Tropical Hemato-Oncology

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Springer

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Preface

Tropical hematology and oncology. So, what is special about it? It may not be obvious at first sight. There are excellent textbooks of hematology and oncology. Yet, these textbooks do not take completely into account the tropical perspective. Never before, to our knowledge, has a book specifically dedicated to this subject ever been published. Therefore, it appeared to be an interesting topic to some of us. This was enough to undertake this work. We want to tell its story. It is first a personal story. It later became a collective story.

Late in 2009, I had retired from my medical oncologist activity in Comprehensive Cancer Centers, specifically the Institut Gustave-Roussy (Villejuif) and the Centre Léon-Bérard (Lyon) and from professorship of medical oncology at the Claude Bernard Lyon 1 University (Lyon). The Hospital of Cayenne (French Guiana) needed reinforcement in medical oncology. I worked at this hospital for almost a year and for periods of 15 days every 2 months until now, in collaboration with a colleague from Lyon. French Guiana is a French territory with the same administrative organization as in mainland France. The health system is the French one; the European rules apply as in metropolitan France. I discovered different pathologies from those seen in Lyon and Paris, a different distribution of cancers. But mostly I discovered other cultural visions, problems related to distance and geographical characteristics. In addition, the hospital had a strong orientation toward tropical medicine (including traditional medical disciplines). These observations led a small group of friends and professors of medicine to agree about the idea of editing a book dedicated to tropical hematology and oncology. It is this small group that formed the editorial board of this book.

We wanted this book to be built on several principles:

- To consider all aspects of the subject: organization, public health, cultural diversity, specific mechanisms of carcinogenesis, etc.
- To not take into account the major principles of hematology and oncology, which are developed in high-quality textbooks.
- To try to discuss specific issues related to the occurrence of these diseases in a particular area: the tropics.

- To have a panel of authors as wide as possible. We tried to find author pairs from the north and the south. This has not always been possible, but the effort succeeded for many chapters.
- To be quite short and, as much as possible, to be practical. In particular, we asked the authors to highlight the management adjustments based on local opportunities and to try to answer the question "what can we do when we have few resources?"

We thank all the authors who have answered this challenge. We were very pleased to invite well-known friends of the hematological and oncological communities, but even more to get to know colleagues from different disciplines and from different countries. We tried, according to our readings, references, and acceptances, to write, to bring authors from all backgrounds and from as many countries as possible. We sometimes had to make difficult choices. For example, we planned a chapter on the biological characteristics of carcinogenesis in the tropics. Eventually it became clear that it was treated across the different chapters and, therefore, that some subjects were redundant. We have not included a chapter on CLL, Hodgkin's disease, and myeloma. In fact, there was no real specificity for these diseases, but the treatment of myeloma is discussed in the chapter on medical treatments. Other concepts have been treated several times in different chapters. We nevertheless kept these repetitions because they may allow giving different perspectives on the same subject. During the 6 months of preparation of this work, we have had many exchanges with the authors. Special thanks to Ian Magrath who agreed to write a foreword. We had a lot of discussions together to finalize the objectives and perspectives on this book. We also thank Springer who accepted the challenge. In particular we thank Nathalie Lhorset-Poulain who accompanied us during the preparation of this book.

This book aims to be a resource to help practitioners in the tropics; we hope it will be useful in this regard. We warmly thank the authors who have agreed to participate; nothing would have been possible without them.

