flags at the peak, to commemorate the uphill struggle of cancer patients around the globe. They read: "Dedicated to all those people affected by cancer in this small world. Keep Climbing!"

"I hope people get some inspiration from this and realize that nothing's impossible," Swarner wrote to friends and supporters back home before his Kilimanjaro ascent."I know everyone has his own proverbial mountain to climb and I hope that when people see someone out here doing the actual physical climbing of spectacular mountains they recognize that they can also plan goals, dream big and never give up hope."

Before tackling Mt. Everest, Swarner happened to visit the Bhaktapur Cancer Center in Nepal, where INCTR assists with cervical cancer prevention programs. "While

I was there, the doctors told patients there that I was a two-time cancer survivor, and that I was leaving the next day to climb Mt. Everest. Their faces just lit up. I know I provided them some hope that they could survive cancer too."

When Swarner is not training in Colorado's Rockies for his next climb, he is giving motivational talks or organizing fundraisers to benefit children with cancer. He and his brother operate Cancer Climber Association to raise money to support summer camp outings and other wilderness adventures for youngsters. The fundraisers themselves are typically outdoor activities—foot races, wall climbing, bungee jumping, whitewater rafting—that encourage active lifestyles.

In conjunction with his next expedition to Alaska's Denali,the highest peak in North America, Swarner is planning a fundraising challenge to fitness buffs willing to climb 20,000 feet on a Stairmaster in their local gym. The knowledge that other climbers are behind him will be helpful as he makes the ascent, but Swarner admits he gets his true inspiration from those who can't leave their beds.

"I've seen death," he says, "and I know that if you don't take chances, you're not really alive. We're put on this earth to experience as much as we possibly can. I want to live my life with no regrets,in the knowledge that anything is possible."

For more information about past expeditions and upcoming events, or to invite Swarner to give an inspirational presentation to your organization, visit **www.CancerClimber.org**, or call 720-890-2716. ■

Marcia Landskroener for INCTR

GOLDEN JUBILEE CELEBRATION OF THE CANCER INSTITUTE (WIA), CHENNAI

In February 2004, the Cancer Institute (WIA), an INCTR Associate Member and for long a valued collaborating institution, celebrated its 50th year. It was Dr. Muthulakshmi Reddy, India's first woman Medical Graduate, who conceived the idea of building a cancer center in India in 1927. Having recently cared for her sister during the terminal phase of her rectal cancer (which had been misdiagnosed),she visited the Royal Cancer Hospital in England, where she saw patients who had been cured of the same disease. Upon her return to India she resolved to develop a similar institution in Madras. The vision was not to become a reality for many years since Dr. Muthulakshmi was initially unable to persuade local authorities to support her project. Not willing to give up, she established the Cancer Relief Fund (WIA) and collected 200,000 rupees (approximately $4,000). With this, a donation of land, and additional funds (totaling 150,000 rupees) provided by the Governments of India and Madras, the first block of the CI (WIA), which included only 12 beds, was finally opened in June 1954. Patients began to be seen in January 1955. The medical staff (honorary) consisted of Dr. P. Arunachalam (the first Director), Dr. Krishnamurthi (Dr. Muthulakshmi's son) and Dr. Shanta (the first recipient of INCTR's Nazli Gad-el-Mawla Award and a member of INCTR's Special Panel). The remainder of the staff consisted of two auxiliary nurses and one boy. In the subsequent 50 years, the CI (WIA) has grown into a large, well equipped cancer center with 301 beds, which has been selected by the Government of India as the Southern Regional Center of Cancer Research and Treatment.

View of the outpatient department of CIA(WIA) taken at the time of the Golden Jubilee.

