# The contribution of Enrico C. Vigliani (1907-1992) to the international development of Occupational Medicine and Industrial Hygiene

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### **KEY WORDS**

Enrico Carlo Vigliani; Occupational Health; history

# PAROLE CHIAVE

Enrico Carlo Vigliani; medicina del lavoro; storia

### **SUMMARY**

Background: One of the last century's greatest personalities in Occupational Medicine was Enrico Carlo Vigliani (1907-1992), director of the "Clinica del Lavoro" in Milan (1942-1977), editor-in-chief of "La Medicina del Lavoro" (1942-1991), Secretary-Treasurer and then President of the "Permanent Commission and International Association on Occupational Health" (1957-1981), the original nucleus of the ICOH. Objectives: The 20th anniversary of his death provides us with the opportunity to discuss the role of this brilliant scholar in the international development of Occupational Medicine and Industrial Hygiene. Methods: A comprehensive analysis of Vigliani's scientific works was conducted. In addition, his close collaborators and pupils were interviewed. Results: In the 1930s, as a young doctor, Vigliani, first in the world, demonstrated the effect of lead on porphyrin metabolism. Afterwards he conducted pioneering studies on occupational oncology (benzene-induced leukaemia, bladder cancer due to aromatic amines, asbestos-related tumours), pathogenesis of silicosis, encephalopathy in carbon disulfide poisoning, byssinosis and metal fume fever, so influencing international research and the implementation of preventive measures against these conditions. Vigliani's scientific authority was widely recognized internationally, as confirmed by his role in ICOH. During his period of active service, the Commission developed from an academic institution to a more open association, substantially increasing its membership. Furthermore, he contributed to establishing subcommittees devoted to specific topics (now called "scientific committees"), one of the strengths of the present Commission. Conclusions: Vigliani's contribution to the development of Occupational Health may be considered as an expression of his genial eclecticism which ranged from clinical medicine to the environment.

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# RIASSUNTO

«Il contributo di Enrico C. Vigliani (1907-1992) allo sviluppo internazionale della medicina del lavoro e dell'igiene industriale». Introduzione: Enrico Carlo Vigliani (1907-1992) è stato una delle personalità più rilevanti nel campo della Medicina del Lavoro nello scorso secolo: direttore della "Clinica del Lavoro" di Milano (1942-1977) e della rivista "La Medicina del Lavoro" (1942-1991), Segretario-Tesoriere e Presidente della "Permanent Commission and International Association on Occupational Health" (1957-1981), nucleo originario dell'ICOH. Obiettivi: Il ventesimo anniversario della sua scomparsa offre l'opportunità per definire il ruolo avuto da questo illustre scienziato nello sviluppo internazionale della medicina del lavoro e dell'igiene industriale. Metodi: Oltre ad un'analisi dettagliata dei lavori scientifici di Vigliani, sono state condotte interviste ai suoi più stretti collaboratori ed allievi. Risultati: Negli anni Trenta, Vigliani, primo al mondo, dimostrò l'effetto del piombo sul metabolismo porfirinico. Successivamente condusse studi pioneristici nel campo dell'oncologia professionale (leucemia da benzene, tumori vescicali da amine aromatiche, tumori connessi all'amianto) e nel campo della patogenesi della silicosi, dell'encefalopatia nell'intossicazione da disolfuro di carbonio, della bissinosi e della "febbre da fumi metallici", influenzando così la ricerca scientifica internazionale su queste tematiche e l'implementazione di misure preventive nei confronti di queste patologie. L'autorevolezza scientifica di Vigliani era ampiamente riconosciuta all'estero, come confermato dal suo ruolo nell'ICOH. Durante il suo mandato, la Commissione si trasformò da istituzione accademica a vera e propria associazione medica, aumentando significativamente il numero di membri. Inoltre Vigliani contribuì a fondare i comitati scientifici dell'ICOH, uno dei suoi attuali punti di forza. Conclusione: Il contributo di Vigliani allo sviluppo della medicina del lavoro può essere considerato espressione del suo geniale eclettismo che spaziava dalla clinica alle tematiche ambientali.