Professor Jean-Pierre Droz
and members of the editorial team:
Professor Bernard Carme
Professor Pierre Couppié
Professor Mathieu Nacher
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Foreword

It was not until the end of the nineteenth century that academic institutions' focus on tropical medicine arose, the first being the Liverpool School of Tropical Medicine in 1898, with the London School of Hygiene and Tropical Medicine (LSHTM) being opened the next year. The schools in the Netherlands and in Belgium were established in 1910 (Amsterdam) and 1931 (Antwerp), respectively. It is no coincidence that each of these schools was located in a port city, for this was where the seamen suffering from diseases picked up in the tropics were to be found. Sick seamen meant that ships could not sail on schedule, with consequent loss of revenue by the trading companies. Given the large profits to be made by trading in exotic spices, cotton, silks, tea, and opium (at one time the East India Company accounted for half the world's trade), it is not surprising that international trade was largely conducted by joint-stock private companies owned by wealthy European merchants and the nobility. The East India Company, for example, at one time accounted for half of all the world trade and between 1757 and 1858 controlled large areas of India by means of its own private army and administrators. It was not until technological advances made in the nineteenth century – particularly improvements in microscopy – and Pasteur's final proof that "germs" cause infectious diseases that research could be conducted on the major tropical infections, although at that time there was little that could be done to alter the course of the debilitating diseases from which so many inhabitants and visitors suffered. One exception was malaria, which had for long been known to respond to treatment with cinchona bark, thanks to Peruvian Indians who passed on their knowledge to Jesuit priests in the early seventeenth century. The active constituent of cinchona bark was later shown to be quinine. So it was that in relatively quick succession, Sir George Manson and Sir Ronald Ross (particularly known for their work on the transmission of malaria), Sir Aldo Castellani (who showed the association between sleeping sickness and trypanosomiasis), Robert Leiper (a helminthologist noted for his discovery of the life cycle of the guinea worm), Carlos Chagas (who first recognized the American form of trypanosomiasis and established its transmission by triatomid bugs), Theodor Bilharz (who discovered schistosomiasis in Egypt), and Pirajá da Silva (who established its life cycle), among others, were able to rapidly move forward the understanding of tropical

diseases, a term which was particularly applied to the diseases caused by parasites, which were largely, though by no means exclusively, confined to tropical regions for reasons discussed below and about whose life cycles considerable evidence was accumulating. There was little if any discussion of cancer, although some cases must have been seen. Presumably, this was because the classification of cancer was in its very early stages, and signs and symptoms may have been misinterpreted. Cancer accounted for a relatively minor fraction of sick people in the tropics, and treatment was extremely limited, even in Europe, until well into the twentieth century. Cancer may also, in some cultures, be stigmatized (e.g., women with breast cancer) and hence hidden from other family members to the extent possible. However, although not foreseen at the time of the research, understanding the life cycles of various parasites, especially trematode worms, proved to be important to the development of measures designed to prevent certain cancers that in tropical regions have been responsible for a large proportion of cancers in the past and, in Africa particularly, may still be seen (e.g., schistosome-related bladder cancer). The availability of funding from the companies that made enormous profits from the high demand (at least in the upper echelons of society) for the products available from tropical countries was more than enough to establish schools of tropical medicine, which focused also on public health and epidemiology as the mechanisms of parasitic infestation were gradually uncovered. Cancer was not a major item on their agendas, and the cancer burden, both in the tropical colonies and among those who returned from the colonies, was small. Nonetheless, there are differences in the distribution of various cancers throughout the world and in different socioeconomic subgroups, and a book focused entirely on tropical cancers may well serve a valuable purpose in emphasizing the importance of environment and lifestyle in the causation of cancer. Moreover, chronic infection as a cause of cancer remains important in certain populations. There is, for example, a Schistosomiasis Control Initiative focused on schistosomiasis in Africa, since, unlike Egypt, whose efforts to control schistosomiasis extend back to early in the twentieth century, some countries in which schistosomiasis is common have only recently developed control programs.

