IARC celebrates 50 years of cancer research

The International Agency for Research on Cancer (IARC) held its 50th anniversary conference in Lyon, France, this week. John Maurice spoke to cancer experts about the agency's achievements.

As birthday parties go, the celebration of the 50th anniversary of the International Agency for Research on Cancer (IARC) was a fairly serious affair. On June 7, nearly 1000 scientists convened in the congress hall of Lyon, France, the Agency's home city, to listen, over the next 3 days, to presentations of scientific papers on cancer. The event aptly reflects the worldwide reputation of IARC as a WHO research agency. As Margaret Chan, WHO Director-General, puts it in a preface to a recent history of the Agency: "IARC has provided the indispensable cancer evidence base for WHO's public health work. It is the only WHO body that conducts its own research programme and disseminates its findings to the world."

Christopher Wild, director of IARC since 2009, sees the Agency as unique in several respects. "To start with", he tells *The Lancet*, "it has a unique dual status. It is part of WHO and at the same time it is autonomous. As part of WHO we enjoy an international standing that makes it easier for us to bring together scientists from all parts of the world to collaborate with us than if we were a national institution. As part of WHO, we are not beholden to the interests and policies of any one country. At the same time we have autonomy within WHO. We have our own Governing Council, which oversees policy and administrative issues and whose members represent our 25 participating countries. And we have our own Scientific Council, which oversees our research activities and is made up of top-level scientists from our participating countries."

Union of cancer researchers

The death of the wife of French journalist, Yves Poggioli, from cancer marked the birth of IARC. In 1963, he persuaded a well-connected public personality, Emmanuel d'Astier de la Vigerie, to convince Charles de Gaulle, President of France at that time, to create an institution of excellence devoted to cancer research and funded by 0·5% of the military budgets of several rich countries. Taken with the idea, de Gaulle called on the governments of the (then) Federal Republic of Germany, Italy, the UK, and the USA to join him in creating "a union of [cancer] research workers that extends beyond national frontiers". All four countries agreed (although ultimately the 0·5% idea fell by the wayside). In May, 1965, the World Health Assembly formally created IARC as WHO's first autonomous WHO agency. The Agency could start working—initially in WHO's Geneva headquarters until May, 1967, when it moved to Lyon.

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"The first scientists who landed in Lyon decided that their primary objective would be to find ways of preventing cancer", Wild explains. "And the first thing they looked at were the strikingly different epidemiological patterns that cancer registries were showing between different countries and different continents. "One of IARC's first achievements", Wild says, "was to describe systematically the global patterns of cancer and to try to understand what was driving these different geographical patterns and how they were changing with time. Work was also under way to improve the quality and coverage of the data flowing in from cancer registries around the world." Speaking to *The Lancet*, Richard Peto, professor of medical statistics and epidemiology at University of Oxford, UK, gives high marks to the Agency's efforts at putting an international perspective on cancer, which included, for the first time, the poorer countries of the world. "The data the Agency produced on the extreme variability of cancer mortality and incidence between different countries could only have been produced by an international institution like IARC. The Agency also, in those early days, added impetus to the growing realisation that human cancer can be avoided."

A distinctive attribute of IARC, Wild noted, is its mandate to train scientists in developing countries in cancer research. The cancer research needs of these countries is expanding, Wild says, especially the need for cancer prevention and early detection. In 2012, 14 million cases of cancer and 8 million cancer deaths occurred in the world, according to the latest available estimates from IARC's Globocan database, which covers 27 common cancers in 184 countries. By 2030,

IARC/R Dray

IARC's headquarters in Lyon, France

those figures are predicted to surge to 22 million and 13 million, respectively. Already, low-income and middle-income countries account for 70% of the world's cancer burden.