The Golden Jubilee included a speech by the President of India,and scientific and medical presentations by distinguished Indian and guest speakers. INCTR was honored by an invitation to Dr. Magrath to deliver the Dr. Muthulakshmi Oration. ■

MEETING OF THE INDIAN LEUKEMIA STUDY GROUP (PART OF INCTR'S LEUKEMIA STRATEGY GROUP)

The ILSG met on two of the evenings in the course of the CI (WIA) Golden Jubilee Celebration to discuss progress in finalizing requirements for implementing the new treatment protocol for acute lymphoblastic leukemia, assisting smaller centers to use protocol MCP 841, and working in collaboration with other countries, particularly Egypt and China. It is hoped that patient accrual to the new protocol will begin this summer. ■

CHENNAI MEETING ON ACUTE LYMPHOBLASTIC LEUKEMIA, 9-11 FEBRUARY, 2004

Immediately following the Golden Jubilee Celebration of the CI (WIA) a meeting was held to discuss the development of effective therapy for acute lymphoblastic leukemia (ALL), with special emphasis on progress made in India in the last 20 years. The meeting was jointly organized by CI (WIA) and INCTR and was supported by local funding and the NCI's Office of International Affairs. The treatment protocol, MCP 841, which has been of particular importance to the treatment of ALL in India, was first used at CI (WIA) in the mid 1980's and has been subsequently adopted by many other treatment centers in India. This has resulted in marked improvement in five year survival rates from perhaps 20% or less to over 50% (Indian centers represented at the Chennai meeting reported survival rates of between 50-80% at five years). The conduct of this protocol in collaboration initially with the NCI and more recently with INCTR,provided incentive to develop high quality data management in participating centers, and has revealed that there are differences not only between Indian and "western" patients with ALL, but also among participating Indian centers - both with respect to patient characteristics and to treatment outcome. In general, Indian patients tend to have more advanced disease than patients in the USA or Europe and a higher proportion of a subtype of leukemia known as precursor T cell ALL. Fittingly, a review of the development of ALL treatment with protocol MCP 841 in three major Indian centers - CI (WIA),Tata Memorial Hospital and the All India Institute of Medical Sciences - has recently been accepted for publication in the *European Journal of Cancer*. ■

Members of the Leukemia Study Group of India (a subcommittee of INCTR's Leukemia Strategy Group) at their meeting in February 2004.

ANNUAL GENERAL ASSEMBLY AND GOVERNING COUNCIL MEETING

The annual meetings, including a combined element, of the active members of INCTR and INCTR's Governing Council took place on 12th March at the INCTR offices in Brussels. In addition to approving the past year's expenditure and accepting the proposed budget for 2004, the progress report for 2003 was presented, and several important decisions were made. One was to develop an INCTR Charter, in which the principles governing the organizations collaborative activities would be clearly stated. All elements of the organization will be expected to adhere to these principles. Once completed, the Charter will be approved by the Governing Council, and presented at the Members

Assembly in October 2004, in the course of the Annual Meeting. Another was to establish a funding committee. This will consist of Raj Shah (chairman), Nausherwan Burki and Sultan Al-Sedairy. ■

ESTABLISHMENT OF A TELESYNERGY® SYSTEM AT THE NCI LIAISON OFFICE

A meeting was held at the NCI Liaison Office, on 12th February, to discuss the use of the TELESYNERGY® equipment that had just been installed in space adjacent to the NCI Liaison Office (kindly provided by EORTC). Participants included Norman Coleman, Frank Govern and Ellen Feigel of NCI, Susanne Radtke of the NCI Liaison Office, and Ian Magrath and Melissa Adde of INCTR. The TELESYNERGY® system is a state-of-the-art telemedicine system developed by the Radiation Research and Radiation Oncology Sciences Programs of NCI in conjunction with members of NIH's Center for Information Technology. TELESYNERGY® is capable of linking several centers by high speed telephone lines to enable videoconferencing and sharing of information, including high quality digitized images of X-rays or scans and histopathological sections of tumor biopsies, computer files (including slide shows), and prerecorded material. This equipment has been generously made available to INCTR by Drs. Coleman and Govern of the NCI. INCTR will use it to enhance communication with associate members and collaborating centers, to improve management of research projects, and to add a multimedia dimension to a variety of educational programs. ■