Since anemia is widespread and carries with it important social and economic implications due to poor development in children, an inability to learn, and a predisposition to infectious diseases, some hematologists focused on hematological diseases that occurred predominantly in tropical reasons, such as the inherited thalassemia and sickle cell disease. These diseases were shown to lessen the severity of malaria, the distribution of which, prior to eradication programs, was remarkably similar to that of thalassemia, such that patients did not die, but neither were they in full health. Tropical hematology, however, was primarily focused on nonmalignant diseases, and the inclusion of malignant hematological diseases in this book stems from the editor's desire to cover the full spectrum of malignant diseases in tropical countries. But are there differences between the spectrums of malignant diseases in the tropical regions compared to temperate climates? Before addressing this question, it is important to know what is meant by "tropical" and how a tropical environment might influence the spectrum of cancers and approaches to their prevention and control.

The Tropics Precisely Defined

The tropics comprise – as will be reiterated in multiple chapters of this book – the region between the two imaginary lines of latitude that presently encircle the globe at 23°26′14.3″ north and south of the equator, respectively (the precise positions are drifting slowly toward the equator). The northern latitude is called the Tropic of Cancer or Northern Tropic, and the southern, the Tropic of Capricorn or Southern Tropic. This region has a number of unique characteristics. It is the hottest part of the planet, being closest to the sun, and the temperature does not fall below 18 °C (64 °F) throughout the year. This means that the four seasons (spring, summer, autumn, and winter) that occur in all other parts of the planet do not occur in the tropics. The tropical sun remains high in the sky throughout the year and is directly overhead at its "culmination" (approximately noon) on 2 days of the year at the latitudes of the tropics and the regions between them. Necessarily, from this observation, the point at which the sun sets (or rises) appears to move between the latitudes of the Tropic of Cancer and the Tropic of Capricorn throughout the year. This is the result of the plane of the Earth's axis not being at right angles to the plane of the ecliptic, i.e., the plane of the Earth's orbit round the sun. The axis is inclined at an angle of approximately 24.4° which is fixed in relationship to the stars, such that as the Earth orbits the sun, the degree of tilt presented to the sun varies between 0 and 24.4°. As a result, the point on the horizon at which the sun rises or sets moves back and forth between the two tropics as the Earth traces its orbital path, reaching its most northerly point in June, precisely on the Tropic of Cancer, and its most southerly point in December, precisely on the Tropic of Capricorn. The days on which the rising or setting of the sun appears to stand still before reversing its direction are known as *solstices* (*Latin for* "*sun*" *and* "*to stand still*"). The June solstice is the longest day of the year and the first day of summer north of the Tropic of Cancer. It is the shortest day of the year and the first day of winter in the southern hemisphere south of the Tropic of Capricorn.

The climate in the tropics is of three main types – tropical rainforest, tropical monsoon, and savanna, the last of which has a pronounced dry season. These climatic zones result in a broad range of ecosystems, some of which change little throughout the year. Tropical regions account for 80 % of the world's biodiversity, 40 % of its population, and 20 % of its economy. Using the World Bank's classification of countries into low-, middle-, and high-income countries, only Singapore and Hong Kong – now a part of China – are among the 30 countries ranked as high-income countries by the World Bank. Thus, the cancers of these countries, and the cancer services, with the two exceptions mentioned, are similar to those in other low- and middle-income countries. According to Jeffrey Sachs (National Bureau of Economic Research, working paper 8119), the GNP per capita in the tropical zone in 1820 was approximately 70 % of that in the temperate zone, but this had fallen to 25 % by 1992, reflecting the difference in economic growth throughout this period. The major reason for this was the difference in the development of technology, particularly that related to agriculture and health, but difficulty in mobilizing energy

