N E T W O R K

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INCTR

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THE PRESIDENT'S MESSAGE

THE MEASURE OF CANCER

Part 2. Analysis

by Ian Magrath

Such harmony is in immortal souls; but whilst this bloody vesture of decay doth grossly close it in, we cannot hear it. Lorenzo, Merchant of Venice Act V, Scene I, William Shakespeare.

Plato, in *The Republic*, advocated a lengthy process of education for the prospective leaders of his ideal city-state, culminating in the study of "pure philosophy" or dialectic - in essence an ability to reason on the highest plane. Only penetrating logic unbiased by appearances would, he believed, lead to knowledge of the ultimate reality that lies beneath the ever changing world of the senses, and only individuals capable of this level of objectivity and integrity were fit to govern. In preparation for the final phase of the intellectual development of prospective guardians of society Plato recommended a thorough grounding in all branches of mathematics, which then included arithmetic, plain and solid geometry, astronomy and musical harmony.

Fibonacci spirals (see Figure 2) are found everywhere in nature since they provide optimal spacing and packaging. In daisies, marigolds, chrysanthemums and sunflowers, the seed arrangements in the flowers form such spirals, in which the numbers of seeds in clockwise and anticlockwise spirals are adjacent in the Fibonacci series.

This educational prescription was remarkably prescient, for our present concepts of energy and matter and of the laws that describe their interactions derive largely from the work of theoretical physicists using the tools of mathematical analysis. Such illustrious minds, unfortunately, have rarely been applied to political leadership.

Plato taught that there are several levels of comprehension, ranging from those based purely on sensory impressions to eventual understanding, through dialectic, of the first principles, or *Eidos* (Ideas, or Forms), which he took to be the unchanging constants underlying the varying manifestations of the objects we perceive (*aisthetón*). He illustrated these mental states by the use of his now well-known similes - the Sun, the Divided Line and the Cave (Figure 1). Scientific understanding is perhaps the modern equivalent of Plato's *Eidos*, but present ideas of the "underlying truths" are scarcely less tangible than the Forms, being enveloped in words which conjure up only vague images (such as *quark*, or *anti-matter*), or expressed as mathematical equations, sometimes complex and sometimes disarmingly simple (e.g., $E = mc^2$). Effectively, the words and equations *are* the understanding. But in contrast to the imprecise nature of Plato's Forms, the equations of modern physics can be tested to an exquisite degree of particularity, thanks to the emergence of scientific methodology some 2000 years after Plato's death. Henceforth, the dialectic of natural philosophers, renamed "scientists" by William Whewell in the 19th century, would derive from far more substantial fare than that available in ancient Greece. Thought alone, however erudite, can never approach reality unless founded upon fact. Such facts we refer to as *data*. Data (singular, datum, from the Latin for something "given"), are derived from the observation of natural events (such as the occurrence of specific cancers at different incidence rates in different environments), or from experiments, whereby the results of carefully designed and executed interventions (such as the uniform administration of a particular therapy) are equally carefully measured. Plato recognized the importance of mathematics - that is, the rules of numerical calculation, whether arithmetical or geometrical - as the foundation of logic. But he lived in an era when numbers dealt with specific circumstances and were largely fixed to the tangible objects they enumerated, when the concept of zero did not exist, and when even movement (and hence change of any kind) was seen as mathematically paradoxical, at least by one school of thought (that of Parmedides and Zeno). Logic, inevitably, remained as tightly tethered to the world of the senses as were the numbers from which it derived, prohibiting anything more than the most superficial penetration beyond outward appearances. The very idea of "laws" of nature, in essence fundamental generalizations that apply to a broad, if not infinite, range of circumstances, was inconceivable. Modern science, in which elementary particles or unimaginably small effects on a gravitational field are sought entirely on the basis of predictions derived from mathematical equations, stands in dramatic contrast. As such, its emergence became possible only after a profound revolution in the very concept of number, and hence in calculation - a slow, stuttering revolution that occurred in the course of many centuries, eventually giving birth to a third major branch of mathematics - *algebra*.

This seminal step exceeded the capacity of a single human mind, however great. It came about, therefore, as series of smaller steps, each taken without a clear sense of where it might lead. The embryo of the central idea - that of abstract numbers - had lurked in the minds of the ancient philosophers for centuries. It underwent further development by mathematicians in the great library of Alexandria who continued in the tradition of the ancient Greeks. But the critical element was the development of much more flexible number systems in India in the course of the 4th and 5th centuries CE. The brilliant Muslim cultures, geographically interposed between the two main branches of the Indo-European races and nourished by the wisdom of their Near Eastern forebears, including Babylonians,

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Egyptians and Persians, as well as mathematicians from distant China, were ideally placed, physically and mentally, to bring these intellectual worlds together. After a lengthy gestation period in the courts of the Caliphs, algebra was born in its modern form in renaissance Europe and grew to maturity as successive mathematicians developed new analytic methods, bringing together the once separate domains of arithmetic and geometry and leading to new mathematical approaches to the analysis of data. The logical foundation of scientific understanding is truly a child of all of mankind.

ABACISTS AND ALGORISTS

The remarkable tool of mathematical analysis is named after a book imposingly entitled *Hisab Al Jabr wa'l Muqabala* (Transposition and Reduction) written by the Persian/Arab astronomer and mathematician, Muhammad Al-Khwarizmi, born around 783 CE. Al-Khwarizmi lived at the court of Caliph Mu'Am and worked in the famed "House of Wisdom"- the equivalent, in medieval Baghdad, of a scientific academy - translating the works of the ancient Greeks, Romans and Byzantines. Al-Khwarizmi's book described two important steps in the solution of equations, and although his descriptions were in words rather than symbols, his book made a sufficient impression for an abbreviation of its title to become the name of the new branch of mathematics. Al-Khwarizmi also studied Indian texts and it is from the title of the extant Latin version of his book *Algoritmi de Numero Indorum* (Al-Khwarizmi on the Hindu Art of Reckoning) that the use of the word *algorithm* to describe a series of steps in a mathematical or logical operation is derived. Al-Khwarizmi and his followers, who became known as *algorists*, eschewed the abacus (used widely in those days as a calculating machine by mathematicians known as *abacists*) in favor of calculations performed with Indian numerals, including the zero, written in dust or sand. Today, the sand has transformed into silicon chips, for algoriths are the building blocks of computer programs.

Our modern numerical notational system, consisting of nine symbols and zero, derives from the numerals invented by Indian astronomers and mathematicians at the time of the 4th century CE Gupta dynasty. The zero, as well as indicating *no-thing* at all, was used for the first time as a place holder in a place-value system. Such systems use multiplication of a base number to generate different sized sets of numbers which are then enumerated, the value of each set in any given number being represented by a different position. They differ markedly from additive systems in which each number simply follows the next and has its own name and symbol. This works well for small series of numbers, but would require prodigious feats of memory for large series. In contrast, place-value systems require only one less numeral than the base. Such systems are intrinsically more abstract than additive systems, since numbers tend to lose their individual characteristics and an infinite series of numbers can be generated by a simple rule. Moreover, zero itself is an abstract concept. Most place-value systems are decimal, that is, based on ten (the original "digital" system!) and its multiples. Many other bases have been used in the past, and their remnants persist today - for example, the sixty-based Babylonian system has given us our circle of 360° and triangle of 180°. In the decimal sys-

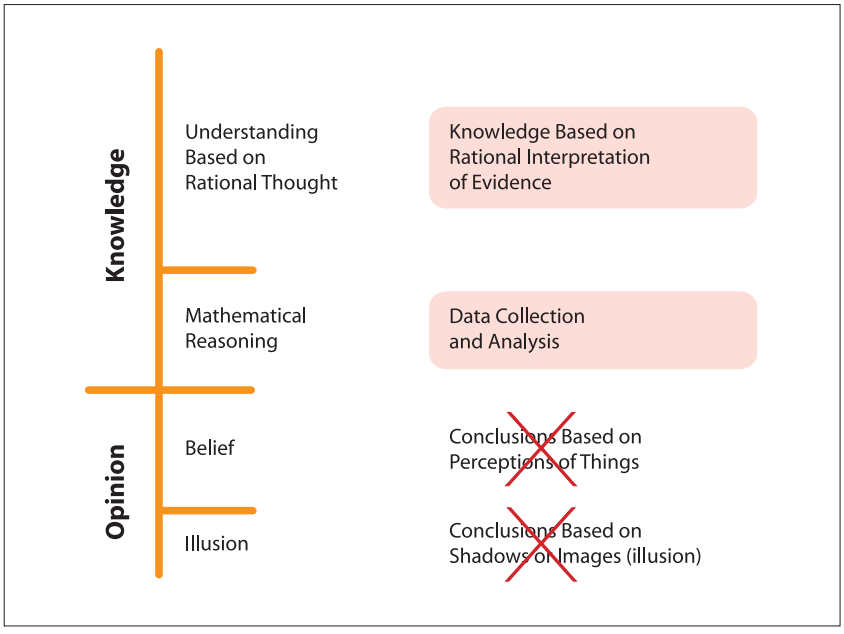

Figure 1. Plato's Divided Line simile showing the various mental states, from lowest to highest. Modern science, as shown on the right, has no room for unsupported opinion.

tem, the nine numbers and zero are used repeatedly to indicate, in any given number, the value (number) of the sets of hundreds, tens, units, etc., or the absence of a particular set. In the late Middle Ages, this system of counting was transmitted to Europeans by Arab scholars, along with the works of Greek mathematicians such as Archimedes, Euclid and Diophantus and their own important contributions. For this reason our modern numerals are still referred to as *Arabic*.

