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## THE PRESIDENT'S MESSAGE

### CAUSING AND CONTROLLING CANCER

by Ian Magrath

*Golden lads and girls all must,  
As chimney-sweepers, come to dust.  
William Shakespeare, Cymbeline. iv, 2.*

Cancer control is a term used to refer to all attempts to reduce death and suffering caused by cancer. It includes prevention (primary and secondary), early detection, specific treatment and palliative care (see Figure 1). Effective cancer control can only be based on science, although it involves a constituency that extends well beyond the health practitioner since it includes a major public health component. Because cancer encompasses many diseases, each of which may be more or less amenable to prevention or treatment, notions such as "a cure for cancer" are oversimplifications and tend to distract attention from the even more attractive goal of preventing cancer. Many patients with cancer can be cured— 50% or more in the affluent countries are alive at five years—and it is theoretically possible to prevent at least 50% of cancers in these countries—particularly

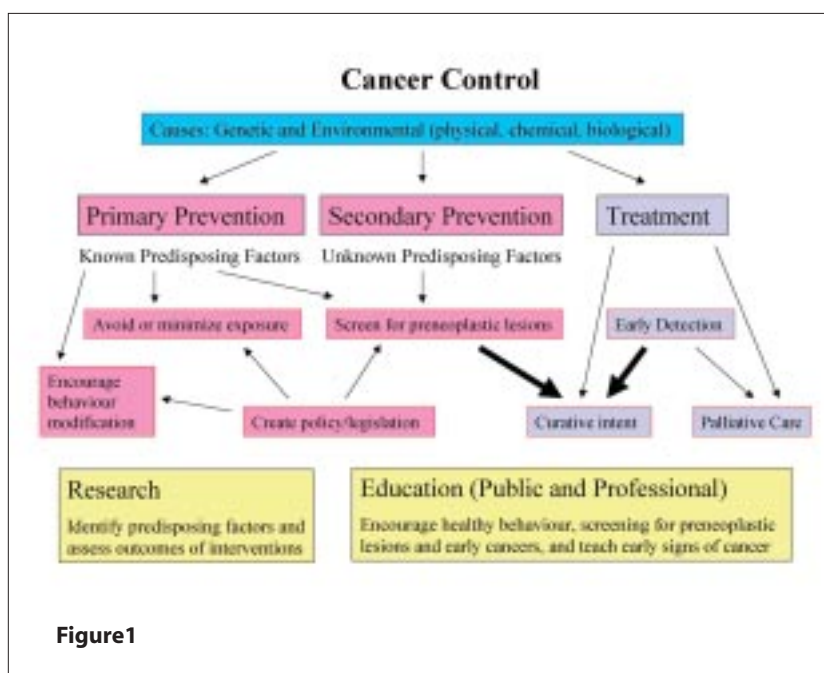


Figure 1

those caused by tobacco and dietary factors (estimated to be two-thirds of all cancers in affluent nations). Unfortunately, more than 60% of patients with cancer live in developing countries and have poor access to therapy, so that a much lower fraction receive appropriate treatment, while the populations of these same countries are poorly informed about cancer, inadequately protected against envi-

ronmental risks, and have limited access to screening programs that could prevent some cancers.

For each cancer, the optimal approach to its control depends upon available knowledge of its causal factors, its natural history and its response to current therapy. The risk posed by cancer-causing environmental factors can be reduced by primary preventive measures such as

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lifestyle changes (e.g., not smoking) or actions that limit or avoid exposure (e.g., to toxic chemicals, sunlight, radioactivity or certain infectious diseases). Many of the preventable cancers (e.g. lung cancer) are often poorly responsive to treatment unless detected in a very early stage. Diseases in which the early stages, including pre-malignant lesions, can be readily detected and removed by simple surgical methods, (e.g. cervical intraepithelial neoplasia, a precursor of cervical cancer), may be well controlled by screening appropriate target populations and ensuring appropriate treatment. The success of prevention programs at a public health level is dependent, of course, upon achieving good population coverage. Diseases in which the causal factors are not known or cannot be readily avoided, or in which preneoplastic lesions are not readily detected, may be effectively treated, sometimes, even when in advanced stages (e.g., most childhood cancers).

Given that cancer control must be disease-specific (although tobacco and diet are relevant to many cancers), systematic strategies directed towards controlling cancer must take into consideration the relative proportions of different types of cancer within the targeted geographic areas or population sub-groups, as well as existing resources for cancer control and their distribution within the regions in question. While primary cancer control is largely a public health problem, secondary cancer control and treatment rely upon primary care health practitioners and cancer specialists. Consequently, the successful establishment of systematic cancer control strategies is dependent upon a variety of cultural, social, economic and political factors, including the priority given to cancer by governments, the type of health care system and the diligence and knowledge of individual practitioners.

Figure 2 (opposite) shows the geographic variability in cancer incidence at a global level for the year 2000 (adjusted to an age-adjusted standard

world population), based on cancer registry data and, where this is not available, estimated information. The variability in overall incidence shown here reflects an even greater variability in the incidence of each type of cancer throughout the world, and confirms the need for individualized cancer control plans at national or regional levels. It must also be recognized, however, that this map gives no indication of the constantly evolving patterns of cancer resulting from changes in population age-structure and lifestyles, and changes in the prevalence of, or exposure to causal factors. Although developing countries presently have a lower incidence of cancer, the fact that their populations are growing much faster than those of affluent nations, the increasing proportion of elderly in the population, and the rapid changes in lifestyles and environments are leading to both a higher incidence of cancer and a trend toward cancer patterns that increasingly resemble those of affluent nations. The progressive rise in the incidence of tobacco-related cancers is particularly worrisome and will impose a heavy burden of chronic disease on these countries, further challenging their healthcare systems. This implies an urgent need to focus more attention on cancer control in developing countries now, even though cancer incidence is relatively low.

Inevitably, the concepts and strategies of cancer control have evolved with our understanding of cancer itself. Prior to the modern era, cancer was only dimly perceived as a discrete set of diseases, although the existence of inexorably progressive swellings or tumors, or festering sores which eroded adjacent tissues, has been recognized since ancient times. Before

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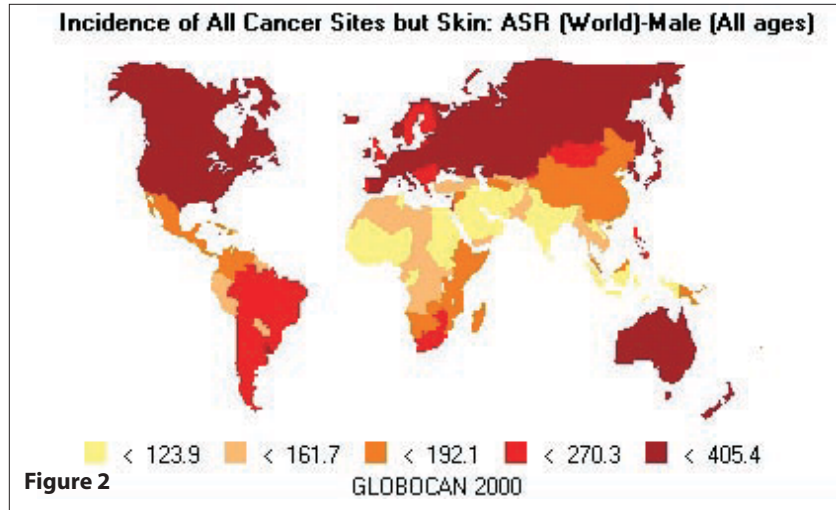
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pathological diagnosis became feasible, it was often impossible to distinguish between cancer and many chronic infectious or inflammatory diseases, but in the absence of effective therapy for any of these conditions this scarcely mattered. Treatment was sometimes attempted by the simple and obvious expedient of surgical removal or cauterization, but since the available techniques were primitive, such attempts were rarely successful and achieved, at best, a temporary delay in the progression of the disease. Unfortunately, any such prolongation of life was bought, in the absence of anaesthesia and effective pain control, at the high price of the excruciating suffering of the patient, while the infectious complications that followed the primitive attempts at extirpation were likely to prove fatal. Doubtless, such treatments often shortened the life of the victim while managing to make it even more miserable, or, in Hobbesian terms, "nasty, brutish and short."