resources in tropical zones was also important. Sachs also recounted that in 1995, productivity per hectare of grain in tropical zones was 50 % of that in temperate zones. This is a result of soil formation and erosion, losses related to various pests and parasites, the availability of water, and the effects of tropical climates on plant respiration. Poor agriculture gives rise to poor nutrition and poor health. Poor health results in a reduced ability to learn and a lower capacity for work. This feeds back into the more limited development of technology, and correspondingly low economic growth rates, although it must be said that many colonies have only achieved their independence in the mid-twentieth century and part of the lack of concern about technological growth may have related to the colonial plan to maintain the less developed countries as the providers of raw materials and their colonial masters as the producers of the end product – a means of ensuring that the wealth of a country was, to a large extent, concentrated in the hands of the colonialists. Although some hospitals and schools were built, most of the very sick colonialists were sent back to their own countries. These remarks apply particularly to the French and British colonies since the Spanish and Portuguese colonies (except for Cuba and Puerto Rico) had gained their independence by 1826. A third reason for the poorer performance of tropical countries is the fact that many of them are considerable distances from the sea – particularly African colonies – which tend to disadvantage them from the perspective of exporting goods to the rich countries. In the context of health care, this also meant that as more technology developed, the delivery of medicines and equipment became an increasing challenge, for not only do the poorest countries produce few drugs but importation offers many opportunities for taxation (official and "nonofficial"), e.g., in Africa, where the cost of many generic drugs, especially those for cancer, can be several times higher than in the country of manufacture! In the context of new drugs, most patents provide for 20 years of monopoly and, therefore, during this time, a lack of market competition except by completely different compounds which have similar activity. The less developed countries, with their small pharmaceutical industries (if they exist at all), therefore have limited access at best to many of the newer drugs, which are usually priced too high for them to afford, although special circumstances may sometimes apply, such as the provision of imatinib free of charge by Novartis to the 40 poorest countries in the world. They must, however, demonstrate the presence of the relevant translocations, such as the 9;22 translocation in chronic myeloid leukemia and a subset of acute lymphoblastic leukemia, in order to receive the drug free of charge.

Poor health in low- and middle-income countries is not solely the result of lower agricultural yields. Tropical countries have a larger burden of disease even after controlling for GNP per capita. The infant mortality rate is 50 % lower in temperate-zone countries and life expectancy 8 % higher. Due to constantly improving technology pertaining to disease control in temperate zones, coupled with improved housing, nutrition, public sanitation, and the introduction of immunization, infectious diseases which had affected all parts of the world in the nineteenth century were more readily controlled in temperate-zone countries (e.g., tuberculosis and malaria). In general, the more limited health workforce of tropical countries led to much slower progress with respect to vaccination of children against the common,

but potentially, serious infections. Further, many infections in the tropics are caused by vectored parasites and viruses, and these, along with helminthic infections, some of which are listed below, have proved to be difficult to control. Arthropod vectors have the advantage in the colonies that they have no winter to survive, and their adult forms continue to spread disease throughout the year. The difficulties in controlling these diseases, however, are in considerable part due to their neglect at an international level during a period when health technology was growing rapidly in temperate-zone countries. The World Health Organization, for example, lists 17 neglected tropical diseases. It is likely that the lack of a winter season favors the maintenance of insect vectors, some of which may be confined to the tropical regions, such that appropriate vectors for some diseases do not exist outside the tropics, but there are often multiple possible insect vectors as has been shown by the occasional appearance of tropical virus infections in temperate countries. Malaria, for example, now considered a tropical disease, was once a disease that was present almost everywhere in the world. Although only transmissible to humans by female Anopheles mosquitoes, there are some 430 species of Anopheles which overlap in distribution such that vectors for malaria are available everywhere. The parasite develops more rapidly in the mosquito at higher ambient temperatures – it requires 10–18 days to complete its production of sporozoites in the mosquito (the infectious particles injected into a new host when a female mosquito takes a blood meal), such that it may be somewhat more readily eradicated in temperate regions. Malaria is not known to cause cancer, but there are reasonably strong data that indicate a role for it in Burkitt lymphoma in Africa. The enormous difference in geopolitical power between temperate and tropical countries is clearly also a major factor in the poorer economic performance of the latter. Huge challenges face tropical nations, such as environmental degradation. Tropical forests, for example, are either overharvested or cut down to make room for large international agricultural corporations – or small homesteads for subsistence farmers, who clear the forests in order to create agricultural lands from which they can eke out an existence. Population growth, although slowing, is markedly higher in tropical countries which already lack the resources to ensure good nutrition and the health of their citizens. These socioeconomic circumstances have a considerable impact on the health of the people who live in the tropics who, to a large extent, are dependent upon natural resources for their livelihood.