One of the most important, and earliest links between the Hindu-Arabic number system and European mathematics was the Italian mathematician Fibonacci, otherwise known as Leonardo of Pisa (1170-1250). He began and spent much of his life in Pisa, Italy, but was brought up and taught mathematics in North Africa, in a port town called Bugia (now Bejaia) in modern Algeria, where his father represented Pisan merchants to the customs authorities. In his book, *Liber Abaci* (1202), which had little or nothing to do with the abacus (the title was, in its day, religiously correct, for the church frowned upon any form of islamic influence), he described the nine Indian numerals and zero, which he had learned about in Bugia. He also provided a large collection of problems aimed at merchants and described the famous *Fibonacci series* thus: *A certain man put a pair of rabbits in a place surrounded on all sides by a wall. How many pairs of rabbits can be produced from that pair in a year if it is supposed that every month each pair begets a new pair which from the second month on becomes productive?* This series, in which each number is the sum of the two preceding numbers, occurs

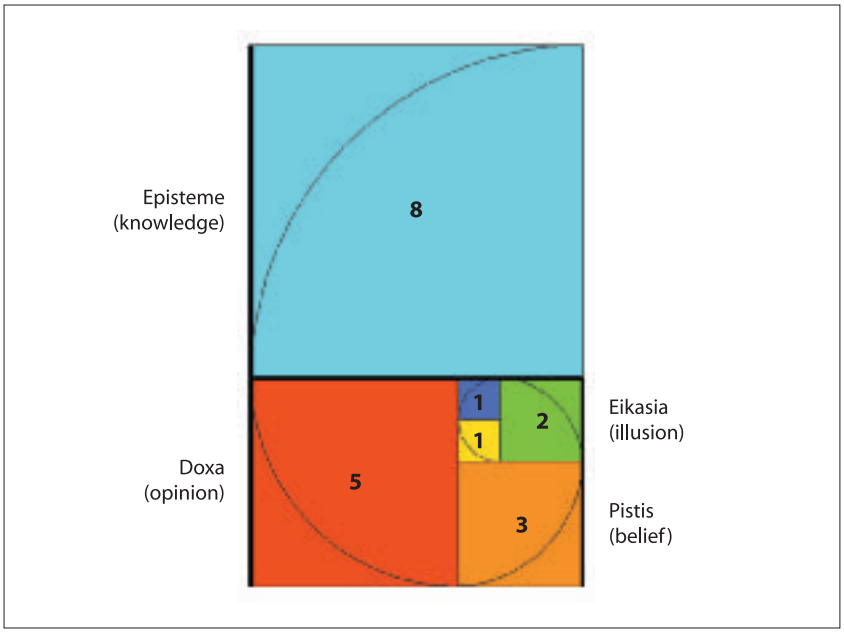

Figure 2. Fibonacci numbers, showing how the use of this sequence to create a series of squares leads to the Fibonacci spiral, which is seen in the Nautilus shell (a cephalopod related to octopuses and squids that has existed for 500 million years). See also the photograph on the front page. The Divided Line simile is superimposed.

frequently in nature, being the mathematical basis of a type of spiral curve which occurs in the Nautilus shell (Figure 2), as well as in various seed, leaf and petal arrangements. The numbers in a Fibonacci series also lead to the Golden Proportion or Ratio (1.618034), said to have been derived by the Greek sculptor, Phidias, (hence its symbol, the Greek letter, phi) from the proportion of limb length to height of women "pleasing to his eye." The golden ratio is converged upon as the Fibonacci series tends to infinity, being the ratio between one number and the preceding number. Because it allows a limit to be reached in the smallest number of steps, a modified Fibonacci series has often been used as the basis for dosage increments in "phase I" clinical studies in which the maximally tolerated dose of a new drug is sought.

ARS ANALYTICA

Muslim and early European mathematicians lacked a means of symbolically representing generalized numbers, and it was Francisco Vieta (François Viète, 1540-1603), a French jurist who studied cosmology and astronomy in his spare time, who laid out the foundations of symbolic algebra in his work In *Artem Analyticem Isogoge* (Introduction to the Analytic Art). Vieta drew upon the writings of two Alexandrian mathematicians, Diophantus, whose *Arithmetica* dates from the 3rd century CE, and Pappus, whose somewhat later *Synagogue* (Mathematical Collection) dealt mainly with problems in geometry. He recognized that algebra was a general theory of proportions, expressed in equations, and that it could be applied to both geometry and arithmetic. He was well aware that "*things that are new*

are wont to be set forward rudely and formlessly, and then must be polished and perfected in succeeding centuries," but nevertheless, appreciated that algebra, the "Ars Magna," had a fundamental place in the system of knowledge, enabling the world to be perceived in terms of its underlying harmonious structure or symmetry, and as a *"lawfully" ordered course of events*, rather than simply a collection of countable entities.

Mathematical analysis gradually came to be perceived as a process whereby solutions to specific questions can be obtained by inserting numbers (data points), into previously established equations that express general relationships between one thing and another. Improvements in symbolic representation and methods of calculation created ever more powerful means of expressing such relationships, and hence of predicting the outcome of a broad variety of interactions. In 1582, Simon Stevin of Flanders greatly simplified calculations by using decimal fractions in place of ordinary fractions. Pierre de Fermat, another French magistrate, and his contemporary, René Descartes, invented analytic algebra, whereby the sets of points that define lines, curves and surfaces could be represented by algebraic equations. Descartes' treatise on this topic, *Géométrie,* appeared in 1637, but Fermat, who claimed to be content simply to discover the truth, failed to publish his work, thereby involuntarily ceding primacy to Descartes. Descartes used the later letters of the alphabet, *x, y* and *z,* as symbols for variables and the early letters, *a, b* and *c*, for constants in algebraic equations. This convention superceded Vieta's earlier system, and has persisted to the present day. Descartes also introduced the superscript notation to indicate positive powers, such as 10^3, and a system of coordinates to represent points in space - a critical element in the graphical depiction of change. In the latter part of the 17th century Newton and Leibnitz invented differential and integral calculus - methods for analyzing continuous change (*fluxion* was Newton's term), including shape, quantity, position, movement, speed and time. Ironically, Zeno's paradoxes, which had appeared to show that motion, if considered as the successive halving of distance *ad infinitum*, is mathematically impossible, were finally resolved by a method based on the mathematical manipulation of infinitesimally small changes. As Plato had recognized, the natural world is about change, and the powerful mathematical techniques developed to express interrelationships quantitatively led to major advances in scientific understanding. But knowledge cannot be derived from the mere manipulation of numbers, or algebraic symbols. It relies heavily upon an additional ingredient - imagination. Science is driven by hypothesis, i.e., a proposed explanation for a set of observations (data). The ability to use reason to create hypotheses goes beyond mathematics, and corresponds, perhaps, to Plato's dialectic. It is the testing of such hypotheses by seeking additional data (*re-search*), experimentally where necessary, that distinguishes scientific knowledge from beliefs that are not based on the rational interpretation of factual information.

Scientific analysis is the necessary foundation of all attempts to improve socioeconomic conditions and to control disease, including cancer.

DATA VERSUS DOXA

Plato, in his paradigm of the Line, separated knowledge (*episteme*) from opinion or supposition (*doxa*). *Doxa*, according to Plato, derives purely from sensory impressions, i.e., from the appearance of things. Direct experience results in belief (*pistis*), but shadows or reflections can only create impressions or illusions (*eikasaia*). Whilst Greek words used some 2,500 years ago cannot always be precisely translated, Plato's message is not only clear, but as valid today as it was then - knowledge cannot be based on unsubstantiated belief or conjecture. And without knowledge, human actions or interventions in the physical world will be both irrational and entirely ineffective. Much of medical treatment in the past (with a residuum that persists today) has been based on *doxa* unsupported by data (e.g., purging, bleeding, cupping) and has often resulted in more harm than good. Successful prevention or treatment of disease, including cancer, does not necessarily require a detailed understanding of the causes of the disease or of therapeutic mechanisms, although such knowledge permits more precise interventions with fewer side effects. We stand, today, at the beginning of an era of rationally designed cancer therapy, but much of the progress in cancer control to date has derived from empirical observations, which also provide the raw material for

the development and testing of hypotheses. Meaningful analyses of this kind must begin with high quality data, much of which is in the form of simple counts. The countable entities (e.g., the number of cancers in a population, or responses to a given drug) must, as always, be carefully defined and the data meticulously collected, documented and stored.

