

Lorenzo Tomatis and environmental cancer risk

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Summary. Lorenzo Tomatis and Benedetto Terracini have shared study and research experiences since 1948. This paper describes various phases of Tomatis scientific adventure leading to outstanding results (in particular as Director of the International Agency for Research on Cancer) despite the various difficulties met and the tendency to ignore scientific findings which in fact were adequate to implement preventive measures addressed to environmental carcinogenic hazards.

Key words: international agencies, history, medical oncology, portraits as topic.

Riassunto (*Lorenzo Tomatis e il rischio cancerogeno ambientale*). Lorenzo Tomatis e Benedetto Terracini hanno condiviso, a partire dagli anni 40, esperienze di studi e ricerca. Questo lavoro descrive le diverse fasi dell'avventura scientifica di Tomatis che ha condotto a risultati di notevole rilievo, malgrado le difficoltà incontrate e la tendenza ad ignorare i risultati scientifici che invece erano adeguati a prevenire il rischio cancerogeno di origine ambientale.

Parole chiave: enti internazionali, storia, oncologia medica, ritratti come argomento.

INTRODUCTION

In the summer of 1948, I used to bike to Renzo Tomatis's house in Turin to prepare our exam in histology. After our graduation in 1953, we both were attending the Department of Pathology of the University of Turin headed by Giacomo Mottura. In 1959 we met in the Division of Oncology of the Chicago Medical School whose Director was Philippe Shubik, where the two of us were trained in experimental carcinogenesis. I had gone to the United States because I wanted to see the world. He was inspired by more profound motivations: he was perceiving that unravelling the mechanisms of carcinogenesis could be important for public health. Neither of us intended to remain permanently in the US. In Turin, I had entered the department of Pathology of the University some time before him: according to the rules of the time (which, alas, have not changed much over the last half a century), I was ahead of him in the rush to get a university position. He remained in Chicago and I returned to Italy in 1960 without many second thoughts about my scientific future.

In Shubik's laboratory, Renzo worked on two topics of chemical carcinogenesis which later turned out to be crucial milestones in order to understand cancer mechanisms: carcinogenesis in tissue cultures and transplacental and transgenerational effects of carcinogens in laboratory animals. By the mid Sixties, his papers were well known worldwide. In spite of the quality of his scientific curriculum, hav-

ing been away for some years (which meant not having contributed to the reinforcement of the power of any Italian university barony), Renzo's chances to get a position in an Italian research institution in Italy were meagre, to say the most. Further, in 1965 he published his first literary production, *Il laboratorio*, a lucid description of the difficulties through which future academic scientists had to go in Italian universities in those days (indeed, the book also described the human frailty in the scientific milieu in the US). It was clear soon after the book's publication that he would never be able to pursue his career in Italy. What may have been Italy's loss has certainly been the world's gain. Incidentally, Renzo's latest frustration from the Italian academy came some twenty years later, when he was gently persuaded to withdraw from a national competition for a position of full professor of Oncology on the official basis that the number of publications enclosed to his application was too small compared to other candidates (indeed, he had enclosed to his application only the most relevant papers out of the lot, which in those days amounted to more than one hundred, but the selecting committee was entitled to ignore the others). Had he got the position, decisions on the future of Italian oncologists taken by the barons in the intimacy of their private telephone calls would have been upset.

Renzo Tomatis was among the scientists joining the International Agency for Research on Cancer at the time of its creation in the 60s. He wanted to

come back to Europe, and his personal philosophy was consonant with the grounds on which the Agency had been created following General De Gaulle's proposal. The basic ideas were that:

a) diverting to cancer research a small percentage of the huge amounts of money worldwide addressed to military expenses would have produced an efficacious international effort to understand cancer and

b) the underlying generosity and altruism would have contributed to the development of solidarity between nations.

Renzo's name and scientific prestige are intimately linked to the International Agency for Research on Cancer (IARC) programme on the *Monographs on the evaluation of carcinogenic risk of chemicals to man*, three volumes of which have been prepared every year since 1972 and whose 100th volume (for a total of well over one thousand agents) is expected for 2009. Around 1970, the Unit of Chemical Carcinogenesis of IARC was submerged by requests of lists of chemicals used in industrial processes "proven" to be carcinogens. Both unions and industries – for different reasons – hoped that the recognition of occupational carcinogens could be tackled in a simple and straightforward way. In addition, leaving the responsibility for indicating carcinogenic hazards in the workplace to an international body such as IARC would have relieved national governments from a delicate task. Renzo was well aware of the ambiguities and omissions underlying a "black list" endorsed by IARC without any explanation of reasons for inclusion/exclusion. Producing separate lists for "human" and "only experimental" carcinogens was even worse. The alternative was a responsible elaboration of the scientific observations based on manifest and standardized criteria and on an explicit statement that hazard identification and risk assessment are two completely different things. Catalogs would come later. Indeed, lists of IARC evaluations using standard terms started to be produced in 1987, with the praiseworthy "supplement 7", which was translated in several languages.