Destruction of the Rainforests

Some 90 % of the 1.2 billion people living in extreme poverty worldwide live in the vicinity of rainforests and depend upon the forests for their livelihood (57 % of all rainforests and almost all tropical rainforests are located in developing countries). While the judicious use of *renewable* sources provides wood (an energy source) and foods (various plants and animal species) and protection of the land against erosion, flooding, and drought, the permanent destruction of large regions of the tropical

rainforests will lead to the loss of countless species of animals and plants (estimated at the present time as 5–10 % per decade) and, quite probably, to lost opportunities to develop new medications due to the elimination of the valuable resources mentioned. The destruction of the rainforests results in flooding in the rainy season and drought in the dry season, creating enormous hardships for the vulnerable people living in or near the forests (i.e., people with very limited or no reserves that can carry them through difficult periods) and resulting in markedly decreased productivity in these regions. Long periods of drought in the arid savanna regions have a similar effect on the pastoral way of life, a lifestyle that is absolutely dependent upon the animals herded by the pastoralists. When sources of water dry up, the animals die, leaving their owners with no source of nourishment. They have little choice but to move to the cities – only to find they cannot make a living there either.

Urbanization

While we associate the word "tropics" with a rural lifestyle, the cities that are within the tropical zone are undergoing rapid expansion as a result of the population growth resulting from the demographic changes caused by the industrial revolution – or those parts of the industrial revolution that people in poorer countries can take advantage of. According to John R Wilmoth, director of the population division of the UN, many countries are urbanizing at lower levels of development than in the past. People who leave the countryside are by no means assured of a livelihood because many cities will not have an industrial economy that can provide jobs and an infrastructure that would allow new residents to live in acceptable conditions. The result is large slum areas and dumping grounds for waste of all kinds, particularly on the vaguely defined peripheries of such cities, because the city does not have sufficient equipment to remove waste. This has a major effect on the development of new housing, clean water, education, electricity, transportation, and health care which, because of the density of the population, would normally be more efficiently provided in cities than in rural regions. Already, many of the largest cities in the world are in tropical regions, such as Delhi, Kolkata, and Mumbai in India, Manila in the Philippines, Jakarta in Indonesia, Guangzhou and Shenzhen in China, Lagos in Nigeria, and Mexico City, Lima, and Rio de Janeiro in Latin America. All of these cities are among the largest 30 cities (in terms of population) in the world and suffer from massive pollution, mostly due to the high volume of traffic occupying a space not designed to contain it and lax regulations on industrial discharges into rivers, the sea, or the air. Many respiratory diseases ranging from asthma to lung cancer result, and more health services are almost certainly required than was the case in the past, where tropical environments were exclusively rural. In these megacities the slum dwellers often live, quite literally, on the detritus of their wealthier fellow citizens, but the latter, although vastly better off, may still have higher rates of cancer due to smoking coupled with air pollution, although they may have some respite from the massively polluted air in

their air-conditioned offices. But worse still, low- and middle-income countries are undergoing urbanization at an increasing rate. The UN estimates that presently, 22 % of the world's population lives in urban regions, but this will increase to 27 % by 2030. In a word, the unique climates and habitats of tropical regions are being destroyed with major consequences for the world. As these regions are degraded, and urbanized, there is a loss of environmental stability and changes in lifestyle patterns and in the diseases which are associated with them. Even the ancient myths that bound tribes together no longer provide the psychological support and "cultural glue" that make people feel part of a community that, whatever the myths used, gives meaning to people's lives. The loss of these cultural ties may be as devastating psychologically as the physical consequences of disease – particularly complex diseases, such as cancer, that usually require complex impersonal treatment by highly trained personnel as well as expensive equipment for imaging and treatment (e.g., radiation therapy machines). Modern myths must be created, which teach illiterate people something about cancer and more gently lead them toward a world that at least resembles the technological world in which the wealthier societies live – although not all that the rich have to offer is good, and care must be taken to differentiate the good from the bad (smoking, drinking, overeating, and lack of exercise should become the evil spirits that must be exorcized).