One of the last century's greatest personalities in Occupational Medicine was Enrico Carlo Vigliani (1907-1992), director of the "Clinica del Lavoro" of Milan for 35 years (1942-1977) and editor-in-chief of "La Medicina del Lavoro" for nearly half a century (1942-1991). The contribution of Vigliani to Occupational Medicine was immense and widely acknowledged at international level, as shown by his active service in the Permanent Commission and International Association on Occupational Health - the original nucleus of the ICOH (International Commission on Occupational Health) - contributing to the evolution of the association, first as Secretary-Treasurer and later as President. The 20th anniversary of his death provides us with the opportunity to recall the life of this remarkable man and to describe his tireless activity in improving knowledge in the field of occupational medicine and industrial hygiene. Since the results achieved by Vigliani as director of the "Clinica del Lavoro" and his role played in the Italian academic world and in the improvement of the health and safety of Italian workers have already been described in previous publications (5, 13, 29), this paper sets out particularly to investigate the contribution provided by this brilliant scholar to the international development of Occupational and Environmental Health. For this purpose original articles, documents and manuscripts from the Library of the "Clinica del Lavoro" and from the ICOH Archives were examined (6). Moreover, his closest collaborators and pupils were interviewed to collect direct information on his personality and his way of working and teaching.

### THE BEGINNINGS OF A LONG CAREER

Enrico Vigliani was born in 1907 in Turin, one of the most industrialized cities of Italy, famous for its automobile industry. He was educated in a traditional family, developing a typical Turinese temperament: reserved and not inclined towards bold emotional displays, but also thoughtful and ready to make a thorough analysis of any problem. In 1930 Enrico graduated in Medicine in his hometown, attending the clinical institutes of Benedetto Morpurgo (1861-1944), Ferdinando Micheli (1872-1937) and Carlo Gamna (1886-1950) (13, 23). In addition, he had several training experiences abroad, in some international research centers, such as the "Psychotechnic Institute" in Dresden (Autumn 1930), the "Electrodiagnostic Labo-

ratory" of the Salpêtrière Hospital in Paris (Spring 1931), the "University Institute for Occupational Diseases" in Berlin (Autumn 1932 and 1933), and the "Johns Hopkins Institute" in Baltimore, USA (Summer 1934) (23). In particular, the Institute in Berlin – founded by Ernst W. Baader (1892-1962) in 1925 as the third institution of modern occupational medicine worldwide after Milan and Moscow – enabled Vigliani to learn the fundamentals of modern occupational pathology. Furthermore, the Italian physician used his stays abroad to visit the main plants and industries of those countries and to study their industrial hygiene regulations, so that he could introduce them in Italy.

He inherited this passion for workers' health and safety from his father, Giovanni Antonio Vigliani (1877-1958), who was a pioneering occupational physician (13). Giovanni had initially worked at the Turinese automobile manufacturer "FIAT" and in a private workers' insurance company, called "La Vigile" until he established the medical section of the "Ente Nazionale di Prevenzione degli Infortuni" (ENPI, National Bureau for the Prevention of Accidents) in 1936. Giovanni Vigliani also stimulated scientific research in this new field, as reflected in the journal "Rassegna di Medicina Industriale" (Review of Industrial Medicine) that he founded in 1930.

On completion of his studies, Enrico Vigliani started to work with his father in the medical section of ENPI but continued academic research at the University of Turin, becoming a lecturer in Occupational Medicine when he was only 28. At that time his primary research interests were lead poisoning and biological monitoring, a field where he achieved pioneering results. Indeed, in 1934 the young Vigliani, first in the world, demonstrated the effect of lead on porphyrin metabolism showing, in collaboration with Claudio Angeleri, that the incorporation of iron into the heme group was impaired by exposure to lead, resulting in accumulation of protoporphyrin IX in the erythrocytes (7, 9, 36, 37). Furthermore, standardizing a fluorimetric method for the measurement of porphyrins in urine, he was able to assert that an increase in porphyrin levels in urine is the first sign of lead present in the organism, so revolutionizing the biological monitoring of lead poisoning (1, 26).