The generation of knowledge through the analysis of accurate data is a very different process from the proof of a mathematical theorem. The latter involves the application of a series of formal (mathematical) rules to already proven theorems which themselves depend, ultimately, upon a number of foundational assumptions taken to be self-evidently true (such as Euclid's five axioms, updated by Hilbert in 1899). Once established, a mathematical proof is absolute and stands for all time. Many theorems were proven in ancient times. Indeed, Euclid's *Elements* remained the primary source of the proofs of geometrical theorems and of mathematical rules in geometry until the 19th century. In contrast, the validity of a hypothesis is examined by making a judgement as to whether the relevant data support or refute it. While occasionally, the result of an experiment, or trial, designed to test a hypothesis is sufficiently obvious as to require no formal analysis (e.g., the cure of a high fraction of patients in a formerly fatal disease) this is not often the case. Since different informal observers may draw different conclusions from the same data set, the scientific method includes the use of objective methods to measure the degree of certainty, i.e., the *probability*, that a hypothesis is correct.

ARS CONJECTANDI

Probability theory has become a critically important branch of mathematics and is as important to the design of clinical experiments involving human subjects (clinical trials) as it is to the analysis of the results obtained. Its foundations were laid by Blaise Pascal and Pierre de Fermat in a series of letters they exchanged in the course of the summer of 1654 dealing with the mathematics of games of chance, such as the likelihood of throwing a double six with two dice. Just as a hypothesis cannot be absolutely proven, there is never absolute certainty that a double six will be thrown. However, with a sufficiently large number of throws (trials) the likelihood of *not* throwing a double six becomes extremely small, and as Fermat and Pascal showed, it can be calculated. In December of the same year that Fermat and Pascal corresponded in France, another gifted mathematician was born in Switzerland. Jakob Bernoulli was responsible, among other things, for major advances in probability theory, building upon the work of his French predecessors. His name is associated with the "Bernoulli trial," an experiment with a dichotomous outcome, that is, the result is one of two possibilities, in this case, independent of each other,

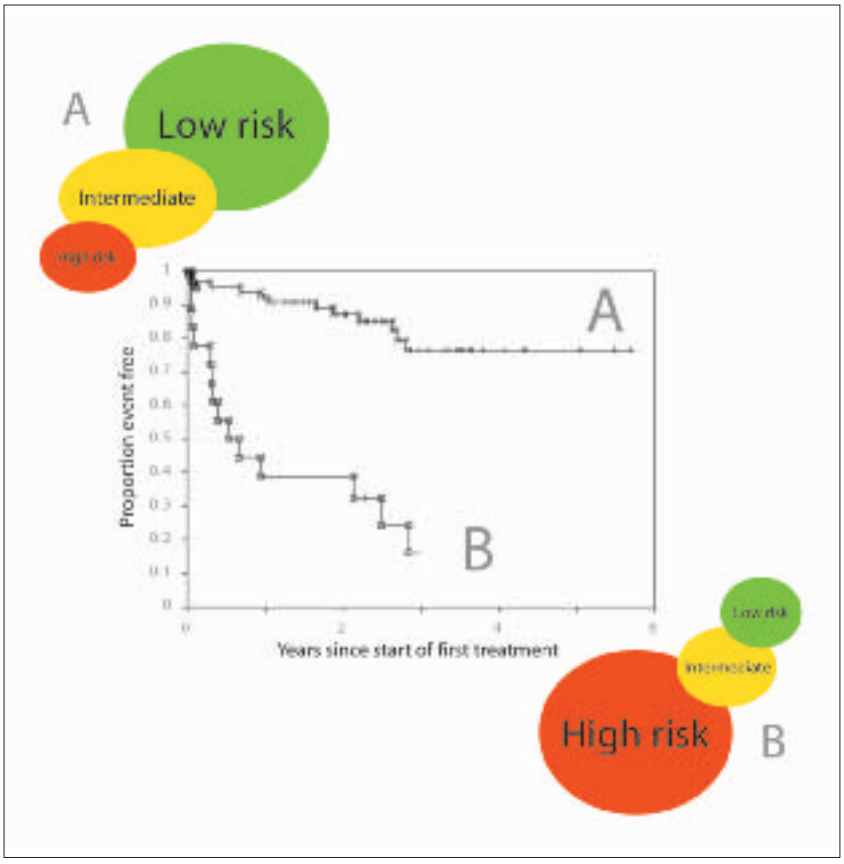

Figure 3. Survival curves demonstrating how different patient populations (A and B), in which there are different proportions of high, low and intermediate risk patients, may have quite different outcomes with the same therapy.

i.e., the outcome of one trial (usually referred to as a success or failure) has no impact on the outcome of another (as in tossing a coin). For any given number of Bernoulli trials, the probability of there being a specific number of successes and failures can be calculated precisely, as Jakob Bernoulli showed in his book, *Ars Conjectandi* (The Art of Conjecturing). In clinical trials designed to test the value of a particular treatment, the outcome for each patient can be dichotomous (e.g., survival or death), but the complexity of this situation is far beyond that of tossing a coin since there are many factors (or variables) which determine response, including the treatment itself and various patient characteristics, some of which are dependent, while others may be independent. Mathematical approaches (multivariate analyses) to determining the relative weights of such variables have been developed and are used to identify independent risk factors that predict prognosis in a particular disease with a particular treatment. Such information permits treatment decisions to be rationally made, i.e., *evidence-based*. Care must be taken to ensure that evidence is not inappropriately misapplied, which can happen when all the relevant factors are not taken into consideration. Cancer treatment, for example, is largely based on data from affluent countries, yet similar approaches are often applied, untested, to very different patient populations in developing countries (Figure 3). To *assume* their universal validity is to use doxa instead of episteme in guiding treatment policy. Probability theory is also used to calculate the number of patients that are required in a clinical trial designed to test the hypothesis that one intervention is superior to another. The calculation of the *power* of a study to demonstrate a difference, which reflects the degree of certainty that the difference between the interventions, if present, would be detected, can be used for this purpose - by specifying the anticipated difference and the degree of certainty required.

Cancer treatment is largely based on data from affluent countries, yet similar approaches are often applied, untested, to very different patient populations in developing countries.

Another major contribution made by Bernoulli is his Law of Large Numbers, or as he called it, his Golden Theorem. This law states that the more trials that take place, the closer the proportion of successes will be to the proportion that applies to an individual trial (namely, for the tossing of a coin, 0.5). Although it may seem to be self-evident, Bernoulli was able to provide a mathematical proof of this theorem, which is a cornerstone of probability theory. It permits the determination of the probability that any given number of successes in a sufficiently large series is more, or no more, than could be expected by chance alone - a determination that is critical to epidemiological and therapeutic research. It allows rational judgements to be made, for example, as to whether exposure to a particular substance, or the presence of an inherited genetic abnormality, increases the risk of developing cancer. Today, the quantification of risk has evolved from the simpler calculation provided by the Russian mathematician, Pafnuty Chebyshev, in which the observed value (e.g., the number of cancers in an exposed population) is compared to the expected value - i.e., that observed in a control population. Once again, the validity of the conclusion is dependent upon the number of observations made and the population size. These statistics are taken into consideration in the calculation of the *relative risk*, i.e., the ratio of the risk of an event happening in one group to its risk in another.

Plato was probably correct in his belief that the ideal civil society he proposed would never exist. But his idea that the guardians of society should be trained in mathematics and the ability to reason has proved, in another sense, to be correct; scientific analysis is today the foundation of all attempts to improve socioeconomic conditions and to control disease, including cancer. The *Ars Magna*, well polished in the course of four centuries, provided a critically important tool which has been successful in revealing much of the harmony of a lawfully ordered world. The challenge, in the context of cancer control, is to increase the rate at which knowledge is acquired, particularly in the developing countries, while simultaneously translating existing knowledge into broad, effective action. For, ensuring that all peoples benefit from their collective invention would surely fall within Plato's definition of justice, which he offers in the pages of *The Republic*. ■

PERSPECTIVES IN PALLIATIVE CARE IN TANZANIA

Tanzania, in East Africa, is one of the least developed countries in the world. In 2002, it had a population of 36 million people and an annual population growth rate of 2.4% per annum, although this is expected to fall. In the same year, the life expectancy at birth was 43.5 years, and the Gross Domestic Product per capita for Tanzania, US$580 (purchasing power parity, PPP) - compared to an average of US$4,054 for all developing countries, US$2,149 for low income countries and US$28,741 for high income countries (data from United Nations Development Report, 2004).