Identifying carcinogens

Arguably the best-known achievement of IARC, is its Monograph programme, which brings experts from around the world to form "working groups" that decide whether there is enough scientific evidence to judge whether a potentially carcinogenic "agent" is or may be a carcinogen. "The Monographs have made a hugely positive contribution to cancer prevention over the years", says Wild. "They have brought about changes in areas such as tobacco control, occupational carcinogens, sun exposure, air pollutants, and many more." Since 1971, when Monograph programme started, 1000 agents suspected of being carcinogenic have gone through the evaluation process and almost half have shown evidence of being carcinogens. Very strong evidence was found in 118 agents. They include some long-known culprits, such as tobacco, alcohol, air pollution, aflatoxin, and also viruses, such as hepatitis B and C and human papilloma viruses. Some recent controversial additions include processed meat.

Monograph experts base their decisions on the strength of evidence that an agent is or might be a carcinogen and not on the extent to which an individual exposed to an agent risks developing a cancer nor on the extent of exposure needed to cause cancer. Peto complains that the Monograph process does not place enough emphasis on quantifying the risk of exposure to a carcinogen and the benefit that could accrue by avoiding or controlling the exposure: "The result can be a long list of carcinogens that includes relatively unimportant or uncertain carcinogens and diverts attention from the more important ones. A more quantitative approach is needed."

Wild notes that the Monograph experts report dose-response data if and when the data are available from epidemiological studies. Over the years, IARC has drawn criticism about possible conflict of interest in some working group members who have links with manufacturers of an agent under evaluation. "We do come under criticism sometimes, from different vested interest groups", Wild admits. "It's a natural consequence of our evaluation role. We take these criticisms very seriously and make every effort to ensure that the experts we bring to Lyon are free from conflict of interest."

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In addition to the Monograph programme, IARC has added an impressive number of achievements to its name. In the mid-1970s, its studies in Africa confirmed aflatoxin and hepatitis B virus infection as causes of liver cancer. Wild mentions the epidemiological research done by the Agency on cervical cancer in the late 1980s. "That work allowed us to link the risk of cervical cancer to several types of human papilloma virus and then to assess the impact of screening and vaccination programmes on cervical cancer incidence and mortality."

Then in 1992, the Agency launched the European Prospective Investigation into Cancer and Nutrition (EPIC) to study the link between dietary, nutritional, lifestyle, and environmental factors, and the incidence of cancer and other chronic diseases. One of the largest cohort studies ever undertaken in the world, EPIC recruited more than 500 000 participants from ten European countries who were followed up for 15 years.

On a less positive note, Wild admits that IARC has not given the prevention of cancer the priority ranking it requires. "Up to now there has been generally a lack of investment in cancer prevention. The Agency vision was and is to conduct cancer research for prevention. In this vein we promote cancer prevention through handbooks, articles, and interviews but our lack of funds is a formidable constraint."

Bang for its buck

Some IARC observers wonder how the Agency manages to work on so many projects on an annual budget of €20 million ($23 million), which is dwarfed 200-fold by the €4·4 billion ($5·0 billion) annual budget of the US National Cancer Institute. As Peto remarks: "IARC accounts for a tiny fraction of the world's cancer research spending but that fraction has clearly produced a number of worthwhile achievements." For Cary Adams, chief executive officer of the Union for International Cancer Control (UICC), an umbrella organisation which represents 950 members in 155 countries, "the work of IARC is outstanding and I would put the Agency among the top in the world in terms of the quality of data they produce. I only wish it had greater support and funding". Paolo Vineis, now with the School of Public Health at Imperial College London, UK, agrees that "IARC is small in terms of its means but it has done extremely important transdisciplinary work that I have seen nowhere else. I have worked in the Agency for many years and really enjoyed the atmosphere of collaboration it has created".

Wild sees international collaboration as the lodestar of the Agency. "You see it in the atmosphere here at our headquarters where we have 300 people from over 50 countries working together on a common purpose. But you'll also see it in the rural areas of India, of Brazil, of China, or any countries where we have projects, with papers and files stacked on every table and dedicated staff working intensely together. This is really where you see what the Agency is all about."

John Maurice