Another occupational health problem emerging in the 1930s was asbestosis. In 1939 Vigliani, acting as chief physician at the Turin section of ENPI, conducted one of the first European cross-sectional studies on 439 asbestos workers at four Italian factories, two of which were the largest asbestos manufacturing plants in Italy at that time (10, 24, 28). In his investigation Vigliani found that 47% of the subjects in groups doing the dustiest jobs had asbestosis and this percentage increased to 90% when analyzing workers who had been exposed for more than 6 years. On the basis of several clinical observations and industrial hygiene measurements, he concluded his research suggesting improvement of working conditions through ventilation, pre-employment medical examinations and regular medical check-ups (11). Even if those modern recommendations were never implemented, this groundbreaking study, carried out in parallel with an industrial hygiene survey, contributed to field experience in developing and testing exposure assessment tools and methods for determining airborne fibre concentrations (11).

## DIRECTORSHIP OF THE "CLINICA DEL LAVORO"

After his undeniable scientific successes as director of the Clinical Institutes of Industrial Medicine of ENPI in Turin and Milan (1937-1941), Vigliani was appointed director of the "Clinica del Lavoro" in 1942, when he was 35 (13). In his inaugural lecture, held on 26 February 1943, he well described the emerging topics in the field of Occupational Medicine at the time: pneumoconiosis and occupational cancer (particularly asbestos-related cancer and benzene-induced leukaemia), occupational toxicology and biological/environmental monitoring, industrial hygiene and industrial psychology and, lastly, the training of occupational physicians (25). Vigliani and his collaborators accurately studied and developed all these issues in the golden age of the "Clinica del Lavoro", often achieving important results at international levels thanks to the scientific intuitions of its director (3).

In the period between the 1940s and 1950s, occupational oncology became one of the main re-

search topics in all the world's Occupational Health institutes. At the first post-war International Congress on Occupational Medicine (London, 1948), Vigliani and Mario Barsotti statistically demonstrated the carcinogenicity of benzidine, by analyzing the occurrence of bladder cancer in 280 workers exposed for more than one year to aromatic amines (2). In this way benzidine was demonstrated to be at least as carcinogenic as beta-naphthylamine (3). Vigliani was the first to understand the value of laboratory research in occupational oncology, since he had the insight to establish a modern laboratory of diagnostic cytology and occupational cytogenetics at the "Clinica del Lavoro" in 1948, sponsored by the "Società Montecatini" (13) and purchase a "Siemens Elmiskop I" electron microscope (the first at the University of Milan) sponsored by INAIL (Italian Workers' Compensation Authority) (4). These technological innovations supported another international success of Italian occupational medicine in the field of workrelated cancer: the demonstration of the haematologic alterations due to benzene. In 1938 Vigliani had already reported ten cases of benzene-induced leukaemia in a critical survey of the available literature from the previous ten years, in collaboration with Fausto Penati (39). Actually, this groundbreaking report was little known in the international scientific community, since it was published in an obscure journal. Moreover, he had already reported that benzene could produce proliferative blood disease at the 8th congress of the "International Permanent Commission on Occupational Health" in Frankfurt (Germany) in 1938, but the meeting was interrupted due to the fear of the impending outbreak of the Second World War (27). After the war, Vigliani resumed his research in this field in the modern laboratory of the "Clinica del Lavoro" in collaboration with Giulio Saita, who had investigated 23 cases of leukaemia attributed to benzene in 1945 (21), and Alessandra Forni, who had been trained in molecular biology at the "Memorial Sloan-Kettering Cancer Center" in New York. In the 1960s his team published two landmark works based on retrospective studies in France and Italy that involved 77 deaths in benzene workers, approximately half due to leukaemia

and half to aplastic anaemia (33, 40). He subsequently reviewed data from Italian benzene-exposed workers between 1928 and 1938, reporting 60 cases of aplastic anaemia and 10 of leukaemia (34). These original studies on benzene-induced leukaemia contributed to the recognition of the carcinogenicity of this solvent by the *International Agency for Research on Cancer* (IARC), leading to its international ban (22).