**REVOLUTIONARY IDEAS**

Treatment, however unsuccessful, at least was conceivable before there was any grasp of the nature of cancer. In contrast, the primary prevention of cancer requires an understanding of its causes. Such understanding had to await the industrial revolution when the exposure of large numbers of workers (and, via pollution, others living in industrial regions) to a wide range of noxious substances, led both to a dramatic surge in a broad range of diseases, including cancer, and to the recognition of the potential role of environmental agents in their cause. The same advances in manufacturing capabilities led to the industrial production of cigarettes, and the consequent



onset of tobacco-related diseases, including cancers, of epidemic proportions. Infectious diseases, whose pattern was dramatically modified by changes in the environment, the management of sewage, improved personal hygiene and, eventually, by the development of antibiotics, became less important both as diseases in their own right, and as causes of cancer. Finally, the increased affluence brought by the industrial revolution translated into increased consumption of all kinds and altered patterns of reproduction. After the deprivations induced by the World Wars and the rapid economic development of the major combatants in the second half of the 20<sup>th</sup> century, the ill effects of a diet increasingly rich in fats and poor in fruit and vegetables became apparent. Doll and Peto have estimated that diet is involved in the causation of as much as a third of cancers in affluent countries; a high lipid intake and obesity have been associated with the development of colon cancer, endometrial cancer, prostate cancer and probably breast cancer, while a number of cancers have been shown to have a lower incidence in populations with a high intake of

fruits and vegetables. The high incidence of breast cancer in more affluent societies is also linked, at least in part, to decreased fertility and a reduction in breast feeding.

**CHIMNEY SWEEPERS PROVIDE A MODEL FOR CANCER PREVENTION**

The importance of the environment in the genesis of illness is by no means a new concept. Hippocrates himself stressed the influence of climate and geography, and sometimes of local features such as marshes, the water supply and the habits of the people, on prevalent patterns of disease. At a practical level, the toxic effects of certain minerals to which miners were exposed was recognized from the beginning of recorded medical history. Galen, however, who further developed Hippocrates' theories, considered cancer to be due to an excess of black bile (melancholia)—hardly a basis on which rational preventive measures could be undertaken. Although many other theories were put forward over the next 2,000 years, none provided any real insights. Sir Percival Pott, a surgeon at St Bartholomew's Hospital in London famous for his descriptions of tuber-

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culosis of the spine and fractures around the ankle joint—he sustained one himself, narrowly avoiding amputation and greatly stimulating his interest in this particular fracture—is generally credited with making one of the first scientifically sound connections between cancer and an environmental agent. Pott recognized, in 1761, that men who had been chimney sweeps as children frequently developed scrotal cancer. He postulated that chimney-sweepers' cancer was due to the "lodgement of soot in the rugae of the scrotum." Pott became a staunch advocate of legislation to deal with this problem. Unfortunately, the first bill passed to protect workers, the Chimney-Sweeper's Act of 1788, required only that apprentices be at least eight years old, and that sweeps could have no more than six "apprentices"! In Denmark, the chimney sweeps' guild approached the problem differently, urging its members to take daily baths. This simple, if revolutionary, measure effectively prevented the cancer, although it was not until 1892 that an article in the British Medical Journal, "Why Foreign Sweeps Do Not Suffer From Scrotal Cancer," revealed the advantages of a bath to the British. While hardly a controlled trial, there was little doubt that a critically important principle relating to the prevention of cancer—avoidance of exposure to a carcinogen—had been identified.

Meanwhile, doctors had noted similar cancers among gas plant workers in Germany and oil shale workers in Scotland, and in the early 20<sup>th</sup> century certain constituents of tar, soot, and oils, known as polycyclic aromatic hydrocarbons, were found to cause cancer in laboratory animals, thus identifying the specific sub-

stances responsible for cancer among workers in these occupations. Fortunately, protective measures taken in affluent countries today have largely relegated occupational exposure to a minor overall role in cancer causation, although rapid industrialization in developing countries, and the widespread use of agricultural chemicals, frequently in the absence of adequate worker protection or advice, and of pollution controls, may result in such exposures causing relatively high rates of particular cancers in specific populations or communities.

## THE DANGERS OF TOBACCO SMOKE

Oxidation is a risky business, as vouched for by the numerous cellular enzymes that exist to limit the potential damage to our genes caused by the production of dangerous oxidation products, such as cancer-promoting free radicals. Oxidation, in the form of the burning of fossil fuels, provided the energy needed to drive the industrial revolution, but the resultant pollution of body and soul had numerous ill effects, chimney-sweepers' cancer being just one of them. In-

"Currently two million deaths from smoking occur each year in developed countries and 1 million in lesser developed countries. By 2025, this ratio will alter to 3 million per year in developed countries and 7 million in lesser developed countries. Based on current trends, the death toll from smoking will rise to 10 million people per year by 2025." - WHO

deed, "soot-wart" was a minor public health problem compared to the 20<sup>th</sup> century blights brought about by the increasing availability of fatty foods for oxidation *in corpore* and the growing addiction to inhalation of the smoke of the dried leaves of the plant, *Nicotiana tabacum*. An astute thinker might have guessed, from a survey of the grim cities shrouded in soot, and the plethora of occupational diseases related to the dramatic increase in the use of carbon-based fuels, that inhaling tobacco smoke would be injurious to health. Some did, but the importance of smoking in the causation of cancer was not widely accepted until enough cigarettes had been smoked by enough people for long enough to produce a veritable epidemic of cancer.

Tobacco had been a valuable trading commodity ever since the colonists of the New World discovered it among the native peoples they encountered. By the 1700s it had become a major international industry and the smoking of pipes, cigarettes and cigars was widespread. But in spite of the many who opposed its use on moral, health and social grounds, centuries were to pass before the extent of its negative medical consequences was fully recognized. Samuel Thomas von Soemmering of Maine reported on cancers of the lip in pipe smokers in 1795, and Benjamin Rush, the most famous American physician of his day and a signatory to the Declaration of Independence, wrote of the medical and moral dangers of tobacco in 1798 (he was concerned primarily with its promotion of thirst and, consequently, drunkenness!). The first association of lung cancer with smoking was made in 1912, by Isaac Adler, although at that time the incidence of

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lung cancer was only approximately 0.6 per 100,000 per year in the USA. At its peak, around 1990, it had risen to 75 per 100,000 in males. The industrial manufacture of cigarettes began in the late 19<sup>th</sup> century but already, by 1900, annual sales had reached 4.4 billion. The First World War brought with it a dramatic increase in smoking, and a consequent increase in the incidence of tobacco-associated cancers. By the 1920s pathologists and physicians had begun to report a relationship between smoking and lung cancer as annual global cigarette sales reached 600 billion (1929). The Second World War gave an added stimulus to the smoking habit and the connection with cancer was established beyond any doubt in solid epidemiological studies conducted in both Great Britain and the USA. In 1950 Doll and Hill found that heavy smokers in Britain had a fifty-fold increase in the incidence of lung cancer while Wynder and Graham reported that 96.5% of lung cancer patients they interviewed in the USA were moderate to heavy smokers.

In spite of these findings, cigarette sales continued to climb, reaching more than 5000 billion between 1990 and 2000. Doll and Peto have estimated that tobacco accounts for approximately one-third of cancers in the affluent nations. It has also become clear that Rush's concern, some 200 years ago, of the dual ills of tobacco and alcohol consumption was well-founded, since cancers of the upper digestive tract and liver are greatly increased by a combination of high alcohol intake and smoking.

## THE CHALLENGE

Prior to the Industrial Revolution, the incidence of cancer was much lower, perhaps one-third of its present level

in affluent nations. Infections were much more important causes of cancer, as they are today in developing countries where infections can account for 25% or more of all cancers. The social and medical changes that dramatically reduced the incidence of many infectious diseases in affluent societies, ought, then, to have led to a reduction of the incidence of cancer. Unfortunately, while infectious diseases today are a less important cause of cancer in the affluent nations (accounting for perhaps 15% of cancers), this advantage has been far outweighed by the increase in cancer relating to smoking and dietary excesses. As developing countries become increasingly industrialized, they are likely to witness a similar increase in cancer. But whereas the emergence of the "cancer epidemic" associated with the ready availability of manufactured cigarettes and the increased consumption of more affluent populations in the 20<sup>th</sup> century was largely unanticipated, today, the growth of science and technology has provided sufficient knowledge to be able to establish effective cancer control programs across the globe. The challenge, as highlighted recently by the Director of the National Cancer Institute of the USA, is to use that knowledge to markedly reduce mortality from cancer.

The incidence of cancer caused by infections is likely to decrease in developing countries, perhaps dramatically, in the course of the next 20 to 30 years, both as a result of increasing socioeconomic development, and from the introduction of more effective anti-infection measures (e.g., vaccination against the Human Papilloma Virus, responsible for over 90% of cases of cervical cancer). Unfortunately, it is likely to prove much more

"In no one view, it is possible to contemplate the creature man in a more absurd and ridiculous light, than in his attachment to tobacco."