Infection and Infestation as Causes of Cancer in Tropical Regions

In spite of the growth of cities and the frequent loss of traditional lifestyles in rural regions of the tropics, chronic infectious diseases, e.g., human papillomavirus (HPV) infection, human immunodeficiency virus, *Helicobacter pylori*, or parasitic diseases (trematode worms or flukes in particular), account for a much higher fraction of cancer than in temperate regions. It should be understood that there is no sharp boundary from the biological perspective around tropical regions, and some of the diseases, and certainly the problems encountered by LMIC populations, are similar in many nontropical countries. It is also necessary to beware of "averages" and global figures if the true picture is to emerge. For example, the International Agency for Research in Cancer (IARC), which collects cancer registry data from all over the world, estimates that in 2008, approximately 16 % of cancers worldwide were associated with infections. However, in LMIC, the fraction of cancers associated with infections was estimated to be 23 %, with high-income countries accounting for only 7.4 %. Even these figures remain composite, i.e., the average of many countries. In Australia, for example, it is estimated that only 3.3 % of cancers were caused by infection in 2008, while in the Gambia, approximately 62 % of new cancer cases in males were diagnosed in the same year with hepatocellular carcinoma – caused by hepatitis B and aflatoxin – and there can be no doubt that some other cancers are also related to chronic infection, suggesting a figure slightly higher than 70 % for the

fraction of cancers in males caused by infection in the country. In women the annual incidence rate of hepatocellular carcinoma was lower and accounted for 24 % of cancers, but cervical cancer, caused by HPV, was estimated to be 38 % of new cases, so that the fraction of infection-related cancers in both sexes was similar, but much higher than the average fraction in all LMIC combined. Interestingly, the incidence of gastric cancer, once the most common cancer in the world, was quite low. These findings are important, since they suggest that the majority of cancers in the Gambia are preventable by affordable vaccines. Cervical cancer can also be effectively controlled by simple screening techniques, particularly if they involve the detection of HPV in cervical secretions. In Egypt, there is a high prevalence of schistosomiasis (both hematobium, causing severe chronic bladder damage, including fibrosis and progression to squamous carcinoma of the bladder, and mansoni causing granulomata of the bowel and, again, the possibility of progression to colon cancer, although the data for this are less compelling than carcinogenesis relating to *S. hematobium* and *S. japonica*, a fluke that occurs predominantly in China). The Egyptian government has attempted for decades to prevent schistosomiasis. Attempts to poison the intermediate host, a water snail, failed, but eventually, a nationwide policy of selective therapy with praziquantel, provided free of charge to individuals diagnosed as having schistosomiasis, had a major impact, such that the incidence of schistosomiasis countrywide is believed to be less than 3 %. Some years after these efforts, it was also thought that the incidence of bladder and bowel cancer caused by schistosomiasis has been markedly reduced, but there is insufficient registry data to be sure. Bladder cancer at one time was thought to be the commonest cancer in Egypt (although this was based on data from the National Cancer Institute in Cairo (NCIC) and not population-based). At that time, squamous bladder cancer accounted for 80 % of bladder cancer cases, but the proportion of squamous cases has been falling at the NCI and a few years ago accounted for approximately 50 % (the remainder being transitional). In support of the role of schistosomiasis in bladder cancer is the observation that most cases are in farmers or their families, while patients with transitional bladder cancer usually work in Cairo.