INCTR'S NEW PORTAL

In the course of the winter, CTIS, an INCTR associate member and partner organization, has worked hard to develop a web-based portal for use by INCTR's network. This powerful system consists, in essence, of a dynamic, interactive cluster of linked web sites which can be managed by INCTR staff. The completed system will provide electronic locations whereby INCTR branches, offices, programs, strategy groups and committees will be able to store and exchange information, including images and documents, and to create shared "work spaces." In addition to enhancing communication and permitting the more effective management of a broad range of INCTR activities, the portal, which will include powerful databases, will eventually be used as a research and educational tool which will greatly improve access of INCTR members to a broad range of information relevant to cancer control. INCTR is grateful to CTIS, and particularly to its Founder and CEO, Raj Shah, for this generous and valuable contribution. ■

Members of INCTR's Governing Council and invited guests posed for this picture after the February 2004 meeting.

MEETING OF INCTR'S NEW INFORMATION TECHNOLOGY (IT) COMMITTEE

INCTR's considerably enhanced access to sophisticated information technology has led to the need for a committee to ensure that IT is used to maximal advantage throughout the network. A first meeting of this newly formed committee, chaired by Raj Shah, took place on 8th March at the Brussels offices. ■

MEETING OF THE CORPORATE LIAISON COMMITTEE

The Corporate Liaison Committee, chaired by Dr Nassir Habboubi, met on 10th March. The main topic of discussion was corporate sponsorship of INCTR activities, and in particular, seeking donations of drugs from pharmaceutical companies for ongoing clinical trials developed by INCTR strategy groups. ■

NETWORK

OBAFEMI AWOLOWO UNIVERSITY TEACHING HOSPITALS COMPLEX

With a population of approximately 120 million people, Nigeria is the most populous country in Africa.

The entrance to the OAUTHC, Ile-Ife, Nigeria.

Sadly, the country's public health infrastructure has been eroded as a result of national economic difficulties, drastic cuts in foreign aid, and continuing political uncertainties. Consequently, most public health institutions lack basic facilities. Nigerians suffer from an array of preventable and curable diseases and must face, in addition, the problems caused by the growing prevalence of HIV/AIDS. In this environment, it is no surprise that Nigeria has no facilities devoted exclusively to cancer treatment. Yet despite critical shortages Nigeria has sustained key primary health care initiatives. In this context, the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife (OAUTHC), is one of the few bright spots in Nigerian health care.

The OAUTHC is one of the first-generation teaching hospitals established by the Nigerian government to deliver quality health care to its people, and until very recently the only teaching hospital in Osun State, drawing patients from the whole of Ondo, Ekiti and parts of Oyo and Kwara states, a predominantly Yoruba ethnic population of about 20 million.

Launched in 1977 at the then fledgling University of Ile-Ife (now Obafemi Awolowo University), the hospital complex has grown to encompass two major hospital facilities, one dental hospital and three primary care centers. The major centers include the tertiary referral center in Ile-Ife and the Wesley Guild Hospital at Ilesa, located in a rural setting 30 kilometers from Ile-Ife. The dental center is located within the main campus of the Obafemi Awolowo University, ten minutes from the main hospital.

CANCER CARE

Between January 2001 and December 2003, 860 cancer cases (all ages and sexes) were seen at OAUTHC. The most prevalent cancers seen there are breast, prostate and cervical cancers, followed by non-Hodgkin's, non-Burkitt's lymphoma, and Burkitt's lymphoma, respectively. Other cancers include colo-rectal cancer, stomach, sarcomas, liver and skin cancers other than melanomas. In recent months, the hospital has been coordinating the free Glivec treatment for chronic myelocytic leukemia and gastrointestinal stromal tumors, under the Glivec International Patient Assistance Program sponsored by the Max Foundation.

The hospital is involved in collaborative research programs with the INCTR and with the International Agency for Cancer Research in Lyon, France, on the treatment and epidemiology of malignant lymphomas, and is also collaborating with the Meharry Medical College in Nashville, Tennessee, (USA), on the genetic epidemiology of breast cancer in African women.