In the same period, Vigliani again took up his work on pneumoconiosis and in particular on damages caused by asbestos and silica. As editor-inchief of "La Medicina del Lavoro", he initially contributed to the diffusion of the German studies on the carcinogenicity of asbestos, forerunners of the 1950s studies by Richard Doll (1912-2005) (18). Also, he gave his immediate support to the studies by Chris Wagner (1923-2000) on pleural mesothelioma. In fact, he attended the "Pneumoconiosis Conference", held in Johannesburg in 1959, where Kit Sleggs and Chris Wagner presented their first results on the relationship between pleural cancer and asbestos. Vigliani's interview given to a local South African newspaper "The Sunday Times" led to the first announcement of Wagner's studies in the media (18). Vigliani also attended the famous conference on the "Biological Effects of Asbestos" chaired by Irving Selikoff (1915-1992) in 1964, presenting the first Italian study that showed a higher mortality for lung cancer and pleural mesothelioma in Italian workers compensated for asbestosis (35).

In the 1950s-1970s the "Clinica del Lavoro" was a national and international reference point for respiratory physiopathology, as shown by the funds provided for research in this sector by the "European Coal and Steel Community" (ECSC) (3). At that time the ECSC economically supported studies on etiopathogenesis of pneumoconiosis, funding the main research centres in Europe. The "Clinica del Lavoro" was able to receive substantial economic funding since Vigliani had a large case series thanks to an agreement with INAIL to send all cases of pneumoconiosis from Lombardy (and the most severe cases from the rest of Italy) to the "Clinica del Lavoro" which had 90 beds for admission of patients (60 beds for men, and 30 for women). Between 1948 and 1982 the Milanese institute promoted a long series of clinical and experimental research on respiratory physiopathology and the pathogenesis of silicosis, substantially influencing Italian and European research in this field. Vigliani and Benvenuto Pernis (1923-2011) demonstrated the immune pathogenesis of silicosis, showing that the stimulation of the immune system in this disease was a consequence of an effect of the mineral dusts on the macrophages, mediated by the production of interleukin-1 (12, 14, 15, 37, 38). Until then, no explanation had been found for the mechanisms by which the damaging action of silica could persist after cessation of exposure.

The collaboration with Pernis was not limited to silicosis. For example, they showed that the pathogenesis of vascular encephalopathy in carbon disulfide poisoning - described by Vigliani and the psychiatrist Carlo Lorenzo Cazzullo (1915-2010) was caused by an inhibition of the clearance factor in the blood (32, 36). His partnership with Pernis also led to some fundamental studies in the comprehension of the pathogenesis of respiratory problems due to inhalation of vegetable dusts, highlighting for the first time that byssinosis was due to the inhalation of bacterial endotoxins contained in cotton dust (17). Lastly, Vigliani and Pernis, the first at international level, identified the cause of the so-called "foundry fever" or "metal fume fever" as due to the liberation of endogenous pyrogen by granulocytes that had phagocytised minute particles of the fumes (16).