In equatorial Africa, the case is still that 80 % of the people live in rural regions in which a higher fraction of cancers are caused by infections or infestations that can be prevented or treated. Incidentally, there are a number of other flukes, mostly found in SE Asia or China, such as the so-called “food flukes” that are believed to cause liver or biliary tract cancers. They infect an additional intermediate host (a fish or crustacean) which, when eaten, spreads the disease.

Challenges in Cancer Control in the Tropics: The Epidemiological Transition

The industrial revolution resulted in major changes in lifestyle and had major social, economic, and demographic impacts. Populations of countries (e.g., the UK) moving through the epidemiological transition that it precipitated first began to grow

rapidly due to improved living conditions and hygiene. Premature deaths (less than 70 years) are reduced, so that the population also ages. Then a gradual reduction in the birth rate follows which does not initially slow population growth since people live longer. During this period the burden of cancer increases, since on average the population is larger and older. All LMIC, which account for 85 % of the world population, appear to be going through a period of rapid increase in the cancer burden – they accounted for an estimated 8 million (57 %) of the 14.1 million cancer cases that occurred in 2012 (IARC) and 65 % of the cancer deaths. The age-adjusted incidence rate is 267.2 and 147.7 for more and less developed countries, respectively, so that the incidence of cancer is higher in more developed countries. However, death rates are quite similar, indicating that treatment results are worse in the less developed countries as expected. In the UK following the Industrial Revolution, the population size stabilized as the birth rate and death rate found a new equilibrium but at a much lower level than prior to the transition. While this pattern is not invariably followed and, indeed, can hardly be said to be following an industrial revolution in the less developed countries, the increase in the cancer rate in LMIC is presumably due to improving standards of living. Population growth and aging appear, as would be expected, to be invariable in such a time, but there is uncertainty about when and to what degree the growth rate will slow and the cancer burden stabilize. It may well differ in different countries, but the IARC predicts that in 2030 the number of cancer cases will be 7.6 million in more developed regions and 13 million in less developed regions. Thus, the less developed regions will need to be prepared to cope with a much larger increase in cancer patients in this 15-year period. In fact, the increasing cancer burden is likely to cause major catastrophes in the poor countries, which cannot take care of their present cancer burdens because of the lack of facilities (including radiation therapy units, skilled surgeons, and medicines) and well-trained pathologists and oncologists. A number of countries (e.g., the emerging economies) have been able to overcome the problems caused by the demographic changes and resultant epidemiological transitions, however, and now manufacture sophisticated goods such as motor vehicles and electronic goods and often take high market shares because they can produce high-quality goods more cheaply. Such countries are able to create enough wealth to be able to care for their cancer patients who, in turn, are generally supported by health insurance, which is, for the most part, lacking in LMIC, where patients must pay for most or all of their care out of pocket. Even now, many patients in LMIC cannot afford even the relatively cheap medicines or procedures available and die. Sometimes they return home having had no or partial therapy because of financial costs or the fact that there is no one to look after their children. Families are frequently large, such that although the parents can support the family by subsistence farming, or other source of livelihood, they are extremely vulnerable to crises such as cancer in the family because they have little or no money (they often barter for goods) or other forms of support. Unfortunately, all too often, the necessary treatment is not available. Large family sizes increase the vulnerability because the parents have more children to look after – and if and when the economic situation improves, more elderly parents to care for too.

Countries at a low level of scientific development who do not make major investments in scientific education will continue to compete poorly and have an ever