—Dr. Benjamin Rush,  
*Essays Literal, Moral and Philosophical, 1798*

difficult to curb the growth of smoking habits and to ensure healthy eating. The World Health Organization estimates that since 1950 at least 10 million people have died from smoking in developing countries, and in the next 20 years, there could be an additional 70 million deaths. But some countries are still in the early stages of the epidemic, e.g., many African and South Asian countries, where the incidence of lung cancer is still less than 10 per 100,000 and cigarette consumption is less than 500 per person per year (compared to over 2500 per year in the countries that consume the most cigarettes). In such countries, preventing more people from smoking would have an enormously beneficial impact. Meeting this challenge will require the combined will of individuals and governments, the active cooperation of industry and the transfer of knowledge and resources from richer to poorer countries. One might be forgiven, in the light of history, competing interests and the limited resources of developing countries, for believing it more likely that the prediction of the International Agency for Research on Cancer—that cancer incidence will have increased by at least 50% (based on predicted population growth alone) and probably more, by the year 2020—will be fulfilled. ■

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## PERSPECTIVES IN CERVICAL CANCER PREVENTION IN INDIA

Carcinoma of the uterine cervix is the most common cancer in South Indian women and occupies the top rank among cancers in women in most developing countries, constituting 34% of all women's cancers. To an estimated annual global incidence of 500,000 cervical cancers, India contributes 100,000, i.e. 1/5 of the world burden.<sup>1</sup> The magnitude of the problem is thus more than evident. The world pattern of cervical cancer, together with the age adjusted rate and ranking, clearly indicate that cervical cancer is predominantly a problem of poorer socio-economic societies.<sup>1</sup>

On the other hand, uterine cervical cancer is a favourable site for an effective control program. It is easily accessible and there is usually a long latent period of intraepithelial neoplasia which is easily recognizable by the Pap smear. Furthermore, treatment at this stage is very effective.

The burden of cervical cancer in India, taken in the context of the additional problems of advanced disease at presentation, the country's limited resources and health infrastructure, and the paucity of trained personnel emphasize the urgent need for a control program.

### PRIMARY PREVENTION

Accumulated evidence based on etiologic associations and the differential world pattern points to cervical cancer being a preventable disease. Sexual hygiene and the use of barrier contraception (condom) may largely achieve this objective but there is a need for long-term education and acceptance. Improvements in socio-economic standards would automati-



Photo courtesy of FreeStockPhotos.com

**The married women of rural India are most at risk for cervical cancers.**

cally reduce morbidity and mortality<sup>2</sup> but this again is a long-term process.

Primary prevention, then, involves the education of a large segment of the population, especially the high risk groups, through mass media such as radio, TV & video cassettes, about sexual hygiene, barrier contraception and control of HPV infection.

### SECONDARY PREVENTION

Secondary prevention assumes vital importance in the context of the hurdles in implementing primary prevention methods. In a large country such India with a large, growing population and limited resources, population screening by Pap smear is neither pragmatic nor cost-effective. It is thus essential that we evolve our own strategies.

### HIGH-RISK GROUPS

The risk factors for cervical cancer in India are socio-economic, viz. they relate to education and income, personal lifestyle, religion, multiple partners and sexual exposure prior to the

age of 18. There is no doubt that cervical cancer is closely associated with sexual activity and promiscuity. There is no recorded case of squamous cell carcinoma of the cervix in a nun.

Extensive viral carcinogenesis studies the world over point to Human Papilloma Virus (HPV) as an important factor in cervical carcinogenesis. Of the many HPV types, types 16 and 18 are documented as high-risk HPV associated with genital neoplasia. Although a cause and effect relationship between HPV and cervical cancer is yet to be proven, over 80% of cervical cancers today are associated with HPV infection.

The first IARC-sponsored case control study on HPV and cervical cancer in India, which was carried out at the Cancer Institute, Chennai, documented that 99% of uterine cervical cancers were HPV-positive compared to only 22% in the controls.

Preventive vaccination is under intensive study.

### TARGET POPULATION

Based on our registry data, the women most at risk for cervical cancers are married women over the age of 35 years, in the low socio-economic strata, with little or no education. Since over 80% of the population of India is rural, the focus has to be on rural women, essentially agricultural workers. This however is precisely the group that resists any progressive health program unless handled with understanding, circumspection and sympathy.

Accepted methods for early cervical cancer detection and control for a developing environment include:

1. Education; access to health care
2. Unaided visual inspection and clinical downstaging
3. Aided Visual Inspection (VIA)<sup>3</sup>
4. VIA with magnification (VIAM)
5. HPV testing
6. Cytology

### CERVICAL CANCER SCREENING IN AFFLUENT COUNTRIES

Cervical cancer screening has been documented to be effective in many affluent countries. After the successful British Columbia screening campaign in 1949, it is estimated that 85% of the population now at risk are screened annually, with a sharp drop in the incidence of invasive cervical cancer by about 78% and a similar reduction in mortality. Organized screening programs in Nordic countries have demonstrated a 50% reduction in mortality in Iceland and Finland which have instituted nationwide screening. In Denmark, 40% coverage resulted in a 25% reduction in mortality while in Norway, with only 5% coverage, the mortality fell by only 10%<sup>4</sup>. In the UK cervical cancer screening program, it is estimated

that 800 lives are saved annually, at a cost of £124 million/year<sup>5</sup>.

While effective, the cost effectiveness of such screening programs has yet to be demonstrated.

### INDIAN STUDIES

A number of screening projects by individual institutions, conducted either in collaboration with IARC or on their own, have been undertaken or are ongoing. The ongoing IARC collaborative projects comprise both randomized and non-randomized, controlled intervention studies for evaluation of different methodologies in early detection. A total of 457,000 women are being evaluated in the eight ongoing studies, but this constitutes hardly 0.25% of the total eligible women at risk.

From the available studies, the most useful and affordable methodology now appears to be aided visual inspection. Cytology, colposcopy and HPV DNA testing can be included wherever possible. A study undertaken by the Nargis Dutt Memorial Cancer Hospital at Barshi, in collaboration with IARC<sup>6</sup>, demonstrated a significantly higher percentage of women with early stage cancers reporting for treatment in the intervention arm, 66% with Stage I and II disease compared with 25% in the control arm. The intervention group was provided with an effective education and awareness program; no such programs existed in the control group. This highlights the vital role of education in any prevention program.

### EVOLUTION IN CONCEPTS FOR CERVICAL CANCER CONTROL – THE CANCER INSTITUTE EXPERIENCE

*Chingleput survey:* The first hospital-based, rural survey of cancer conducted in Chingleput district in 1961-



**A healthcare worker from the Cancer Institute in Chennai visits women for cervical cancer screening in the privacy of their homes.**

62 clearly demonstrated that routine clinical screening of *all women* attending the rural hospitals for whatever complaint could detect cancers in the early stages (70% as compared to 5.7% in the hospital registry (61-62)<sup>7</sup>. This finding underscored the imperative need for a rural cervical screening program to clinically downstage the disease which would contribute to more effective treatment, and laid the foundation for the first WHO pilot cancer control program, established in Kancheepuram in 1969.

*Feasibility Project:* It is on the basis of this background that the feasibility study to train village health nurses (VHNs) in the visual and digital detection of an abnormal cervix was undertaken in 1991-92 and was funded by the ICMR.<sup>8</sup> 101 VHNs were trained, 6450 eligible women were screened and abnormalities were detected in 985 women. All cancers and pre-cancers were referred to the Institute for treatment, free of charge. The project concluded that the VHN is competent and capable of being trained in the visual detection of an abnormal cervix with a concordance rate of over 90%.

The feasibility project in South Arcot also concluded that a rural cer-

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vical screening program was very worthwhile with a cervical cancer pick-up rate of 115.92/100,000 women and that a cervical smear is desirable but not mandatory. A simple visual and digital examination could detect 45% of early disease. It is realized that precancers were missed but the introduction of aided visual inspection may overcome this.

## PLANNING A DISTRICT CANCER CONTROL PROGRAM, 1992

Our experience in oncologic care over the last 50 years has taught us that India has to evolve her own screening strategies. The concepts of cancer control and prevention have to be based on the pattern of cancer incidence, health infrastructure and economy of the country. We cannot attempt to replicate the strategies of the affluent countries. The conclusions that we have drawn based on our experience can thus relate only to our area—India and a few other countries such as Sri Lanka and Nepal. They cannot be applied to countries like Bangladesh and Pakistan where the cancer patterns and cultural practices are different, nor to other Asian countries like China, Korea and Singapore, which have excellent healthcare infrastructure.