# HIS ROLE IN THE "PERMANENT COMMISSION AND INTERNATIONAL ASSOCIATION ON OCCUPATIONAL HEALTH"

From the end of 1950s Vigliani's scientific authority was widely recognized internationally, as confirmed by his prominent role in the "Permanent Commission and International Association on Occupational Health". In this he was helped by the fact that he could fluently speak four languages (French, German, English, and Spanish) in addition to Italian. Vigliani was initially Secretary-Treasurer from 1957 to 1975 under the "Scandinavian" presidencies of Sven Forssman (1957-1969) and

Leo Noro (1969-1975) and subsequently he was President himself for six years (1975-1981), with Robert Murray (UK) Secretary. During his period of active service, the Commission developed from an academic institution to a more open association, which brought a substantial increase in membership. Indeed, until 1957 the strict membership policy of the Commission fixed an upper limit of 200 members and allowed no more than 12 members from the same country (27). During the Secretariat of Vigliani a new policy was adopted, making the acceptance of members more liberal. Thereafter membership increased rapidly, exceeding 500 members in 1970 and 1,000 in the 1980s (8). In 1957 the new membership policy led to a change in the name of the organisation, from "International Permanent Commission on Occupational Medicine" to "Permanent Commission and International Association of Occupational Health", since the term "association" was believed to better describe the new features of the Commission (27). As Secretary, Vigliani also promoted the publication of a newsletter, circulated to all members of the association and containing congress reports, reviews of publications, a list of coming events, and information on research and other activities of interest to the members. During his mandate, he also contributed to setting up subcommittees devoted to specific topics (now called "scientific committees"), one of the strengths of the present Commission. A decision to set up such committees was made at the Helsinki Congress in 1957, and soon committees on "absenteeism", "maximum allowable concentrations", "shift work", and "lead poisoning" began to function (8). During his presidency, Vigliani improved the quality of the committees, increased their number and established general rules for their activity in article 6 of the 1975 Constitution. Chairmen were scientifically and financially responsible for their committee activities: financial contributions by the Commission to committees were envisaged as well as, at a later stage, some income in favour of the Commission based on the Scientific Committees' activities. The names of the first scientific committees in 1975 (table 1) well represented the main issues of research in the field of Occupational Health in that period (iron and steel indus-

**Table 1** - List of the Scientific Committees of the Permanent Commission and International Association on Occupational Health in 1975

- Absenteeism (Sickness Absence Statistics)
- Asbestosis
- Behavioural Toxicology
- Byssinosis
- Electropathology
- Industrial Hygiene
- Permissible Limits for Airborne Potentially Toxic Chemicals in Working Areas
- Mental Health in Industry
- Occupational Health in the Production of Artificial Fibres
- Occupational Health in the Chemical Industry (Medichem)
- Occupational Health Services in Developing Countries
- Occupational Geographical Pathology
- Occupational Health in the Iron and Steel Industries
- Occupational Health Nursing
- Occupational Health Services in Small Industries
- Pesticides
- Shift-work

tries, asbestosis and artificial fibres, pesticides and chemical industries, permissible limits and industrial hygiene, shift-work, behavioural toxicology and mental health), but also reflected some emerging problems (small enterprises and developing countries) and the growing role of non-medical professionals (e.g. nurses) in the life of the association. In the 1970s and 1980s the Scientific Committees became not only the backbone of scientific activity of study and research but also a major organization in its own right that greatly contributed to the aims and progress of the Commission.

### VIGLIANI'S LEGACY

Even after his retirement from the "Clinica del Lavoro" and from all international appointments, Vigliani kept up with the development of science and maintained his role of a renowned senior scientist with a profound knowledge of most of the current problems in occupational medicine. In particular, he continued to promote and organize conferences and meetings on this subject at the "Fondazione Carlo Erba" in Milan (where an Occupa-

tional and Environmental Health Section had been set up in 1976) until a few months before his death.

The figure of Vigliani as a man is remembered for his charismatic personality, his self-control in reactions and interpersonal relationships, his penetrating rationality, his practical approach and his self-assurance in projects and choices, rigorous selfdiscipline (expected also from his collaborators), his continuous search for the best both professionally and in his personal life, his charming elegance in manner and allure, and his moral force when his authority was severely contested during the social protests in the early 1970s. If not attending conferences or seminars, Vigliani used to spend the morning in the wards and later, after a one-hour lesson at 11 am (open to students, post-graduate students and the whole medical staff of the Clinica) he dedicated a couple of hours to national and international contacts. Generally the afternoon was spent in the research laboratories and towards evening in his study to read attentively the national and international scientific literature. This, in addition to general administrative and organizational duties involved in running a Clinic and University Institute.