The most recently measured doctor-patient ratio in Tanzania was 1 to 25,000 and health expenditure (PPP) US$26 per capita. Each year about 0.5% of the total population of Tanzania die from HIV/AIDS and cancer and few of these patients receive any palliative care. The World Health Organization defines palliative care as *an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness through the prevention and relief of suffering by means of early identification and careful assessment and treatment of pain and other problems, physical, psychosocial and spiritual*. Unfortunately, this is simply not available to the vast majority of patients in Tanzania, and most endure a great deal of pain and suffering in the terminal phases (and often also before they become terminal) of their disease. However, the HIV/AIDS epidemic has had a major impact on Tanzania's policy makers who have now accepted that palliative care is greatly needed in order to improve the quality of life and minimize suffering among patients with incurable conditions – and to help their families cope in these difficult times. Accordingly, a number of palliative care programs have been initiated, both by the government and also by non–governmental (NGO) organizations, in an attempt to provide care and support to people living with HIV infection and other terminal illnesses.

PALLIATIVE CARE INITIATIVES IN TANZANIA

The government, through the Tanzania Commission on AIDS (TACAIDS) and the Ministry of Health, developed a mid-term strategic plan for 2003-2006, which addresses measures relating to care and support for terminally ill patients. The strategy includes both clinic and home-based palliative care initiatives and although stimulated by the AIDS epidemic, also covers cancer, given that many HIV-infected individuals present with, or develop HIV-related cancers, such as Kaposi's sarcoma and lymphomas.

PALLIATIVE CARE CENTERS

So far palliative care has been introduced in the following centers in the country:

Ocean Road Cancer Institute (ORCI) - a government institution situated in Dar es Salaam which provides care for cancer patients, some of them with HIV-related cancers. ORCI has a hospital-based palliative care team whose main activity is to identify and manage the palliative care needs of cancer patients. Over 80% of patients seen in this institute receive cancer treatment (i.e., radiotherapy or chemotherapy) as palliative treatment, since there is no possibility of curing them of their disease. At the ORCI, pain management is based on the WHO pain control ladder, and liquid oral morphine is being used as the step 3 drug.

Muheza Hospice Care - an NGO working within a designated District Hospital in Muheza, in the Tanga Region of northeastern Tanzania. The hospice provides hospital-based palliative care services, a hospital support team, a day care center, home care and education and training. Care is provided for both HIV/AIDS (70%) and cancer patients (30%).

Pastoral Activities and Services for people with AIDS Dar es Salaam Archdiocese (PASADA) - the Catholic Church provides services for patients with HIV/AIDS in the Dar es Salaam region.

SELIAN Lutheran Hospital Hospice - an NGO, American-supported hospital-based palliative care program situated in the Arusha Region (in the northern part of Tanzania) that deals mainly with HIV/AIDS patients.

Winmware Hospice - in Mbeya Region (in the southwestern part of Tanzania), Winmware Hospice is developing a home-care service for patients with AIDS.

AVAILABILITY AND ACCESSIBILITY OF PALLIATIVE CARE DRUGS

The essential drugs required for effective palliative care, i.e., those which are required for pain and symptom control, including gastrointestinal, respiratory, urinary or neurological symptoms, are available through a Central Medical Stores Department. These include drugs for opportunistic infections such as candidiasis and tuberculosis. ORCI was permitted to procure powdered morphine from the Medical Stores Department in November 2001. The powder is processed into liquid oral morphine at the ORCI Pharmacy.

All the other centers receive their required oral morphine supplies from ORCI. Bearing in mind that pain is the most common symptom among patients with advanced cancers or opportunistic infections, this arrangement will have to be revised because it may decrease, rather that increase, access to oral morphine. Another area which needs to be addressed is the fact that patients generally develop pain and other symptoms whilst in their home community setting, which makes it necessary to distribute oral morphine at the community level. This need, however, will only be met after training of community-level prescribers and modifying existing policy regarding the use of opioids in Tanzania.

TRAINING IN PALLIATIVE CARE

Currently, palliative care is not included in the training curriculum for the medical/nursing schools in Tanzania. The Hospice Africa Uganda has a distance learning diploma program in palliative care, and so far, three candidates from Tanzania have joined the program. This is not sufficient to meet the needs of Tanzania, however, and it is the intention of ORCI to put in place mechanisms for disseminating knowledge about palliative care and to advocate for the inclusion of palliative care training in the medical/nursing school curriculae. The preparation of palliative care training guidelines for health care providers is already in progress.

PALLIATIVE CARE POLICY

At the moment there is no national policy and no national guidelines for palliative care in Tanzania. Following a WHO-supported situation analysis and needs assessment study for palliative care services in Tanzania in 2002/2003, a proposal for the development of a policy for palliative care was developed and endorsed by the Ministry of Health. The proposal recommends that: 1. Palliative care programs should be incorporated into the existing health care system. 2. Health workers are adequately trained in palliative care. 3. Adequate support is provided for palliative care programs, particularly in the home. 4. National health policies should be revised to include palliative care. 5. Hospitals are able to offer appropriate specialist back-up and to support home care. 6. The availability of opioid, non-opioid and adjuvant drugs is assured.

Ward Units at Ocean Road Cancer Institute.

RESEARCH ON PALLIATIVE CARE IN TANZANIA

Very little research in the area of palliative care in Tanzania has been undertaken. In the year 2002, a multicountry situation analysis and needs assessment study coordinated by the World Health Organization was done. The results from this study, are summarized in the website: **www.who.int/cancer/media/en/614.pdf**. The interviewees expressed the need for comprehensive palliative care and the majority of patients (82%) mentioned home to be their preferred place for care. Some 82.5% of family caregivers expressed a lack of basic knowledge for caring for their sick ones.

THE WAY FORWARD IN PALLIATIVE CARE IN TANZANIA

A Country Palliative Care Team has been formed. It is the intention of the team to lobby for resources for implementing the proposal for countrywide, home-based, palliative care services. In the meantime, the team is striving to create links with the existing programs that are already providing home-based and clinic-based care for HIV/AIDS patients.

CONCLUSION

Palliative care in Tanzania is still in its infancy, despite the existing demand in the community. There is great hope that execution of the country proposal, whether partly or wholly, would dramatically change the existing picture. We look forward to receiving support both from within and outside Tanzania to help us meet this much needed service for our patients. We expect that in the very near future, collaboration with INCTR's Palliative Care Program will be initiated and that this will act as a catalyst to our existing palliative care efforts in Tanzania. ■

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A PATIENT WITH CANCER OF THE BILHARZIAL BLADDER

HISTORY OF THE PRESENT ILLNESS

A 57 year old agricultural worker presented to a hospital with fever and an altered level of consciousness. He had been having bone pain since January 2004, for which he had received non-steroidal anti-inflammatory analgesics without benefit. The condition was aggravated by the development of severe chest pain in May 2004. Investigations performed at the time, including an ECG, showed no abnormality. Cardiac enzymes were elevated; LDH, was 1170 U/L the normal being up to 423. Echocardiography was normal with the ejection fraction of 68%.

A chest X-ray on 9th June 2004 showed a pathological fracture of the 6th rib. A bone scan performed one week later revealed multiple osseous lesions, actively taking up isotope, which were randomly distributed throughout the skeleton. The lesions were considered to be consistent with metastatic deposits (Fig 1). Laboratory investigations on 19th June 2004 included a complete blood count that showed a moderate normocytic, normochromic anemia and moderate thrombocytopenia. Liver function tests revealed hypoalbuminemia. Kidney function tests were normal. An abdominal ultrasound showed liver cirrhosis and splenomegaly and a transrectal sonogram showed a slightly enlarged prostate gland with a heterogeneous pattern and no detectable focal lesions.

Tumor markers, including carcinoembryonic antigen, alpha-feto protein and PSA (prostate specific antigen), were slightly elevated. Because a primary tumor accounting for the bony metastases had not been identified,investigations for multiple myeloma were performed. There was no Bence-Jones proteinuria and β2 micro-globulin level was only slightly elevated. Serum protein electrophoresis confirmed the hypoalbuminemia and also showed hypergammaglobulinemia and beta-gamma bridging. A bone marrow aspiration performed on 5th July 2004 revealed a hypercellular marrow with erythroid hyperplasia but no evidence of infiltration by neoplastic cells. Computerized tomography (CT) of the chest on 15 July 2004 showed a right rib fracture with abundant callus formation but no other abnormalities. CT of the abdomen and pelvis showed mild to moderate hepato-splenomegaly with liver cirrhosis, minimal ascites (Fig 2), left para-aortic and iliac lymph nodes of 8-11 mm in diameter and a soft tissue mass in the bladder measuring 6.5 x 3.2 x 4 cm, involving the right lateral wall and base of the urinary bladder with para-vesical extension (Fig 3). The patient refused cystoscopic examination and biopsy under general anesthesia because of a concern that his liver function would deteriorate as a consequence.

PAST HISTORY

The patient had a history of Hepatitis C Virus (HCV) infection. He was also diabetic and suffered from hypertension, for which he had been receiving medical treatment for 10 years.