greater task in catching up with those countries whose economies are largely built upon manufacturing, particularly complex goods such as motor cars, computers, etc. To reach this stage, however, sound investments in education and good leadership are essential. In countries that have undergone an epidemiological transition, infectious diseases have largely come under control, and the major diseases are noncommunicable, such as diabetes, heart disease, lung disease, and cancer. A reasonably high fraction of such diseases are caused by unhealthy living, and if education and policy are able to modify behavior, the number of premature deaths (less than 70 years) will be reduced. However, at the other end of the spectrum, an increase in the elderly members of the population also creates a heavy financial burden unless universal health insurance has been implemented. In many European countries, their own populations are shrinking, and people from other countries (usually LMIC) must be recruited in order to carry out the tasks necessary to maintain and even improve services provided. While some of these may be uneducated, they may obtain an education in the country to which they have migrated (possibly because they could not obtain an education at home) and often remain in their adopted country. Unfortunately, the technical and scientific skills of such individuals are, for the most part, not available in their own country. The less developed countries have both the least amount of resources for health care and are likely (as per the IARC predictions) to have far greater cancer burdens by 2030 than the more developed countries. In addition, they may still have significant levels of infectious diseases and possibly still some cancers associated with infectious agents. Thus, the less developed countries will be even less able to cope with the ever-increasing cancer burden, short of a major new discovery relating to the control of cancer. Since the health systems prior to the epidemiological transition evolved largely to manage acute problems (e.g., trauma and short-term infectious diseases), they are ill placed to deal with the sudden marked increase in chronically ill people (not just cancer, but all NCDs) who require multiple visits to doctors, including specialists who, in the poorer countries, are in very short supply. In addition, the number of young people sufficiently educated to attend university is far fewer in more developed countries than less developed countries because of the limitations in the education of children at secondary school. The extent to which increased efforts to educate more specialists will offset these predictions is unclear. In addition, the predictions are based on demographic factors only – increased exposure to risk factors, especially tobacco, will make the situation even worse.

Cancer Prevention and Control

Prevention entails the avoidance of risk factors which can be achieved only by changing behavior through education of the public and creating policy that encourages them to do so and/or screening to detect premalignant or early-stage disease. The common risk factors for cancer and noncommunicable diseases include being overweight, obesity, lack of exercise, abuse of alcohol, and, most important of all,

the use of tobacco. The common risk factors tend not to apply to the poorer members of society, who are often undernourished, have little saturated animal fat in their food, undertake physical rather than sedentary jobs, and cannot afford alcoholic drinks or cigarettes. The growing middle class, however, in attempting to emulate their peers in higher-income countries, tend to have poor diets (i.e., rich in fats) and smoke cigarettes. Increasing their awareness of risk factor exposure can be greatly aided by education and policy. Given the broad nature of the common risk factors described, policy must be multisectorial at the government level, while its implementation must involve a broad range of stakeholders.

While prevention, for the most part, takes place in the community, effective treatment planning at country level requires a sound health system built on knowledge of the number and types of cancers and, ideally, knowledge of their distribution in the country coupled with efforts to ensure that referral is early (education of those who refer patients for further investigations as well as the public will be required) and the necessary treatment modalities available along with needed equipment and necessary specialists. Such resources are rarely available in the less developed countries today, and to create institutions and hospitals will be an expensive process, almost certainly out of the range of possibilities of most of the less developed countries. The assessment of the number of cases and trends is usually made via cancer registries at a population level, but there are still too few registries in poorer countries, especially in the rural areas. Registries can also be used to measure the impact of interventions designed to prevent or treat cancer, including mortality and survival rates, but accurate information requires high coverage rates of the population in question. Unfortunately, it is difficult to imagine that the needs will be met, and there is little evidence that much is being done about the enormous gaps that must be filled.

This book covers the entire gamut of cancer prevention and treatment and the characteristic features of the most common cancers as well as general topics such as clinical trials, training, and education. It addresses issues of insurance and socioeconomics of cancer control. It also deals with each of the main cancers individually. Within its pages one can only hope that there are potential answers to the serious questions raised with respect to the predictions of the cancer burden in 2030. Of one thing, we can be certain. Without a scientific approach, none of these problems will be overcome. That must be its ultimate message. Prof Droz is to be congratulated for bringing together an elite group of authors and creating a solid framework for discussion of cancer control in the tropics and in other LMIC.

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Contents

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