Vigliani's pupils well remember the meticulousness of their professor in clinical practice at the bedside as well as in the research activities in the laboratory. As a clinician, he was very thorough and accurate in occupational history collection, believing this approach was fundamental for every physician to diagnose occupational diseases. As a researcher, his genial and pioneering insights (e.g. the establishment of a modern laboratory at the "Clinica del Lavoro") made Vigliani well- known at the international level. He was the first of Italian and European scientists to understand the importance of laboratory research in Occupational Medicine, promoting groundbreaking studies on industrial hygiene and molecular biology. He therefore encouraged the purchase of advanced technical tools, such as radiological and laboratory equipment (e.g. the electron microscope). As a modern European researcher, he completed his education at foreign research institutes (Germany, France, USA), attended many international conferences, and continued his research activities abroad, even at an older age, i.e. the studies he personally conducted in Ankara

(Turkey), Zurich (Switzerland) and Johannesburg (South Africa) between 1971-1974. Like the brilliant scholar he was, he immediately recognized the value of international exchanges in the scientific community, thus making the "Clinica del Lavoro" a reference point and model for new institutes (e.g. the "Finnish Institute of Occupational Health", founded by Leo Noro in the 1950s). As already mentioned, Vigliani's scientific authority was widely recognized internationally, as confirmed by his role in the "Permanent Commission and International Association on Occupational Health", the frequent invitations to attend international conferences as speaker (e.g. the famous conference on asbestos chaired by Selikoff in 1964) and his appointment as member of the scientific board of the ECSC. As editor-in-chief of "La Medicina del Lavoro", the oldest Occupational Health journal in existence today (20), he promoted the publication of high level papers and focused attention on the international literature in the field, thus increasing recognition of the journal in the worldwide scientific community. Vigliani improved the quality of the Library of the "Clinica del Lavoro", subscribing to all the most important journals of that time, so that it became one of the most important libraries in this field. As a teacher, he was able to bring out the talents in his students and collaborators and to surround himself with the best scientists/clinicians of that time in each field, such as Alessandra Forni - cytogenetics and histology, Benvenuto Pernis - molecular biology, Gerolamo Chiappino - pathology, Carlo Cazzullo - psychiatry, Cesare Maltoni (1930-2001) oncology, Antonio Grieco (1932-2003) - ergonomics, Mihrtad Pasargiklian and Emilio Sartorelli respiratory physiopathology, Nicola Zurlo (1916-1990) - industrial hygiene. Vigliani personally checked the work of his collaborators, encouraging them to find new ideas for scientific research in their field. Many of his pupils were themselves appointed as Professors of Occupational Medicine: at Bari (Luigi Ambrosi and Vito Foà), Brescia (Chiappino and Lorenzo Alessio), Genoa (Pernis), Milan (Chiappino, Foà, Grieco), Siena (Sartorelli). He emphasized the importance of education and training of occupation physicians and industrial hygienists and actively promoted the foundation of the "Associazione Nazionale dei Medici d'Azienda" (AMNA, 1987) and the "Associazione Italiana degli Igienisti Industriali" (AIDII, 1969).

Lastly, as a modern Bernardino Ramazzini (19), Vigliani believed that Occupational Medicine should not only be limited to the diagnosis and cure of occupational disease, but had to be based on active research, aimed at understanding the pathogenetic mechanisms of these conditions and modifying their etiological determinants, which is the aim of preventive occupational medicine.

NO POTENTIAL CONFLICT OF INTEREST RELEVANT TO THIS ARTICLE WAS REPORTED

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