ADMISSION TO NCI, CAIRO

The patient was admitted to the NCI, Cairo, on 8th August 2004 and was noted to be febrile, hypertensive (blood pressure 170/100) and tachycardic (pulse 99/minute). The patient was drowsy, but oriented with respect to person, time and place. Heart and lung examination revealed no abnormalities but abdominal examination revealed hepato-splenomegaly and ascites. Laboratory investigations at the time of admission revealed severe anemia (hemoglobin 5.7gm%), an

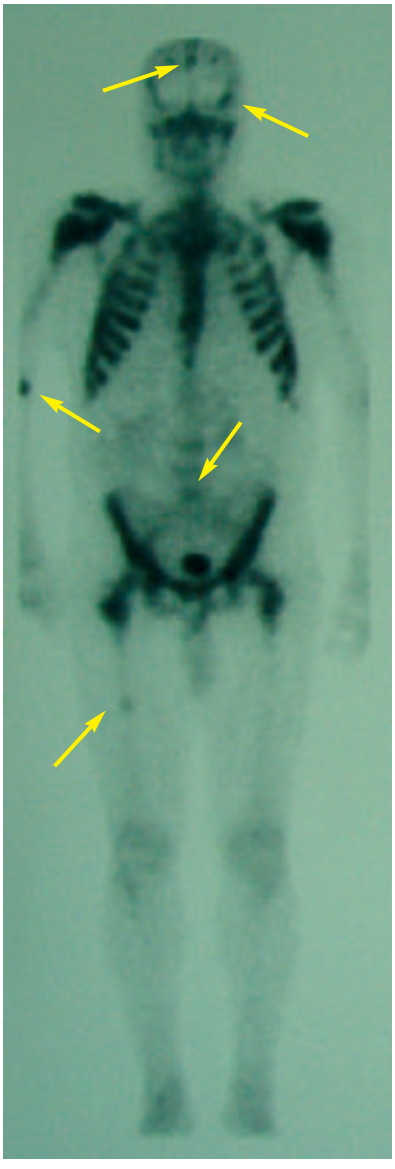

Figure 1. Bone scan showing multiple metastases (arrows).

absolute monocytosis and thrombocytopenia (platelets 39,000 per cu mm.). Liver function tests showed hyperbilirubinemia and hypoalbuminemia. There was mild hyperuricemia and hypocalcaemia and normal renal function tests A random blood sugar was normal. Urine cytology showed malignant epithelial cells consistent with urothelial carcinoma. Additional radiological examinations included a CT scan of the head, which revealed sub-cortical arteriosclerotic leukoencephalopathy with suspected small deep parietal lacunar infarcts. The base of the skull had a patchy osseous texture of uncertain origin.

FINAL DIAGNOSIS

The patient was diagnosed as having bilharzial related bladder cancer with bone metastases at presentation together with HCV infection, diabetes mellitus, severe anemia, hypertension, arteriosclerotic leukeoencephalopathy and a possible acute infection.

DISCUSSION

This patient provides an example of a common oncologic problem faced by physicians in Egypt. The patient had bilharzial related bladder cancer presenting at an advanced stage with bone metastases. Although metastases in bilharzial associated bladder cancer are uncommon, bone is the most common site of metastasis.

The patient also had impaired liver function due to both bilharzial and HCV infections. This difficult medical situation, with compromised hepatic function poses several questions. Firstly, since disease is disseminated, the only realistic therapy is systemic chemotherapy, but this is complicated by the impaired hepatic function and is influenced by the fact that prospects for cure in this patient with widely metastatic disease are essentially zero. Should he be treated with chemotherapy that is either modified, or selected in the hope of causing minimal additional liver impairment or increased toxicity because of the presence of cirrhosis? What is the cost-benefit ratio?

Both the advanced state of this patient's cancer and his several underlying chronic diseases pose enormous and probably insurmountable medical problems. Such complex patients consume extensive resources yet are much more commonly encountered in developing nations where resources are limited. In bilharzial associated bladder cancer, even patients with surgically resectable disease may subsequently die from hepatic schistosomiasis or from renal infection associated with urinary bypass following total cystectomy. Information from studies conducted in affluent nations often provide little help in deciding optimal management of such complex and advanced cases. In the case of bilharzial bladder cancer, there are also important biological differences from the common transitional cancer of western countries – which generally presents at an early stage. Clinical trials in developing countries themselves are essential to determine optimal management, but all too many of these patients may be candidates only for palliative care – which is also not widely available in the setting of poor countries and poses additional problems, such as the availability of opiates and the difficulties of both home and clinic-based terminal care in low-resource populations. Clearly, greater efforts need to be focused on prevention and early detection, and in the case of bilharzial associated bladder cancer, on the underlying parasitic disease as well as the cancer it predisposes to. ■

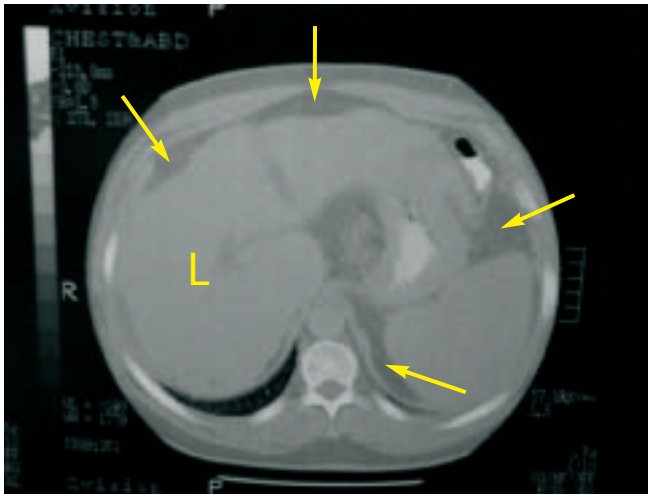

Figure 2. CT scan of the abdomen showing cirrhosis and ascites (arrows). L = liver.

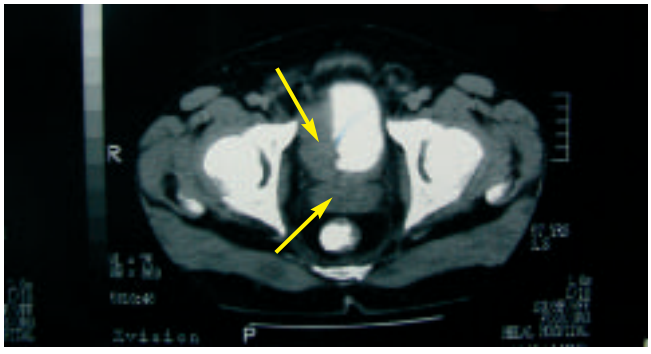

Figure 3. CT scan of the pelvis with contrast (white) in the bladder, showing a large filling defect (mass) extending posteriorly (arrows).

Hussein Khaled
National Cancer Institute (NCI),
Cairo, Egypt

BRINGING HEALTH AND HOPE TO THE PEOPLE OF ARMENIA

Rita Balian recently received the USAID Outstanding Citizenship Achievement Award, as well as the Spirit of Life Award, in recognition of her volunteer efforts in her native Armenia.

What started as one psychologist's endeavor to awaken the artistic instinct within Armenian children has grown into a major health care initiative. Today, the walls of the American Armenian Wellness Center, a state-of-the-art facility in Yerevan, Armenia, are filled with brightly colored children's artwork. The women who come to the Wellness Center for breast and cervical cancer screening are the beneficiaries of the compassion and drive of a pragmatic businesswoman, educator and art lover who never forgot her ethnic heritage. From her home overlooking the Potomac River in Washington, D.C., Rita Balian, President and CEO of the American Armenian Cultural Association (AACA), has accomplished what some might have called impossible — the creation of a thriving, modern women's health care center in Armenia that holds the promise of expansion.

In 1991 Armenia declared its independence from the Soviet Union, becoming the first republic to do so. With Armenia's independence, the Armenian American community, including the Balians, felt a greater responsibility to help the young republic succeed. Rita Balian was struck by the poor health care facilities in Armenia, particularly the utter lack of preventive medicine for women, which she observed during her annual trips. Balian lost five dear Armenian friends - teachers, mothers and grandmothers - to breast cancer, while her two sisters in the United States were saved through early detection. The breast cancer screening equipment in Armenia was decades old and grossly inadequate on the one hand, while radical mastectomies were often performed unnecessarily, on the other.

The AACA initiated the challenge to bring modern mammography to Armenia in the fight against breast cancer, the leading cause of cancer deaths among Armenian women. With the help of her good friend, Hranush Hakobian, who was then Armenia's Minister of Social Welfare and Services, she persuaded Armenia's Minister of Health to allocate space for the women's center at a medical university. Upon her return home, Balian rallied Armenian Americans throughout the United States to support the funding initiative, persuaded U.S. corporate sponsors to donate equipment and supplies, and enlisted the volunteer assistance of doctors from leading U.S. medical institutions to help her initiate and develop a diagnostic center. The U.S. Department of State's Humanitarian Assistance Program also donated equipment and expertise for the project. The Center opened in April 1997.

Since its inception, the staff of the center has grown from three to 36 medical and administrative professionals who have been trained in the U.S. and on site by the best in the field. U.S. medical professionals from Washington Hospital Center, the Greater Baltimore Medical Center, Johns Hopkins University, George Washington University and the University of Southern California have traveled to Armenia to train and have also hosted Armenian doctors and biomedical engineers for advanced training in mammography, breast biopsy, gynecological basic services and Pap smears, cytology and histology. The Center also retains two oncology consultants and one pathologist in order to provide free clinical services to patients with breast lesions.