When the Monograph programme started, forty years ago, three ideas of Renzo were revolutionary: evaluating scientific data meant a multidisciplinary approach by a working group, interpreting findings for the purpose of public health required a major contribution from basic science, and the working group had to explain his rationale and the sequence of thoughts leading to evaluation in a transparent way, using terms understandable also to the lay people, with no loss of rigour. Absence of conflicts of interest of the members of working groups was crucial but in those days it was implicit and not spelled out.

Over the decades, through his intelligence, cultural and social commitment, Renzo was able to recognize and describe the frailty of the mechanisms with which scientific facts are produced, stored and used for public health purposes, as well as the vulnerability of scientists and scientific institutions to the

flatteries of industrial interests. Over the years, he did not miss any opportunity to point out the blindness, laziness and vested interests leading to ignore scientific findings which in fact were adequate to implement preventive measures addressed to environmental carcinogenic hazards. Governments' decisions (or inertia) have often reflected industrial interests (from chemical industries to tobacco multinationals) rather than will to protect against environmental risks. His analyses of the distortions underlying unforgivable delays in decisions to implement primary prevention measures are revealing. Cancer induction in animals in the absence of epidemiological confirmation (which requires decades) has often been claimed to be no proof of hazard for humans, but epidemiological findings in the absence of knowledge on biological mechanisms have also been considered to be an insufficient proof of causality. This was the course of events in the case of aromatic amines, asbestos, tobacco smoke and many other circumstances in which authorities' unjustifiable delays in taking measures corresponded to industries' interests. He was often upset by the excessive attention given by epidemiologists to the purity of their methods compared to the hints for prevention provided by their findings.

Tomatis was elected Director of the IARC in 1982 and he held this position until 1993. During this period IARC started the sequence of studies on the causes of cervical cancer, which is particularly common in developing countries, which led to the identification of HPV as the causal agent. Another major programme in developing countries was the IARC Gambia Hepatitis Intervention study based on the role of hepatitis B immunization in the prevention of HCC and on the consideration of the role of other risk factors, namely aflatoxin B1. These projects, as well as others, led to the recruitment of scientific staff that became recognised by the international scientific community. They contributed to the development of cancer molecular epidemiology, based on the integration of laboratory science into epidemiological studies.

Thus, the attention to the social and political problems underlying the causes of cancer was a major feature of Tomatis' period as Director of IARC. The IARC Scientific Publication on social inequalities and cancer remains a milestone in this context and Renzo's contribution to this publication is a "must" for those who want to understand the mechanisms through which poverty and inequalities explain a large part of the worldwide difference in cancer risk.

In the late '70s and early '80s, cancer epidemiology studies were still largely concentrated in Scandinavian and English speaking countries. Renzo, and other members of the IARC perceived that one of the tasks for the Agency was to encourage the development of epidemiological expertise in other countries: this was largely done through the IARC fellowship programme, the coordination of interna-

tional studies and the support which was given to new cancer registries worldwide and to the Group of Cancer Registries in Latin Language speaking countries. The current high standard of epidemiology in countries such as Italy and Spain would have not been reached hadn't they received scientific and technical support from IARC during the period in which it was headed by Renzo Tomatis.

After his retirement, Renzo was critical of the new lines of activities of the agency and his attempts to continue contacts with IARC did not meet much success. There were changes in the management of the monograph programme. He felt that the aim to provide a scientific basis for cancer prevention was at risk. Indeed, an imprudent and tendentious use was being made of the uncertainties of the relevance to man of some long-term experimental models. This brought about a downgrading of the evaluation of the risk associated to some agents (such as saccharin and some man-made mineral fibres) from categories suggesting a higher risk to categories considered to be at lower risk. Renzo explained his concern in the open literature. He also felt that the monograph programme of IARC was departing from the consid-

eration of the absence of conflicts of interest of the members of the working group as one of the basic criteria for the selection of members of its working groups.

Over the last fourteen years, Renzo commuted between Lyon and his house facing the sea in Trieste, spending every year a period of time as Visiting Scientist at the National Institute for Environmental Health Sciences in the US. He became President of the Italian section of the International Society of Doctors for the Environment. In this capacity, he did not miss any opportunity for inspiring the use of precautionary attitudes and for highlighting the potentialities of medical practitioners in identifying environmental hazards. In his numerous contributions to *Epidemiologia e Prevenzione*, the journal of the Italian Association of Epidemiology, he emphasized the risks that cancer prevention is facing as a consequence of a scientifically misleading strategy profusely supported by industrial corporations and the moral weakness of investigators. After his death, the journal has open a forum to collect witnesses on Renzo's role in the advancement of public health (www.epidemiologiaeprevenzione.it).