Dr. Muheez Durosinmi is the sole hemato-oncologist on staff at OAUTHC. Other cancer professionals on staff include pathologists, radiologists, gynecologists, general surgeons, and pediatricians.

"There is some cancer awareness in Nigeria, although its promotion is not as aggressive as one would want it to be," says Dr. Durosinmi.

Dr. Durosinmi examines a patient in the two-bed Day Ward at OAUTHC, Ile-Ife.

"The Nigerian Cancer Society and some other related organizations are assisting with cancer control and prevention programs," he says, most of which are concentrated in urban centers.

"I wish the government would show more interest in allocating resources

to cancer control," Durosinmi says. "A country as large as Nigeria should have dedicated cancer care centers by now—at least one in each of the six geo-political zones of the country. He notes that cervical cancer could be controlled through routine screening of women, liver cancer through HBV vaccination and compulsory screening of blood for HVB and HCV markers, and lung and several other cancers through avoidance of tobacco use. "It is sad to note that the Nigerian government has recently permitted one of the largest tobacco corporations in the world, British-American Tobacco, to open a new multi-billion tobacco factory in West Africa at Ibadan, Nigeria. This is in spite of the WHO Technical Report 695 of 1983 that states that "25-35% of males between the ages of 18-20 yrs are already addicted to cigarette smoking in the world's most populous nations of India and China", he says. "With over 90% of lung cancers being related to cigarette smoking, we fear there will be a marked rise in the incidence of lung and other tobacco-related cancers in our country in the next two decades."

BURKITT'S LYMPHOMA

OAUTHC, Ile-Ife is collaborating with INCTR on the molecular characterization and treatment of Burkitt's lymphoma. The treatment arm will re-validate the role of the widely used cyclophosphamide, oncovin and methotrexate (COM) combination therapy as the first-line treatment in the management of the tumor. In all cases, individual patients will be followed up for at least two years; a data manager/nursing officer will be employed to facilitate patient monitoring (including home visits) for the duration of treatment. Second-line therapy, in the form of etoposide, ifosfamide (+ mesna) and cytarabine will be offered to patients who fail first-line therapy.

RETINOBLASTOMA STUDY

OAUTHC is also participating in INCTR's retintoblastoma study. The ophthalmology unit of the hospital is gathering data from the parents of children with retinoblastoma at the time of diagnosis of the tumor in order to identify the the problems they face prior to treatment.

BREAST CANCER STUDY

The breast cancer study is aimed at unraveling the genetic epidemiology of breast cancer in African women using a case control study technique. Tissue specimens from cases and appropriate controls are to be studied. The study participants are entered by breast cancer specialists, oncologists and epidemiologists from Ile-Ife, Nigeria and collaborators from the USA.

RESOURCES AT OAUTHC

Total Beds	565
Beds devoted to cancer care	0
Staff Physicians	11
Nurses	569
Dedicated Oncology Nurses	0
Pathologists	14
Oncologists	3
Oncologists in Training	2
General and Specialist Surgeons	21
CT Scanners	1
MRI Scanner	0
Cobalt Radiotherapy units	0
Linear Accelerator units	0

PATIENTS SEEN AT OAUTHC

Total patients in 2003	204.669
Total Outpatients in 2003	156.262
Adult Cancer Patients in 2003	305
Pediatric Cancer Patients in 2003	43
Burkitt's lymphoma	22

OTHER COLLABORATIVE PROJECTS

INCTR is sponsoring a young doctor from OAUTHC to spend a year learning gynecologic oncology at the TATA Memorial Hospital in Mumbai,India. The INCTR is also assisting the hospital with the training of nurses and a social worker who will work with the gynecologist upon his return to Nigeria. This additional training and staffing will complement the limited cervical screening program currently available in the hospital.