"With the introduction of American technology and know-how," Balian says, "the Mammography Center revolutionized women's healthcare delivery in Armenia by providing reliable medical screening and diagnosis, maintaining qualified medical and administrative staff, utilizing state-of-the art equipment, and creating public awareness of the bene-

The Armenian American Wellness Center currently occupies the first floor of this building in Yerevan.

The new American Armenian Wellness Center

fits of early detection. Today, the Center is a clean, modern facility that has won the trust of the public and the confidence of the medical institutions in the region."

In January 2002, with the addition of the gynecological department and a pathology laboratory, the center was renamed the Armenian American Wellness Center. Today, the Wellness Center remains the finest of its kind in the entire former Soviet Union and Eastern Europe. Two satellite clinics have since opened, and regular bimonthly medial missions to vulnerable Armenian regions have been organized. Since its inception in 1997, over 60,000 women have been screened, and of those diagnosed with breast cancer, more than 1,500 women have received treatment.

"This has been a wonderful experiment that has proven so successful," says Michael Lemmon, the former U.S. Ambassador to Armenia. "The Center has great management, good accountability, and transparency in their operations. It's the perfect example of partnership between NGO's and U.S. and Armenian medical institutions, corporations and governments."

Balian adds: "Each time we save the life of a mother, we save a family." ■

Marcia Landskroener for INCTR

MEETING OF THE MIDDLE EASTERN CHILDHOOD CANCER ALLIANCE. KUWAIT, APRIL 4TH

The third meeting of the Middle East Childhood Cancer Alliance (MECCA) took place on April 4 during the Pan Arab Cancer Congress in Kuwait City, Kuwait. The meeting was organized by the King Faisal Specialist Hospital and Research Centre (KFSH & RC) and 12 countries were represented in the meeting – Bahrain, Egypt, Iran, Jordan, Kuwait, Lebanon, Morocco, Qatar, Saudi Arabia, Tunisia, United Arab Emirates and Yemen.

The objective of the meeting was to develop and finalize a MECCA strategy for the most common childhood cancer, acute lymphoblastic leukemia (ALL).

In preparation for the meeting, a survey of existing resources for the diagnosis and treatment of ALL was conducted among many countries participating in MECCA. In addition to gathering this important information, the interest in collaborating in a study using a standardized diagnostic work-up and a common treatment approach was assessed among the participants. All of the countries that participated in the survey have the necessary resources for diagnosis and treatment – including capabilities to perform routine laboratory examinations, imaging studies, diagnostic immunophenotyping, and access to the chemotherapeutic agents necessary to treat ALL. All countries expressed an interest in collaborating in a common treatment protocol for ALL.

A session in the meeting was devoted to the standardization of the diagnosis of ALL. Dr. Tarek Owaidah, Coordinator of Laboratory Diagnosis of Acute Lymphoblastic Leukemia gave a comprehensive presentation on the different components of the pathway for making an accurate diagnosis of ALL. The group agreed to focus on standardizing sample collection and processing for routine diagnosis and to ensure that immunophenotyping is performed as part of making the diagnosis of ALL.

In order to set the stage for developing a common treatment protocol, Dr. Magrath described the 20 year experience of the treatment of ALL in India. The protocol that has been used in India, MCP841, has been conducted among 3 major cancer centers. Many lessons have been learned – most importantly that prognostic factors reported in Western series do not appear to be the same in this Indian series. Over time, as experience was gained with the protocol, particularly with sharing of experiences among the centers, therapy for ALL and supportive care practices were improved and data collection was standardized. Event free survival (EFS) rates have improved over time. In one center EFS is currently 64% at 4 years - comparable to results reported from the UK.

Dr. Abdallah Al-Nasser presented two possible treatment regimens that could be used as a basis for the development of the MECCA protocol – BFM International Protocol and the Children's Cancer Group (CCG) Augmented BFM protocol. He fully explained the objectives, design, and chemotherapy schemas for the two studies.

A group discussion took place of the treatment approaches and it was agreed that a specific protocol should be written. The study will include the collection of prognostic factors in a uniform fashion among all participants.

If possible, molecular profiling studies will also be carried out.

In summary, the group agreed to:
1. Finalize an immunophenotyping algorithm for diagnosis and sub-classification that will be incorporated into a standard treatment protocol.
2. Prepare a draft of a MECCA childhood ALL protocol.
3. Collect data on patients currently being treated on the two most frequently used protocols among the participating countries.

The group will meet again in early October to discuss the draft protocol. ■

AN EDUCATIONAL WORKSHOP FOR IRAQI PEDIATRIC ONCOLOGISTS. KING HUSSAIN CANCER CENTER AMMAN, JORDAN APRIL 18TH - 19TH

In June, 2003, some 3 months after the beginning of the most recent war in Iraq, an international conference entitled "Partners Towards Helping Pediatric Cancer Patients in Iraq", was held to address the exacerbation of the long standing difficulties faced in Iraq in treating children with cancer, and to identify ways of supporting Iraqi medical and nursing staff attempting to provide appropriate care under very difficult circumstances. A follow-up conference was held in December of the same year. These meetings were largely sponsored by the Office of International Affairs of NCI (OIA), and organized by staff of the King Hussain Cancer Center (KHCC) in Amman, Jordan. INCTR representatives were present at both. The major conclusion reached was that the most effective way of ensuring that Iraqi children with cancer receive the best possible care would be through the provision of assistance to pediatric oncology teams currently practicing in Iraq, including educational updates for health care providers. As an interim measure, selected children with cancer – those considered most likely to benefit – would be transferred to centers of excellence in the region, including the KHCC and the King Faisal Specialist Hospital and Research Center (KFSH&RC) in Riyadh. INCTR was asked to take primary responsibility for the development of pediatric oncology workshops designed both to identify problems faced by Iraqi pediatric oncologists, and to provide relevant updates and continuing education in the context of the care of children with cancer. Financial support was made available by the OIA. Accordingly, the First Pediatric Oncology Workshop for Iraqi Oncologists was held at the King Hussain Cancer Center, Amman, Jordan from the 18th – 19th April 2004. Dr Aziza Shad, Chairman of INCTR's sub-committee on Pediatric Oncology Education, took primary responsibility for the design of the program.

Participants in the Educational Workshop for Iraqi pediatric oncologists.

Nine pediatric hematologists/oncologists from Baghdad, Basrah and Mosul attended the two-day workshop, which focused primarily on pediatric leukemia, lymphoma, supportive care and palliative care. A distinguished international faculty consisting of experts from INCTR, St Jude's Children's Research Hospital, Lombardi Cancer Center, KHCC and KFCH&RC participated in the meeting. The current management of pediatric leukemias and lymphomas was discussed in detail and Iraqi pediatric oncologists provided information about the current state of medical care available in their own hospitals. All highlighted the high mortality rates from infectious complications, particularly during induction therapy, and the lack of availability of chemotherapy agents, antibiotics and blood product support. The second day of the workshop was devoted to discussions and presentations on the management of infections in the immunocompro-

mised host, transfusion therapy and end of life care. It was particularly disquieting to learn that morphine is not available in Iraqi hospitals, and that less effective analgesics can be dispensed in small quantities only with the approval of surgeons.

In addition to the presentations at the workshop, the Iraqi physicians were given pediatric textbooks, handouts and relevant articles pertaining to the topics discussed. Several continuing needs were identified – the need for continuing education, which would be greatly simplified by access to internet and televideo linkages, and help with treatment and supportive care protocols. Feedback from the Iraqi oncologists at the end of the workshop was very positive, and a follow-up meeting was planned for early October 2004, as part of INCTR's Annual Meeting, which is to be held in Cairo, Egypt. ■

MEETING OF THE RETINOBLASTOMA STRATEGY GROUP. INCTR, BRUSSELS APRIL 29TH - 30TH

The Retinoblastoma Strategy Group treatment sub-committee met in April in order to finalize the development of a treatment protocol for children with extraocular retinoblastoma and to review and revise the questionnaire used in the on-going group study entitled, "Understanding Problems Faced by Parents of Children with Retinoblastoma Prior to Treatment". A preliminary report of the results of the questionnaire will be presented in the next edition of the newsletter. During the course of the meeting, group members provided updates on local public and professional awareness programs that have been initiated in their respective countries.

Members of INCTR's Retinoblastoma Strategy Group met in Brussels in April.

TREATMENT PROTOCOL

Clinical data about the children of the parents who were interviewed for the questionnaire was presented. Most children seen by the participating investigators have advanced stage retinoblastoma and many of these children present with extraocular disease, which carries a particularly poor prognosis. Therefore, it was considered an important goal of the protocol to improve the disease-free survival of children with extraocular disease. Children with metastatic retinoblastoma that does not involve the central nervous system (CNS) will also be eligible for the new treatment protocol. It is anticipated that approximately 40 to 50 patients per year can be enrolled on this study.