The incidence of late disease in most of the affluent countries is about 10-12%, in British Columbia, about 3-4%, whereas in India it is almost 70-76%. **Our highest priority will therefore be to identify disease earlier, at least Stage IB** where the cure rate can be as high as 85%.

It is fortunate that the uterine cervix is an accessible site with early symptomatology. The negative aspect is the ignorance of the rural women, the traditional reluctance of women to seek medical aid, especially



Photo courtesy of FreeStockPhotos.com

**Cervical cancer screening conducted in rural hospitals as part of a routine physical exam may be effective at improving early detection.**

for gynaecologic complaints, added to the readily available, indigenous medical quackery.

Since the majority of women at risk live in villages, the primary healthcare personnel that need to be motivated for early detection are the village teachers, block health inspectors and the VHN. Such personnel are generally resident in the village. The VHN is readily available and when trained and sufficiently motivated, should be the central instrument of implementation.

The district-level Cervical Cancer Early Detection Program in South Arcot District was initiated in 1992 and funded by the Government of India. The objectives were to train all women doctors in the district and Taluk hospitals and primary health centers in the early detection of cervical cancer, to train VHNs in visual inspection and digital examination for detection of an abnormal cervix and to take a Pap smear. Further aims were to train cytology technicians who would be located in the district

hospital itself, to train district block health educators, village school teachers, nutrition programmers and other volunteers, and provide them with educational material on cancer and early detection. Such health education will be ongoing and the trained VHNs will motivate women to accept screening through health education.

The overall objective of this plan was to integrate the screening and education program with the State's permanent health infrastructure and delivery system, since this could significantly reduce cost.

The project trained 258 doctors, 672 village health nurses and 30 block health educators. 59,314 women were screened, 8,514 Pap smears were done for those with an abnormal cervix on visual inspection and 20 pre-cancers were detected, with a pick-up rate of 230/100,000 screened. In addition, 310 clinical cervical cancers were detected (12.3% early and 87.7% late disease.) However, we faced significant hurdles in implementing the screening at the primary health center level. The majority of women screened were from the District or Taluk hospitals and very few from primary health centers.

## CONCLUSION

Based on the above experience, we feel that a multi-tier model, based on the local healthcare infrastructure, is practical. Our experience however, stresses:

1. The need for a separate cancer network within the framework of the health infrastructure.
2. A very committed and motivated team, preferably supported by a non-governmental agency with adequate financial support, either national or international.



3. The program could be initiated in a limited way and later extended, depending on the results.

4. In all future projects, aided visual inspection should replace unaided inspection.

5. Women with an abnormal cervix should have additional studies including: Pap smear, biopsy, colposcopy and HPV DNA testing wherever possible.

The UICC and IARC have expressed doubts about the value of clinical downstaging, but our experience is different. The discussion on frequency of screening will be academic in our situation. If we can examine all of the eligible women at least once in a lifetime, much will have been achieved. ■

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## ADVANCED CERVICAL CANCER AFTER UNTREATED CIN

### SUMMARY

A case is presented of advanced uterine cervical cancer treatment for CIN (Cervical Intraepithelial Neoplasia) in a Peruvian woman.

### CASE REPORT

A 35 year-old female of low socio-economic background coming from a small village far from the capital, gravida 6, para 5, first coitus at age of 15, with a history of multiple sexual partners, presented with a Pap smear suggestive of CIN III (HSIL). Repeat cytology performed on arrival at the triage clinic was consistent with HSIL. Colposcopy performed next day at the dysplasia clinic showed an area of thick, acetowhite epithelium with a punctation pattern, extending up into the cervical canal (Fig. 1). Colposcopically directed biopsy reported two weeks later was consistent with CIN III; endocervical curettage was negative.

Because of endocervical involvement, the patient was scheduled for cryosurgery to be performed as an inpatient procedure three weeks later due to the great demand for hospital beds. In the meantime, she ran out of money and was unable to stay in the capital any longer. She was lost to follow-up for five years. In May 2002, she presented again with episodes of heavy vaginal bleeding and pain referred to the flank. Physical examination revealed a 4.5 x 3.5 cms. exophytic cervical mass (Fig. 2) extending into both parametria, reaching the right pelvic wall, corresponding to a mid-differentiated, squamous cell carcinoma, clinical stage IIIb. She received external pelvic radiotherapy

with a 60 Cobalt machine to a total of 5,000 cGy, followed by intracavitary radium brachytherapy, reaching an overall tumor dose of 9000 cGy. Follow-up at six months revealed persistence of unresectable disease at the cervix and parametria. She was referred to the medical oncologist for consideration of chemotherapy, but financial limitations prevented her from being treated. She was lost to follow-up again, with persistent disease.

### DISCUSSION

Cancer of the uterine cervix is the most prevalent female malignancy in the majority of developing countries. Worldwide, it is estimated that 500,000 new cases are diagnosed each year, 80% of these in the developing world, and that half of these patients will die. Although in Lima, the capital of Peru, female cancer figures are changing, with breast carcinoma displacing cervical cancer to the second position in incidence<sup>1</sup>, in the rest of the country, as represented by the Trujillo Cancer Registry<sup>2</sup>, cervical carcinoma is the primary cause of cancer-related mortality in women. It is a real public health problem affecting women of reproductive age with heavy family burden, like the present case. It is a compound picture, involving mainly socio-cultural and economic aspects that prevent women from being screened and treated at an early, curable stage of disease. The same factors also account for patients being denied access to modern standards of advanced disease management, such as chemoradiation and radiotherapy using a linear accelerator.

Our patient exemplifies very well the difficulties that face most of the developing world's women in access-

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**Figure 1.** The patient first presented with a preneoplastic lesion, but never received cryosurgery.

ing health care and, specifically, oncologic care. Although she had a Pap smear, she was not able to benefit either from treatment for early disease or from chemoradiation at a later stage. In this setting, the offer of early detection and cancer treatment is scarce. Until a more definitive solution (HPV vaccines) arrives, we are convinced that the most cost-effective strategy to decrease the incidence and mortality of the cervical cancer is to reinforce secondary prevention. Classic, cytology-based screening programs have been successful in achieving that goal in industrialized countries, but they have almost uniformly failed in the developing world. Furthermore, as occurred with our patient, less than 30% of women with a positive Pap smear receive treatment in Perú.<sup>3</sup> They are lost in the course of the expensive and time-consuming diagnostic workup. So, alternative diagnostic and therapeutic approaches, better tailored to our needs and resources, are urgently needed in order to avoid patients being lost to follow-up. Secondary prevention based on visual inspection<sup>4</sup> and single session management<sup>3</sup>, using outpatient cryosurgery or



**Figure 2.** Lost to follow-up, the patient returned five years later with invasive cancer.

electrosurgical loop excision (LEEP) as therapeutic modalities, are promising strategies currently being tested in some protocols and awaiting final validation and wider dissemination in low resource settings.

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## CERVICAL CANCER PREVENTION: IARC/INCTR JOINT PROJECTS IN NEPAL AND TANZANIA

The International Agency for Research on Cancer (IARC), the cancer research agency of the World Health Organization (WHO) located in Lyon, France, is collaborating with the International Network for Cancer Treatment & Research (INCTR) in organizing cervical cancer prevention programs in Nepal and Tanzania where cervical cancer is the most common cancer among women.

Currently, more than 80% of the women diagnosed with cervical cancer in these countries present with locally advanced disease. Although early detection and effective treatment of cervical cancer precursor lesions will prevent the development of cervical cancer, there are currently no organized screening or early detection programs in Nepal and Tanzania as in many other developing countries. Furthermore, it is now widely recognized that cervical cytology-based screening is not feasible in these countries, due to limited manpower and financial resources.

IARC and INCTR are therefore working together with national institutions in both countries, to evaluate the role of alternative, low-technology approaches. Specific projects addressing these issues are supported by the Bill & Melinda Gates Foundation through the Alliance for Cervical Cancer Prevention (ACCP), of which IARC is a member, and by the WHO Regional Office for the African Region (WHO/AFRO). The participating institutions in Nepal are Bhakthapur Cancer Care Centre (BCCC), and the Nepal Network of Cancer Treatment and Research (NNCTR/INCTR), Banepa,

both located near Kathmandu. The Ocean Road Cancer Institute (OCRI) in Dar es Salaam is the partner institution in Tanzania (see pgs 18-19). The prevention programs are coordinated by Dr R. Sankaranarayanan (IARC), Ms. Melissa Adde (INCTR), Dr A. Felipe (Jr) (AFRO), Dr Aarati Shah (BCCC, Bhaktapur), Dr Surendra Shrestha (NNCTR, Banepa) and Dr Twalib Ngoma (OCRI, Dar es Salaam).