"We believe our partnership with INCTR will enhance our understanding of the prevention and management of common cancers in our part of the world, through the introduction of affordable cancer control methods and use of cheaper, cost effective therapeutic agents," says Dr. Durosinmi. "I also believe it will facilitate manpower development and capacity-building in the areas of cancer control and management.

"I am very optimistic about the future for health care in Nigeria," he says. "The federal government is improving the diagnostic capabilities of many tertiary health facilities across the country and is about to introduce a health insurance scheme that will increase funding for health care. With participatory democratic government, my hope for a better tomorrow with respect to our health care system is very high." ■

Muheez Durosinmi provided the information for this article, which was prepared by M Landskroener for INCTR

PROFILES IN CANCER MEDICINE

SHERIF OMAR TACKLES CANCER AT GLOBAL, NATIONAL AND LOCAL LEVELS

Dr. Sherif Omar, former Dean of the National Cancer Institute (NCI), Cairo University, and Secretary General of the Arab Medical Association Against Cancer, is first and foremost a gifted surgeon.His success in building a small cancer center that integrates state-of-the-art medicine with social and educational programs that address the needs of patients is the capstone of a remarkable career with a decidedly international flavor. He is President of the Board of Trustees of an Egyptian foundation supporting cancer research, and is a member of the Governing Council of INCTR Egypt.

Prof. Omar graduated in 1963 from Cairo University and was trained in surgical oncology in Paris. He studied at the Memorial Sloan-Kettering Cancer Center in the United States and spent six months in Japan as a fellow in surgery and endoscopy. He received the World Health Organization's Gold Medal in 1988 for his work on tobacco control. He also received the national first class decoration for science and art. A member of the Egyptian Parliament for 10 years, he was elected to lead the Health and Welfare Committee in 1995, charged with task of cancer prevention. In his country, he says, the primary means of cancer prevention is smoking cessation. "We studied the economic consequences of smoking," he says. "A 1989 report concluded that smoking costs $400 million a year in health care costs and premature death." In response, the government implemented laws constraining sales

Dr. Sherif Omar

of tobacco products, yet disturbingly, the prevalence of smoking is increasing, particularly among women and youth.

In Egypt, the NCI and regional Cancer Centers conduct most cancer control activities. Only one cancer center is not government-sponsored—Fakous Cancer Center. Established 15 years ago, Fakous provides a new model for cancer treatment that integrates tertiary services with primary health care facilities. "We are taking treatment as well as prevention to primitive areas of the country," Prof. Omar says. Fakous is a micro-center with 50 inpatient beds, two efficiently equipped operating rooms and radiotherapy facilities, he explains. The center has facilities for the diagnosis and treatment of both adult and pediatric patients. Most of the physicians employed are associated with NCI, Cairo, or have trained there. These physicians provide follow-up care for patients in their homes, and take educational and screening programs to the villages. "We have a very important ongoing project for the education of the population about protecting themselves from infection with hepatitis C virus, which is responsible for much of the liver cancer in Egypt," Prof. Omar says. "We are also launching a pilot study for screening and early detection of breast cancer in eight villages."

Beyond offering excellent health care, Sharif Omar envisioned a cost-effective cancer center that would meet the social needs of cancer patients. "It provides comprehensive intervention, including prevention, treatment and social support for the local community. Our facilities are inexpensive because of our NGO status. We are using our know-how to devise the best, but also the cheapest and easiest methods to accomplish our goals. We have the support of UICC and are recognized by the European Organization for Research and Treatment of Cancer. We regularly invite professors from other countries to give lectures and to see patients," Prof. Omar says.

The Fakous Cancer Center is also concerned with training medical personnel and providing jobs for local villagers. A program supported by the Embassy of the Netherlands brings senior nurses from Europe to Fakous, and the Center also provides resources for junior doctors to go abroad for training, The concepts of outreach extend to the community of Fakous as well as nearby regions. "One of our main goals is to provide jobs for local people," he notes. "We aim to give them job skills and an opportunity to improve their lives." ■

Marcia Landskroener for INCTR