The treatment modalities that will be used in the protocol will include chemotherapy, surgery and radiotherapy. Children will be stratified into two different treatment arms, depending upon the presence or absence of optic nerve involvement at the time of presentation. Children who do not have optic nerve involvement (either by histopathology or by a negative CT/MRI scan) at presentation will receive an initial 3 cycles of chemotherapy with vincristine, carboplatin and etoposide, followed by surgery (if needed), and then a further 3 cycles of the same chemotherapy with concurrent radiation therapy. The treatment plan for patients with optic nerve involvement will follow the same sequence, but chemotherapy will consist of alternating cycles of two different combinations of drugs. Chemotherapy will begin with a cycle consisting of vincristine, cisplatin and taxol which will be alternated with a cycle consisting of vincristine, carboplatin and

etoposide until a total of 6 cycles are completed.

Other components of the protocol document were also finalized during the meeting including the tests that would be required prior to the start of treatment, during treatment and after treatment has been completed. The group anticipates that the protocol document will be finalized later this year.

PUBLIC AND PROFESSIONAL AWARENESS PROGRAMS

Dr. Epelman provided an update on the retinoblastoma awareness campaign that has been on-going in Brazil. A public service announcement, shown at INCTR's Annual Meeting 2003, has been broadcast on television throughout the country. At the conclusion of the announcement, a toll free number is provided to encourage viewers to call for advice and an address is provided so that viewers may also write in for advice. Many telephone calls and letters (including photographs of children) have been received. Dr. Epelman showed the photographs of many children, some of whom had retinoblastoma and some who did not. The public service announcement video may be seen on the INCTR and TUCCA (tucca.org.br) websites. In addition to the television campaign, one million cards with information about retinoblastoma have been printed and distributed to individuals purchasing telephone cards in Brazil in an attempt to further increase public awareness. Data about the number of cases of retinoblastoma that have been diagnosed and/or referred as a result of the two campaigns are being kept.

Dr. Leal has formed a Mexican Retinoblastoma Group (MRG) comprised of ophthalmologists and pediatric oncologists interested in retinoblastoma in Mexico. All have agreed to work together in the following areas - studying cases of retinoblastoma, making publications about the pattern of the disease in Mexico, developing uniform treatment approaches, and developing and standardizing methods for improving and enhancing early detection of retinoblastoma. In order to increase public awareness, the MRG has created a poster that will be widely distributed and also obtained television time for a public service announcement about retinoblastoma on one of the more popular TV channels in Mexico.

A Retinoblastoma Day that was highly publicized in newspapers was held in Turkey. Dr. Tacylidiz, who is now the secretary of the Pediatric Oncology Society in Turkey, will utilize her role as secretary to address the need to improve early detection of retinoblastoma in Turkey.

Dr. Banavali reported that the Tata Memorial Hospital has efforts underway to develop closer ties with ophthalmologists in Mumbai in order to provide more coordinated care for children with retinoblastoma. ■

MEETING OF THE BREAST CANCER STRATEGY GROUP. INCTR, BRUSSELS MAY 27TH - 28TH

The Breast Cancer Strategy Group project planning sub-committee, comprised of investigators from Peru, Egypt, India and Pakistan met in May in order to finalize a retrospective survey entitled, "Presentation Features of Breast Cancer and Risk Factors for Treatment Outcome" and to decide upon the timing of the survey's initiation. Other objectives of the meeting were to obtain agreement on a treatment protocol for patients with locally advanced breast cancer and to decide upon specific biological studies in breast cancer that could be undertaken.

SURVEY STUDY

In 2003, the group designed a retrospective survey to collect information about breast cancer cases seen at their institutions during the time period beginning in 1993 through 1997. The survey attempts to collect basic epidemiological data, patient history, information related to the presentation features of breast cancer, and data about treatment and treatment outcomes. The major goal of this study is to create a foundation of information about breast cancer among various developing countries representing patient populations in different world regions. It is anticipated that investigators from Argentina, Peru, Mexico, Tanzania, Egypt, Kuwait, India, Pakistan and Nepal will contribute to the study. Another objective of the study is to demonstrate that high quality data can be collected from developing countries.

In this meeting, the survey document was reviewed and finalized. It will initially be conducted by four centers (represented by the project planning sub-committee) in order to evaluate the feasibility of collecting the data as well as the completeness of the information available at the participating institutions. After a preliminary examination of the data obtained from these four institutions, the study will be expanded to centers in other participating countries – Argentina, Mexico, Kuwait, Tanzania and Nepal.

PROTOCOL FOR THE TREATMENT OF LOCALLY ADVANCED BREAST CANCER

During the meeting, the group discussed possible approaches for the treatment of patients with Stage IIIA, B and C breast cancer. A randomized protocol was designed to compare 3 treatment approaches. One arm will consist of an initial 3 cycles of chemotherapy with 5-fluorouracil (5-FU), adriamycin and cyclophosphamide (FAC) with concurrent radiation therapy followed by surgery, and then followed by 3 additional cycles of FAC. The second arm will be 3 cycles of FAC followed by surgery, then post-surgical radiation with 3 additional cycles of FAC. The third arm will consist of 3 initial cycles of cyclophosphamide, methotrexate and 5-FU (CMF) with radiation therapy followed by surgery, then an additional 3 cycles of CMF. Specific guidelines for surgery and radiation therapy will be built into the protocol. Patient accrual is anticipated to be approximately 500 to 600 per year among the centers presented.

It is anticipated that the group will continue its work on the development of the protocol document during the remainder of 2004.

BIOLOGICAL STUDIES

Dr. Guy Leclercq and Dr. Marc Lacroix of the Institute Jules Bordet in Brussels met with the group in order to describe their work studying gene expression patterns in breast cancer, as well as estrogen receptors and the variants of co-regulators of these receptors found in breast cancer in different world regions. There was strong interest among the strategy group in conducting similar studies. A separate study incorporating procedures for sample collection, processing and research into molecular characteristics will be written.

OTHER POTENTIAL ROLES OF THE STRATEGY GROUP

Throughout the course of the meeting many discussions took place about the role that the Strategy Group could play in professional educational activities, including the development of guidelines for the management of breast cancer, early detection programs and public awareness campaigns. There was general agreement that the group should prepare a consensus statement about the management of breast cancer in developing countries, incorporating what is known and not known about breast cancer in such countries. The group also agreed to hold educational meetings on breast cancer. ■

ADMINISTRATIVE MEETINGS

On May 24th, the Assemblée Générale et Conseil d'Administration of the Alliance Mondiale Contre le Cancer (AMCC) met in Brussels to discuss progress and projects relating to the French branch, as well as administrative matters.

On 21st June, the Advisory Board of the UK Branch met in London to discuss new initiatives in the treatment of Burkitt's lymphoma in Africa. ■

NEW STAFF MEMBER

We welcome Cédric Petit-Musin to the Brussels office as Meetings Coordinator. As time goes by and INCTR undertakes or participates in more and more educational events and project-related meetings, the need has developed for a full time staff member to undertake the task of coordinating the organization of such meetings. Cédric has considerable experience in this area through his prior association with the hotel industry. He assisted in organizing previous INCTR Annual Meetings at the Hilton Hotel in Brussels from, as it were, the other side of the fence, so comes to us with considerable experience in this area, as well as with some knowledge of INCTR. ■

Some of INCTR's staff with Cédric Petit-Musin.

MAHAK: AN IRANIAN CHARITY ORGANIZATION FOR CHILDREN SUFFERING FROM CANCER

In affluent countries, childhood malignancies are, after traffic accidents, the leading cause of mortality in children older than five years, and approximately 120 per million children aged 0-15 years will suffer from cancer.

the MAHAK Rehabilitation and Cancer Center

Due to improving socio-economic conditions and public health services in Iran over the past decade, there are strong indications that a change in the pattern of the incidence of various diseases in children is occurring, but Iran's population of 66 million includes a higher fraction of children - 34% are younger than 15 years – such that childhood diseases, including cancer, are a relatively more important health problem than in the West.

The most common pediatric cancers in Iran are acute lymphoblastic leukemia, brain tumors, non-Hodgkin's lymphoma, Hodgkin's disease, retinoblastoma, Wilms' tumor and neuroblastoma. Doctors in Iran are implementing modern western protocols, which are giving promising results. Approximately 70% of children with cancer treated in western countries are alive five years after treatment. The key point to be made is that cancer in children is curable.

The majority of children with cancer in Iran are referred either to pediatric oncologists or pediatric oncology departments. However, the long time-lapse between disease manifestation and referral to specialists remains a matter of concern. Treatment expenses for children suffering from cancer are, to a considerable extent, covered by government insurance services. Expenses for bone marrow transplants are covered by special government funds. In major cities, local charity groups and organizations are keen to provide financial support and assistance to families in need.