The screening tests, using visual inspection with acetic acid (VIA) and visual inspection with Lugol's iodine (VILI), are carried out by trained nurses and female health workers. VIA involves the application of 5% acetic acid to the cervix. Detection of a definite white area touching the squamocolumnar junction constitutes a positive test. Detection of yellow, non-iodine uptake areas in the transformation zone of the cervix, after application of Lugol's iodine solution, constitutes a positive VILI test.

The use of these services does not require a laboratory infrastructure, and the results are obtained immedi-



**Doctors in Bhaktapur, Nepal, learn how to perform the loop electrosurgical excision procedure (LEEP) during a training course sponsored jointly by IARC and INCTR in March.**

ately, allowing for investigation and treatment on the same day. The accuracy of the two methods in detecting high-grade cancer precursor lesions, and the effectiveness of simple treatment such as cryotherapy and loop electrosurgical excision procedure (LEEP), are being evaluated. Cryotherapy involves application of ice-cold metallic probes with surface temperatures below  $-65^{\circ}\text{C}$  to the cervix, leading to the eventual destruction of the abnormal cells. LEEP is an excisional treatment using an electrically activated thin stainless steel wire loop electrode.

Five thousand women, aged 30-59 years, will be screened using VIA and VILI at each project site in Nepal. Those identified

as positive, on one or both tests, will be investigated further with colposcopy, and biopsies will subsequently be taken in those with abnormal findings. Women with histologically confirmed cervical intraepithelial neoplasia grades 2 and 3 (CIN 2 and CIN 3), located on the ectocervix, without extension into the cervical canal will then be randomized to receive 'single'- or 'double-freeze' cryotherapy treatment. 'Single-freeze' cryotherapy involves a single cycle of freezing of the cervix for three minutes, while 'double-freeze' involves two cycles of three-minute freezing, with an interval of five minutes. Comparison of the cure rates with the two methods will be carried out one year after treatment. If the 'single-freeze' treatment is found to be as effective as the 'double-freeze' method, it will lead to savings in costs. The findings from these two studies will be pooled with those from a large multicentre IARC study. Larger lesions that cannot adequately be covered by the



**Doctors in Tanzania learn how to perform examinations with a colposcope during a training session sponsored jointly by IARC and INCTR.**

# NETWORK

cryoprobes, or lesions extending into the endocervix, will be treated by LEEP. The detection rates for high-grade lesions (per 1,000 women) associated with the screening tests will also be compared to indirectly assess the sensitivities of the tests.

In Tanzania, 5,000 women aged 25-59 years will be screened with VIA and VILI. All women will also be investigated by colposcopy (irrespective of the screening findings) and biopsies carried out in those with abnormalities. This study design will help to evaluate the sensitivity and specificity of the screening tests directly, without any verification bias. In this project, all grades of CIN lesion will be treated, either with cryotherapy or LEEP.

A regional training center for cervical cancer prevention has also been established at the Ocean Road Cancer Institute to facilitate the training of staff in all aspects of screening and treatment of cervical neoplasia, with the ultimate objective of catalyzing the development of such services in the region.

Women diagnosed with invasive cancer in these two programs will be referred for treatment in Bhaktapur and Kathmandu, or Dar es Salaam respectively, where surgical and radiotherapy services are available.

INCTR is also working with IARC on the publication and dissemination of simple practical manuals on VIA, VILI, colposcopy and treatment of cervical cancer precursor lesions. Nurses and

doctors involved in the projects described above have been intensively trained in screening, colposcopy, cryotherapy and LEEP, in courses jointly organized by the IARC, INCTR and WHO/



**A health worker explains the cervical screening program to women visiting the Ocean Road Cancer Institute in Tanzania.**

AFRO. The medical personnel will gain lots of experience as these projects progress over the next few months. It is hoped that they will eventually emerge as a core group of master trainers, facilitating further training and the expansion of preventive services in the regions. Cervical cancer preventive services were not available in these countries before the establishment of these projects. Thus, these programs now serve as a platform for screening and treatment. IARC and INCTR will work together to ensure that the research objectives are also successfully addressed and that the projects are sustained and expanded to provide wider services and training opportunities in these countries and regions in the future. ■

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## BBF SUPPORTS PEDIATRIC CANCER INITIATIVES

The Banco do Brasil Foundation (BBF) historically has worked to promote public health and social welfare programs to aid the Brazilian people. With its initiative in pediatric cancer, BBF is developing strategies, providing equipment and influencing public policies that are improving the chances of survival for children with cancer throughout the country, but particularly in Brazil's poorest regions.

In 1997, the prospect for most Brazilian children with cancer was bleak: of the nearly 7,000 cases each year, the majority were diagnosed in advanced stages of the disease, the quality of care available at treatment centers varied from region to region, and there was little statistical data available to help medical professionals determine the evolution of the disease in that country. The data suggested that of those 7,000 cases each year, only 4,600 were effectively treated. In the country's poorest regions—the North and Northeast—cure rates were as low as 30%. BBF launched its Programa Criança e Vida (Child and Life Program) in partnership with the Brazilian Ministry of Health in 1997 and a team of pediatric cancer specialists to turn this scenario around.

José Jaime Bastos, a hematologist and technical manager of the program, says that his organization already is making a difference. Since 1997, the Foundation has been working to establish a national network of hospitals that can provide precise and early diagnosis and adequate treatment. Money is also being directed to enhance, modernize and equip both public and philanthropic hospitals that treat children and adolescents

## MAKING A DIFFERENCE

with cancer. More than 5,100 children and adolescents have been assisted by these endeavors.

Since the inception of *Programa Criança e Vida*, eight strategically located hospitals have been provided with four laboratories for cancer diagnosis, conducting exams of pathologic anatomy, cytogenetics, immuno-phenotype and molecular biology. These eight hospitals will be responsible for working as Reference Centers for pediatric cancer laboratory diagnosis. At present, five laboratories are fully functional in São Paulo, Campinas, Rio de Janeiro, Santa Maria and Recife, and by the end of this year three more will be completely operative in Brasília, Fortaleza and Belo Horizonte.

The Foundation also supported the technical training and continuing education of 2,500 professionals—specialists in pediatric cancer and other medical professionals who are directly working with the children.

An academic study of assistance housing (where children and their parents can reside for the duration of cancer therapy) is under negotiation with a Brazilian university.

With the collaboration of SOBOPE (Brazilian Society of Pediatric Oncology) and of the Ministry of Health, a huge national data bank called CIOPE (Informatized Centre for Pediatric Oncology) has been established to gather and to make available information about pediatric cancer in Brazil, including epidemiology, clinical characteristics, its evolution, and the evaluation of immediate and late effects of treatment.

Of 41 institutions that provide structured pediatric oncology services in the country, 19 have already been selected to receive financial support for the acquisition of equip-



**Children undergoing treatment at the Pediatric Oncology Hospital of the Medical University of São Paulo gather to help celebrate the inauguration of four laboratories for cancer diagnosis, which are supported by Banco do Brasil Foundation.**

ment and furniture in order to improve treatment conditions. Five of these hospitals, located in Teresina, Aracaju, Vitória, Fortaleza and Natal have inaugurated their rebuilding projects and 10 more will be inaugurated this year.

Over the past five years, BBF has invested US \$5.5 million in its Child and Life Program.

"Nowadays regional differences are decreasing," Bastos says. "Soon we will be able to affirm that regardless of the region in which children are treated, they will have an equal chance of being cured." Important progress continues to be made in the areas of early diagnosis and systemizing therapeutic protocols.

The Child and Life Program is also playing an important role in articulating and mobilizing government representatives in order to set new public policies that regulate cancer diagnosis and treatment, and in strength-

ening the Strategic Alliance Against Pediatric Cancer, a Brazilian movement that since last year has been working to coordinate efforts among the many involved in the fight against cancer: government, specialists, medical associations, non-governmental organizations, foundations, volunteers and assistance houses.

"As we started to fight against pediatric cancer we were encouraged on many fronts," Bastos says, "particularly the improvement of work conditions for doctors, and the increase in the number of hospitals providing quality care. We have made a historic step toward the standardization of laboratory routines, the augmentation of information and knowledge exchange between medical professionals, and, most importantly, the increase of cure levels." ■

*M. Landskroener  
for INCTR*

# NETWORK

## TREINTA Y CINCO AÑOS DE ESTUDIOS CLINICOS CONTROLADOS EN HEMOPATIAS MALIGNAS EN ARGENTINA Y LATINOAMERICA

En la década del sesenta el pronóstico de las leucemias agudas era muy pobre con menos del 1% de sobrevida a cinco años en Argentina (1). En linfomas de Hodgkin el 40% de los pacientes pediátricos y adultos estaban vivos a los 5 años, siendo algo mejor el pronóstico en los estadios localizados. *Tabla 1 y 2.* El primer esfuerzo para desarrollar ensayos clínicos se inició en un estudio multicéntrico cooperativo en Argentina creándose el Grupo Argentino de Tratamiento de la Leucemia Aguda (GATLA) con un protocolo para Leucemias Agudas en noviembre de 1967(2). En 1969, se inició el primer protocolo para linfomas (no Hodgkin y Hodgkin) empleando COPP. En 1973, se iniciaron protocolos para Linfomas Pediátricos, Mieloma Múltiple y Leucemia Linfoide Crónica



FUNDALEU is a nonprofit organization devoted to the treatment and research of hematological malignancies.

(3-6).

En 1973 se crea el Grupo Latinoamericano de Tratamiento de Hemopatías Malignas (GLATHEM), con oficina operativa en el GATLA en Buenos Aires. Varios Centros en Latinoamérica de Argentina, Brasil, Chile, Costa Rica, Cuba, Méjico y Uruguay participaron de los ensayos clínicos.(2)

En 1977, el Instituto Nacional del Cáncer de USA bajo el liderazgo del Dr.Franco Muggia del Cancer Therapy Evaluation Program y el Dr Gregory O'Connor del International Affairs Office y con el soporte técnico de la Organización Panamericana de la Salud se inició el Collaborative Cancer Treatment Research Program (CCTRP). El programa incluía 10 Instituciones pares en centros de Cáncer en Latinoamérica y USA. Se desarrollaron numerosos protocolos bilaterales y luego multicéntricos en Tumores Sólidos y Enfermedades Malignas Hematológicas. Este programa funcionó hasta 1986 desarrollando protocolos en cáncer de mama, cuello uterino, cabeza y cuello, melanoma, osteosarcoma, leucemias, mieloma múltiple y linfomas y permitió que muchos investigadores clínicos jóvenes

puieran entrenarse en Centros de Cáncer en USA.

Hasta Noviembre de 2002, el GATLA-GLATHEM iniciaron y completaron 42 protocolos en todas las enfermedades malignas hematólogicas tanto en niños como adultos incorporando 14.385 pacientes.De la evaluación de esos protocolos surgieron numerosas presentaciones a Congresos Nacionales, Regionales e Internacionales (ASH, ASCO, ESMO, SIOP, ISH, UICC). Además se publicaron los resultados de mas de 100 manuscritos en revistas líderes en la especialidad como Blood, J Clin Oncol, Cancer; Cancer Treat Rep, J Natl Cancer Inst, Brit J Haematol, Ann Oncol, Ann Hematol, Am J Pediatr Hematol/ Oncol, Sangre, Medicina, etc)

El progreso en la sobrevida fue mas marcado en las décadas del setenta y ochenta con el comienzo de protocolos terapéuticos y su desarrollo incorporando dosis mas altas de quimioterapia de consolidación, mejor soporte de hemoterapia y complicaciones infecciosas. Estos resultados fueron mucho más evidentes en la población pediátrica, con índices de curación comparable a series en países más desarrollados.La década del noventa

Tabla 1

### Progreso en 5 años de sobrevida en niños con hemopatías malignas según décadas

#### Ensayos Clínicos GATLA - GLATHEM

Enfermedad	<1968 %SV	# Pts 1968-1980 % SV	# Pts 1981-1990 # SV	# Pts 1991-2002 % SV	P= *	Ref
LLA	<1	1137 32	2130 56	1920 66	.001	1,2
LMA	<1	214 2	226 27	282 40	.001	
E. Hodgkin	<40	119 82	268 90	124 91	.045	6
Linfoma	<20	120 36	282 61	254 72	.001	3

\* Comparación entre décadas de tratamiento desde 1968

se caracterizó por desarrollar protocolos más adaptados a los factores pronósticos (edad, estadio clínico, citogenéticos, biológicos como LDH y  $\beta$  Microglobulina, moleculares, etc) con el fin de incrementar los porcentajes de respuesta y cura en los grupos de mal pronóstico y reducir la toxicidad manteniendo los logros en los pacientes de buen pronóstico. *Tabla 1 y 2*

En la presente década nos enfrentamos con nuevos desafíos, como el alto costo de las nuevas drogas por ejemplo anticuerpos monoclonales (Rituximab, Alemtuzumab y Milotarg) y nuevas drogas como los análogos de las purinas para síndromes linfoproliferativos y el imatinib en la leucemia mieloide crónica.

Otro factor a definir mejor es la utilidad de las altas dosis de quimioterapia ablativa y rescate con células progenitoras hematopoyéticas tanto autólogas como alogénicas. El alto costo de los nuevos avances terapéuticos afectan los presupuestos en salud pública de los países desarrollados y con mucho más razón esto se ve reflejado en países en desarrollo, es especial en pacientes que carecen de cobertura médica.

El GATLA está participando en estudios colaborativos internacionales controlados con el aporte de muchos países y en los que se requiere un gran número de pacientes para obtener diferencias significativas entre las estrategias terapéuticas en estudio. ■

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**Tabla 2**

<b>Progreso en 5 años de sobrevida en adultos con hemopatías malignas según décadas</b>									
<b>Ensayos Clínicos GATLA - GLATHEM</b>									
Enfermedad	<1968 %SV	# Pts	1968-1980 % SV	# Pts	1981-1990 # SV	# Pts	1991-2002 % SV	P= *	Ref
<b>LLA</b>	<b>&lt;1</b>	<b>214</b>	<b>22</b>	<b>295</b>	<b>36</b>	<b>112</b>	<b>39</b>	<b>.001</b>	<b>1,2</b>
<b>LMA</b>	<b>&lt;1</b>	<b>485</b>	<b>4</b>	<b>184</b>	<b>9</b>	<b>228</b>	<b>27</b>	<b>.001</b>	<b>2</b>
<b>E. Hodgkin</b>	<b>&lt;40</b>	<b>439</b>	<b>66</b>	<b>387</b>	<b>76</b>	<b>172</b>	<b>86</b>	<b>.001</b>	<b>6</b>
<b>LNH BG</b>	<b>&lt;30</b>	<b>161</b>	<b>57</b>	<b>178</b>	<b>63</b>	<b>108</b>	<b>72</b>	<b>.041</b>	
<b>LNH AG</b>	<b>&lt;10</b>	<b>333</b>	<b>33</b>	<b>506</b>	<b>50</b>	<b>186</b>	<b>57</b>	<b>.001</b>	
<b>Mieloma</b>	<b>&lt;10</b>	<b>320</b>	<b>25</b>	<b>187</b>	<b>27</b>	<b>134</b>	<b>31</b>	<b>.003</b>	
<b>SV: Sobrevida</b>		<b>Pts: Pacientes</b>							

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**THIRTY-FIVE YEARS OF CLINICAL TRIALS IN HEMATOLOGICAL MALIGNANCIES IN ARGENTINA AND LATIN AMERICA**

**Prior to 1967, the prognosis of the acute leukemias, lymphomas and myeloma was poor, mainly due to lack of effective drugs and therapeutic protocols. The Argentine Group of Treatment of Acute Leukemia (GATLA) was created in November, 1967, and the Latin American Group for Treatment of Haematological Malignancies (GLATHEM) in 1973.**

**Up to November 2002, 42 protocols have been used in 14,385 adult and pediatric patients with acute leukemia, lymphoma, Hodgkin's disease and multiple myeloma. A continuous improvement in survival was observed in all the diseases, especially in children (Tables 1 and 2) (1-6).**

**More than 100 manuscripts have been published in peer reviewed journals.**

# NETWORK

## LE RÔLE DES INFIRMIÈRES AFRICAINES DANS LA LUTTE CONTRE LES CANCERS

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A l'heure actuelle la lutte contre le cancer ne représente pas encore une priorité de santé publique en Afrique Subsaharienne. Cette pathologie est pourtant en progression constante dans cette région défavorisée du monde. Le prix élevé des trop rares médicaments disponibles sur les marchés locaux, le manque de structures de soins et enfin la carence d'équipes médicales spécialisées en oncologie ne facilitent malheureusement pas la prise en charge de ce type de maladie.