One such charity is the MAHAK Rehabilitation and Cancer Center, established in 1991 as a non-governmental organization in Tehran. Several socially motivated Iranians, including the parents of a girl with nephroblastoma, were instrumental in establishing the charity organization. Its mission is to alleviate the pain and suffering of children with cancer, to provide financial and psychological support to afflicted families, to build child-friendly wards, to provide accommodation for patients and their parents, and to inform and educate the public about childhood cancer and its curability. Dr. Mardawig Alebouyeh, a hematologist/oncologist, now also in private practice at Mehr Hospital, was one of the founders. Striving to improve the quality of pediatric care available, he helped develop a model approach that concentrates all services in one place. MAHAK addresses the needs of the whole patient and involves the entire family. If a patient dies, MAHAK even pays for the child's burial.

"One of the problems our patients family's used to face was the financial burden of the disease," says Dr. Alebouyeh. "Now, they come to us and ask us for help, which we are able to provide. Similarly, the seven oncology departments in Tehran are short of resources and have problems meeting the needs of patients. MAHAK is also able to provide them with financial support with respect to diagnostic procedures and treatment."

The organization now has more than 20,000 members, including Iranians living abroad. It has funded the construction of a spacious recreation and rehabilitation center with adjacent diagnostic and therapeutic facilities. MAHAK employs 35 professionals who, since its inception, have provided essential medical and financial support to more than 7,000 children suffering from cancer. Teams of volunteer social workers visit seven pediatric oncology wards throughout Tehran six days a week, registering and counseling patients for referral to appropriate centers and services. The MAHAK complex itself offers three components of medical care: rehabilitation for children during treatment, ambulatory clinic and inpatient departments, and diagnostic imaging facilities. In addition, the center offers social and educational facilities, family accommodation, and medical and psychological counseling.

"Not only do we want to give patients the opportunity to survive cancer, to relieve their pain and suffering and to be treated in comfortable and hygienic surroundings," says Dr. Alebouyeh. "We also offer them and their families psychological support in order to help them deal with their cancer."

The challenge for us is to build a good staff of physicians and a qualified nursing staff," says Dr. Alebouyeh. MAHAK endeavors to send physicians

abroad for specialized training. The center is working to establish training partnerships with St. Jude Children's Research Hospital in the U.S., and with Shaukat Khanum Memorial Cancer Hospital in Pakistan. Still, he gets a great deal of satisfaction knowing his facility is perceived as a worthy philanthropic institution where the newest modalities for cancer treatment can be made available to the pediatric oncology departments in Tehran.

In the absence of an efficient national cancer registry, MAHAK has established a preliminary database for childhood malignancies. Colleagues in other major cities have been encouraged to establish similar systems, with assurances that MAHAK will give them help and assistance in their endeavors to combat childhood cancer.

PEDIATRIC SERVICES IN IRAN

The pediatric hematology and oncology (PHO) services in Iran have improved steadily over the past decade. Specialized PHO services are available in nearly all major cities throughout the country, where 43 board-certified or eligible pediatric hematologist-oncologists are giving care to children suffering from cancer or hematological disorders. There is an approved fellowship program for PHO at three university children's hospitals. At the same time, there exists a good training program for pediatric surgery. Today, 74 board-certified pediatric surgeons are providing surgical care to pediatric patients. There is, however, a need for special training programs for teaching nursing staff the principles of caring for children with malignancies. Preliminary actions to establish such a program for interested nurses are now underway.

MAHAK provides a child-friendly environment.

TREATMENT AND OUTCOME

Childhood malignancies are treated according to the conventional multimodality protocols which are mostly adopted from accredited medical institutions in the USA or Europe. There is no shortage of anti-cancer drugs, antibiotics, hematopoietic growth factors, blood products, and even monoclonal antibodies. However, specialized laboratories capable of performing more sophisticated diagnostic procedures, e.g. immunohistochemistry, cytogenetics, viral and molecular studies, are limited in number, and offer their services mainly in Tehran.

Radiotherapy facilities are conventional and available only in a few major cities. Currently, five linear accelerators are in operation in the country - three in Tehran, one in Isfahan, and one in Hamadan. They all have long waiting lists, which limit the expected benefits in some malignancies, such as Wilms' tumor.

There are encouraging reports from single institutions which treat and follow-up results of childhood malignancies, e.g., acute lymphoblastic leukemia, Hodgkin's disease, Wilms' tumor and retinoblastoma. But, in the absence of an effective national cancer registry and cooperative pediatric study groups, comparative demographic, epidemiologic, treatment, and follow-up data are not available. However, according to IARC childhood cancer statistics, 2,682 children contracted cancer in Iran in 2000, and the death toll from cancer in the pediatric age group was 1,703. Considering these alarming data, the Iranian Society of Pediatric Hematology and Oncology is poised to tackle the problem by helping medical and health authorities and support groups to focus on shortcomings and improve the allocation of resources. ■

Dr. M. Alebouyeh provided the information for this article, which was prepared by M. Landskroener for INCTR

RESOURCES AT MAHAK

Total Beds Devoted to Cancer Care:	
120 beds for patients and one parent	
Hostel - 40 patients with parents	
Staff Physicians	volunteer
Oncologists in training	yes
Spiral CT Scanners	1
MRI	1
Linear Accelerator units	1 (of 3 in Tehran)

PATIENTS SEEN AT MAHAK IN 2002

Total pediatric patients	1,724
Total hostel admissions	2,000
Total expenditures	500,000 E.

PROFILES IN CANCER MEDICINE

DR. HUSSEIN KHALED, DEAN OF NCI, CAIRO

After three decades in cancer medicine, Dr. Hussein Khaled realizes that there is a simple cause and effect relationship with the majority of the cancers afflicting the people of his country. Yet rectifying the social and environmental conditions that set the stage for the development of cancer in the peoples of Egypt is a monumental challenge.

Dr. Khaled's research interests include non-Hodgkin's lymphomas, breast cancer, and bilharzial-related bladder cancer. Most urinary bladder cancers in Egypt can be traced to the waterborne parasites in the River Nile. "If we could prevent parasites, prevent smoking, and prevent Hepatitis B and C viral infection," he says, "then we could prevent more than 50% of cancer cases in the country."

A distinguished professor of medical oncology and Dean of the National Cancer Institute at Cairo University—the largest comprehensive cancer center in Africa—Dr. Khaled understands that prevention and early detection is the key to improving the survival rates of cancer patients while also significantly lowering the cost of treatment. To that end, NCI Cairo has established a special unit to promote public awareness about the most common cancers in Egypt: bilharzial-related bladder cancer, breast cancer and hepatocellular carcinoma. Doctors there are also participating in several international projects focused on cancer prevention in high-risk groups. The IBIS-II trial, for instance, testing a new drug called anastrozole, has been called "the next big step" towards preventing breast cancer. Researchers believe that anastrozole could reduce the risk of breast cancer in post-menopausal women by more than 50 percent.

As a young man, Dr. Khaled was drawn to medicine for two reasons. When his father was critically ill, he developed great respect for the physicians who were treating him. And as a top scholar, he was a likely candidate for the profession. After graduating from Cairo University in 1975, he completed internships in several specialties, but he found his calling at NCI Cairo. "I knew then that my future would be in the field of oncology, conducting research, running clinical trials and motivating others in the fight against cancer."

Dr. Hussein Khaled

Throughout his career, Dr. Khaled has been involved with international cancer organizations. He was twice a visiting fellow in pediatric oncology at the National Cancer Institute in Washington, and was a visiting physician with the Grace Cancer Drug Center, Roswell Park Memorial Institute in New York. He is a member of the European Organization for Research and Treatment of Cancer (Lymphoma Group), the American Society of Clinical Oncology, and is Secretary General of the Egyptian Foundation for Cancer Research. He has written more than 90 papers and 40 abstracts in both national and international journals, and has edited three volumes—on lymphomas, on breast cancer, and nutrition and cancer (in Arabic).

As the regional representative for Egypt and Africa with the European Society of Medical Oncology, he encourages closer partnerships with other cancer societies. And as president of INCTR Egypt, he brings a global focus to cancer management. As such, he was instrumental in organizing INCTR's 2004 Annual Meeting in Cairo.

"It is such an honor to be the first country to host such an important meeting," Dr. Khaled says. "I hope that the international community will gain a better understanding of our national objectives in the fight against cancer. The meeting also provides a forum for discussing the common problems of all developing nations in the field of oncology. This will help in finding solutions for specific problems."

NCI Cairo already participates in INCTR's epidemiological studies in breast cancer.

"This study is a very important one," Dr. Khaled says. "I have been trying for many years to form a database for the clinico-pathological profile and the end results of the treatment of breast cancer patients in Egypt as well as in other developing nations. This will give us a better chance to compare our data with those that originate in western countries, and ultimately will help us tailor the general strategies and management guidelines to our own patients."

NCI Cairo is also collaborating with INCTR in the development of new treatment protocols for non-Hodgkin's lymphoma, and is working with King Faisal Specialist Hospital and Research Center (KFHRC) in Saudi Arabia to characterize the disease profile and to define prognostic factors of NHL patients. Another study seeks to identify factors which influence the development of lymphomas in the region. ■

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