Le deuxième congrès médical Euro-Africain, qui s'est déroulé à Yaoundé en mars dernier, a voulu répondre à la question de la pénurie d'équipes médicales spécialisées par une journée de formation et de sensibilisation destinée plus particulièrement au personnel paramédical. Cet atelier a permis de cerner les problèmes auxquels les différents intervenants médicaux sont confrontés dans la pratique ainsi que de mesurer l'importance du rôle que pourrait tenir les infirmiers pour combler le manque de médecins disponibles sur le continent africain.

Les 28 infirmiers camerounais présents lors du congrès ont ainsi pu bénéficier d'une double formation qui leur était tout spécialement destinée : la première étant axée sur les modalités d'utilisation et de surveillance de la chimiothérapie, la seconde sur la dispense de soins palliatifs dans une stricte démarche de soins infirmiers. Bien que travaillant pour la grande majorité dans des structures hospitalières, aucun d'entre eux n'avaient avant ce

jour pu bénéficier d'une « mise à niveau » significative en oncologie.

Au terme de cette journée, médecins et infirmières ont souligné, une fois de plus, l'importance que devait revêtir la formation des professionnels de santé d'une part pour la prise en charge et l'accompagnement des malades, d'autre part pour la mise en œuvre d'actions de prévention et d'information des facteurs de risques notamment pour les cancers viro-induits. Chacun des intervenants s'accordant à demander un enseignement spécifique en oncologie pour les infirmières. La formation continue de ces infirmières, grâce au programme des « Visiting Experts » et la diffusion de brochures d'information adaptées à une réalité rencontrée sur le terrain, est tout aussi cruciale pour une meilleure prise en charge de leurs malades. La création de modules d'information et de sensibilisation plus spécifiquement adaptés aux agents de santé et aux infirmières travaillant en brousse (prévention, diagnostic précoce, dépistage) représente une autre priorité.

Ces différentes actions devraient permettre dans une certaine mesure de rompre l'isolement que ressent le personnel infirmier africain dans le domaine de la lutte contre le cancer.

Mme Sabine Perrier-Bonnet, porte-parole de l'AMCC-INCTR et organisatrice de cette formation s'est engagée à transmettre l'expression de ces besoins en Europe et à donner suite, dans la mesure du possible, à la mise en place d'actions en faveur du personnel infirmier, pilier de la lutte contre le cancer auprès de la population. ■

*Sabine Perrier-Bonnet, AMCC/INCTR, Montpellier, France*

## FORMATION OF A MEXICAN GROUP FOR RETINOBLASTOMA

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INCTR staff members and Dr Judith Kingston, one of INCTR's visiting experts in retinoblastoma from St Bartholomew's Hospital in the UK, participated in a meeting to discuss the formation of a Mexican Group for Retinoblastoma (Grupo Mexicano de Retinoblastoma, GMR). The meeting took place in San Miguel Regla (Mexico), January 23-25, 2003. Supported by INCTR and the Mexican pharmaceutical industry, the meeting was recognized by the National Academy of Medicine of Mexico. Among the 36 participants were pediatric oncologists, ophthalmologists, pathologists and radiotherapists from the major centers involved in the treatment of children with retinoblastoma in Mexico. A number of topics relevant to the function of the group were discussed, including optimal methods of communication, the creation of a national registry for retinoblastoma, available resources, standards of diagnosis and care, and early diagnosis. The next meeting is set for July 2003 in Guadalajara.

After participating in the GMR meeting, Kingston, a pediatric oncologist, visited the INP in Mexico City to participate in ward rounds, clinics and discussions pertaining to INP's retinoblastoma program. She was accompanied by INCTR's Renate Smith. ■

## BREAST CANCER STRATEGY GROUP MEETING

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The second meeting of INCTR's Breast Cancer Strategy Group, this time a subcommittee of four persons (from Egypt, India, Pakistan and Peru), took



place at the INCTR offices in Brussels in late January. INCTR staff and outside expert Dr Leclerq from the Institut Jules Bordet in Brussels met with the group. After each participant had presented information regarding breast cancer at his or her own center, Dr Leclerq discussed his institute's ongoing projects relating to the molecular analysis of breast cancer (BRCA1/2 mutations, studies in estrogen receptors and estrogen receptor-related proteins). The group then had wide-ranging discussions on breast cancer and resources available for diagnosis and treatment in developing countries. Because of the paucity of information regarding breast cancer in many countries, the group decided that it would be worthwhile to undertake a survey of breast cancer in those countries. Participants discussed the design of a data collection form that will be used by participating centers in the survey. The form will be prepared by INCTR's Clinical Trials Office for presentation at the next full meeting of the Breast Cancer Strategy Group, which will take up that matter as well as other topics for future studies, including molecular profiling and therapy, at the Annual Meeting in May. ■

## GENERAL ASSEMBLY AND GOVERNING COUNCIL MEETING

At INCTR's fourth General Assembly in February, expenditure for FY 2002 was reported and approved by the General Assembly and the composition of INCTR's Governing Council was discussed. Progress made in 2002 was outlined and planned programs and projects for 2003 presented. The budget for 2003 was approved. ■

## TRAINING WORKSHOP FOR CERVICAL CANCER SCREENING IN NEPAL

A training workshop was held at the Bhaktapur Cancer Center in Nepal for nurses, gynecologists and data managers who will be taking part in the joint IARC/INCTR cervical cancer screening project. This project will be undertaken at three sites: Bhaktapur Cancer Center, Scheer Hospital and Khoirola Cancer Center in Nepal. The training, which was supervised by Dr Sankaranyaranan of IARC, consisted of formal lectures and clinical training in the direct visualization methods that will be used for the screening process, as well as in colposcopy, biopsy, cryotherapy and loop electrosurgical excision. INCTR staff members attended the training workshop, and will be involved in the data management of this project. ■

## MEETING OF LEUKEMIA STUDY GROUP OF INDIA

Representatives (investigators and data managers) from participating institutions in the next clinical trial to be conducted by the Indian section of INCTR's Leukemia Strategy group met in India on March 15-16 with INCTR staff for the Investigators Initiation Meeting relating to the new treatment protocol. In the course of this meeting all aspects of the protocol itself, data management, data monitoring and regulatory issues were discussed. Each center was provided with a Data Management Manual to facilitate the data entry process. Patient accrual on the study will begin this summer, after necessary notifications and ethical reviews in India are completed. The clinical

trial will be supported in part by the Sir Ratan Tata Trust (Mumbai), and molecular analyses will be conducted in conjunction with the research center of the King Fahad Children's Medical Center in Riyadh. ■

## NCI OF CAIRO FOCUSES ON LUNG CANCER

The Annual Meeting of the NCI, Cairo, one of INCTR's Associate Members, was held in Sharm El Sheikh in South Sinai in late February. The meeting focused on lung cancer and smoking, and was jointly held with the lung cancer group of the European Organization for Research and Treatment of Cancer. Governor of Sharm El Sheikh opened the meeting, which was held while the Arab Summit was taking place in the same city. ■

## WEB SITE REVAMPED

INCTR's website has been updated with pictures from the last annual meeting ([www.inctr.org/meetings/2002photos.shtml](http://www.inctr.org/meetings/2002photos.shtml)) and news relating to strategy group activities ([www.inctr.org/organization/strategygroups.shtml](http://www.inctr.org/organization/strategygroups.shtml)). Comments on the website are welcome. ■

## EXPERT IN PALLIATIVE CARE VISITS NEPAL

Following his first visit to Nepal, reported in the last edition of NETWORK, Dr Brown made a second visit (February 7-14) to continue his work with NNCTR/INCTR to develop a palliative care group serving the Kathmandu region. A palliative care nurse specialist will visit soon. ■

# NETWORK

## OCEAN ROAD CANCER INSTITUTE

Tanzania is in East Africa and is the land of Kilimanjaro and the Zanzibar spice islands. Although it has abundant natural resources, it is one of the ten poorest countries in the world.

Since its independence from British rule in 1961, Tanzania has been spending its meager health care budget on the prevention of communicable diseases. Until very recently even medical students were taught that cancer is not a problem in Tanzania, and national policymakers have taken no keen interest in cancer prevention and treatment. In 1999 a workshop setting Tanzania's health-care and medical research priorities excluded cancer from the top ten diseases. No wonder that raising funds for cancer services in Tanzania is a struggle.

Tanzania has only one specialized center for the treatment of cancer—the Ocean Road Cancer Institute. Established by the government in 1996, OCRI evolved from the radiotherapy department of the university teaching hospital called Muhimbili. The services offered here include palliative care, radiotherapy, chemotherapy and cancer screening services. Surgical services are offered at Muhimbili Hospital.

At the OCRI, both the adults and children on chemotherapy are under the care of a medical oncologist. Until recently, we had a medical oncologist from Germany who has since completed his seven-year contract; local doctors who worked with him are continuing to take care of the chemotherapy patients. Two radiation oncologists who had their training in the United Kingdom are part of the medical oncology team. All cancer pa-



**The Ocean Road Cancer Institute is Tanzania's first and only cancer treatment center. INCTR and IARC recently conducted a cervical cancer screening workshop for OCRI staff.**

tients in Tanzania are exempted from cost-sharing for medical services, with the government paying the costs of services provided at OCRI.

The government of Tanzania in 1997 endorsed the National Cancer Control program. The broader objective is to establish sustainable cancer services which will effectively contribute to the health of Tanzanians. The main activities include cancer research, training of cancer experts, mounting cancer prevention strategies, promotion of cancer detection services, improvement of cancer treatment facilities and palliative care services, and networking with other organizations.

Recent initiatives at the OCRI include cervical screening and palliative care. Since we began a cervical screening program using visual inspection last December, more than 1,500 women have been screened. This project is being undertaken in collaboration with IARC and INCTR.

Last year, we also completed a situ-

ational analysis and needs assessment study on palliative care. This project was funded by the World Health Organization. The Ministry of Health has endorsed our proposal for palliative care nationwide, and we hope to get some funding from the Diana Memorial Palliative Care Fund to implement some of the elements in the project proposal.

About 2,000 new cancer patients, both children and adults, are seen each year. Doctors treat cancers of the cervix, breast and esophagus, Kaposi sarcoma, Burkitt's lymphoma, head and neck cancers, and ovarian cancer, as well as leukemia. In addition to providing cancer treatment services, the Ocean Road Cancer Institute has a cancer prevention division that coordinates education programs and screening services to the outskirts of Dar es Salaam region.

The Ocean Road Cancer Institute manages its patient load with modest diagnostic and therapy equipment. What we urgently need is a new

# PARTNER PROFILE

-70° refrigerator and a high-dose intracavity machine to cope with the increasing number of patients with cervical cancer.

## PARTNERING WITH INCTR

INCTR has proven to be a vital partner for improving cancer services in Tanzania. In addition to opening an INCTR Tanzania office, INCTR has supported IARC's initiatives to undertake a more comprehensive cervical cancer screening program based on visual inspection with acetic acid and visual inspection with lugols iodine. IARC has provided three colposcopes, cryotherapy and LEEP (loop electro-surgical excision procedure) equipment for the treatment of premalignant lesions, and has trained doctors and nurses in screening methods and colposcopy practices. As we continue, we hope to develop collaborative research proposals with INCTR and other institutions such as SAREC.

Already a draft research proposal addressing the most common childhood cancer in Africa—Burkitt's lymphoma—has been completed. An agreement has been reached on the first-line therapy for newly diagnosed patients with Burkitt's lymphoma in the planned collaborative study. We consider INCTR a valuable collaborator in this undertaking as we strive to increase our treatment results and bridge the gap between developing and developed countries in the fight against cancer.

INCTR's keen interest in improving cancer services in developing countries and its goal to send help where it is needed most has proved beneficial for us. Its additional objective to facilitate research activities will certainly help the ORCI to achieve its mission and vision.

Our mission is to work in partner-



**The Ocean Road Cancer Institute encourages women to come in for cervical cancer screening.**

ship with the community so as to create and maintain an integrated, accessible and affordable health system with quality service as the focus and improved health and well-being as the constant standard. The Institute aims to prevent cancers, and for cancers which have already occurred to heal sometimes, to relieve often and comfort always.

Our vision for the Ocean Road Cancer Institute is to be an institute

of excellence for the treatment of cancers in Africa. The staff at ORCI realize that the making of an institute of excellence is a process, not a destination, and that it will take place over many years of good political will, hard work, financial support and collaboration with other institutions/centers of excellence. ■

*Twalib Athuna Ngoma*  
*Ocean Road Cancer Institute, Tanzania*

## DETAILED STATISTICS ABOUT OCEAN ROAD CANCER INSTITUTE

**Facilities – inpatient and outpatient service to cancer patients**

**Number of Hospital Beds – 130**

**Doctors – 5 radiation oncologists; 1 gynecologist; 1 part-time pathologist, 17 junior doctors**

**Nurses – 23 trained nurses; 50 nursing/ward attendants**

**Pharmacists – 1**

**Medical Physicists – 2**

**Therapy Radiographers – 10**

**Laboratory Technicians – 3**

**Total staff – 152, including administrative and ancillary services staff**

**New patients attending OPD – approximately 2,200 per year**

**Follow-up patients - approximately 4,000 per year**

**Women attending cervical smear clinic – approximately 5,000 per year**

# NETWORK

## PROFILES IN CANCER MEDICINE

### STANDARDIZING CANCER TREATMENT

Suresh Advani, the man who pioneered bone marrow treatment for leukemia in India, is one of the most highly-decorated physicians in the country. Last year, in recognition of his significant achievements in medical research and education, he received both the Padmashree Award, a civilian honor for lifetime achievements, and then, in early November, the Dhanvantri Award, India's highest recognition in the field of medicine.

The former Chief of Medical Oncology at Tata Memorial Hospital, Advani also helped to establish the Oncology Department at Jaslok Hospital, Mumbai, where he is now the Chief Oncologist. He is working with the faculty at Mumbai University to standardize the oncology syllabi used in its medical colleges. And he has established the Asian Institute of Oncology at Bombay, providing cancer treatment at affordable cost.

Dr Advani, 56, trained in general medicine and in hematology at JJ Hospital at Grant Medical College in Mumbai, and studied oncology in the United States. He joined the Oncology Department of Tata Memorial Center and Research Institute in 1974. Here, he undertook clinical work along with research in hematology and medical oncology. He devoted the next 28 years to developing a modern oncology center and operating India's most advanced hematology laboratory. He established the first bone marrow transplantation unit in 1983.

Among his research projects were cytogenetic studies in chronic myeloid leukemia (CML) and myeloblastic leukemia (AML); the cytochemistry of leukemias; enzymatic patterns

in leukemias; cell-mediated immunity in CML; cell-mediated immunity in Hodgkin's disease and myelomas; and polyamines in Hodgkin's disease. Advani has published more than 500 papers in international medical journals.

Advani began practicing medicine when oncology was an emerging field in India—and when survival rates for acute lymphoblastic leukemia (ALL), for instance, were less than 25%. During the past 15 years, long-term survival rates for ALL have risen to nearly 60% at the Tata Memorial Hospital. Early on, he recognized the importance of international cooperation, particularly for workforce training and the transfer of technology. The success in treating leukemia is due in large part to hospitals across the country adopting uniform procedures for diagnosis and treatment (recorded in a "protocol" document) developed by Advani and his colleagues at other major centers, in collaboration with cancer experts from the National Cancer Institute (now with INCTR).

Advani believes standardization is critical in the fight against cancer. The treatment protocol outlines how specific drugs should be administered, what side effects might be anticipated, and how those side effects should be treated. The ALL protocol calls for drugs in their generic form, which are more cost-effective than new drugs coming to the market.

"Being a cancer institute in a developing country, we have a tremendous responsibility not only to deliver treatment, but also to promote education and research," Advani says. "All of us need to work together, and INCTR has been really helpful in this area. With assistance from INCTR,



Dr Advani confers with Ian Magrath at the INCTR annual meeting.

we have been able to do more research that helps us advance the understanding of the biology of these diseases. In certain areas where we lack expertise we need to send people out for training; we also are looking for a reverse flow of knowledge—to have experts come to our center to look at our work, to help us upgrade local facilities and to make sure our data are absolutely reliable. The quality of our work output should meet international standards."

Under his guidance, Jaslok Hospital now offers bone marrow and stem cell transplantation therapies in addition to routine chemotherapy and other standard treatments. As a medical researcher, Advani looks forward to moving into DNA microarray—a technology that allows biological information to be stored, integrated, searched, retrieved and analyzed—which is reshaping molecular biology and bioinformatics.

"Everyone is very keen to get into new technology," he says. "Everyone wants to learn how to do things in a better way, but the opportunities are limited and it will take time. The most important thing we need to develop are our human resources—with properly trained doctors and technologists, everyone benefits." ■