

**The Contribution of the Clinica del Lavoro to the
Development of Industrial Hygiene and Toxicology in the
Twentieth Century**

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Abstract

In 1910, the founder of the Clinica del Lavoro of Milan, Luigi Devoto established a chemistry laboratory in the new institute, sustaining its importance in the study of occupational diseases. In 1948, the new director of the Clinica, Enrico C. Vigliani established the first laboratory of industrial hygiene in Italy, in the years of the economic boom. In 1960s, this laboratory, directed by Nicola Zurlo, significantly contributed to the research in the field. In 1980s and 1990s, the laboratory of the Clinica started to explore the field of environmental toxicology, studying the effects of benzene and other traffic pollutants on the general population. The analysis of history of the Clinica del Lavoro of Milan may represent a valuable tool for studying the origin and the development of industrial hygiene, occupational and environmental toxicology in the twentieth century.

Keywords:

industrial hygiene; industrial toxicology; environmental toxicology; Clinica del Lavoro; Milan; history

The “Clinica del Lavoro”, established in Milan at the beginnings of the twentieth century, was the first institute in the world to be devoted to the scientific study and the treatment of work-related diseases, becoming a model for similar institutions in Moscow (1923) and in Berlin (1925).¹ Under the direction of Luigi Devoto (1864-1936), Luigi Preti (1881-1941), and Enrico C. Vigliani (1907-1992), the Clinica del Lavoro significantly contributed to the development of the scientific research in all the fields of Occupational Health.¹ The aim of this historical paper is to analyze the evolution of the industrial hygiene and toxicology during the twentieth century throughout the contributions provided by the Clinica del Lavoro of Milan to ~~the~~ international research in these fields.

The chemistry laboratory in the Clinica del Lavoro (1910-1950)

When the Clinica del Lavoro was inaugurated in 1910, its founder, Luigi Devoto, established a chemistry laboratory on its first floor, above the entrance (Figure 1).² The laboratory was able to support the physicians, providing chemical analyses on biological fluids of their hospitalized patients. When Devoto decided to establish a chemistry laboratory in his new institute, he had a pioneering idea. Indeed, in that period the clinicians were used to conducted basic chemical analyses in their own medical offices or in a small room in the wards without the support of specialized technicians. Clinical pathology was nothing more than simple examination of the urine and blood count.³ Only great hospitals in the United States and in the United Kingdom had their own laboratories, where chemists were employed to provide help to clinicians in analysis.

However, even in these countries the clinical laboratories not always accorded the respect their importance deserves. A comment, made in 1918, well describes their conditions: “Usually after the hospital has been completely erected, certain space, unsuitable for any other purpose, is assigned to the laboratory. It is thus that we find this department frequently located in basements, in out of the way nooks and corners, in outhouses or roof structures built as an afterthought. The laboratory is gloomy, the ventilation unsuitable, and the general conditions such as to make the scientist working

there cognizant of a spirit of depression in his assistants and help".³ Luigi Devoto actually believed that the chemistry laboratory also had a decisive role in the comprehension of physio-pathogenic mechanisms of occupational diseases and in their treatment. This different consideration is demonstrated by the fact that he placed the laboratory on the first floor of the institute, in well-ventilated and bright rooms. Devoto sustained that chemistry laboratory had to "examine the substances commonly used by the workers and analyze the components of the air in workplaces".² It had to evaluate "the effects of occupational toxins on the functions of human organism".² With these considerations, Devoto seems to outline the objectives of a modern laboratory of industrial hygiene and toxicology. So, it does not come as a surprise that the first international technical conference on industrial hygiene was organized by Luigi Devoto in Milan on May 1912. The director of the Clinica del Lavoro invested many funds in equipment for modernizing his laboratory; up to 12 chemists could simultaneously work in the laboratory.² Initially, the physician Luigi Preti (1881-1941) and the chemist Monti co-directed the laboratory, while since the end of the 1920s the head of the laboratory was the chemist Giovanni Battista Lo Faso. In 1928 Lo Faso published a paper on a pioneering method of determining the concentration of mercury in human urine⁴ and, in collaboration with the pathologist Giorgio Boattini, he also wrote a considerable paper on lung anthracosis of coal-miners, determining carbon and iron in the pulmonary tissues of workers affected by this occupational disease.⁵

In the following years, the Clinica del Lavoro, directed by Luigi Preti after the death of Devoto, continued its studies in the field of occupational toxicology. In detail, the chemistry laboratory developed new methods for determining concentration of lead in urine, blood and saliva.⁶⁻⁹ All these studies demonstrated the elevated interest towards occupational toxicology and industrial hygiene in the "Clinica del Lavoro" in the first thirty years of its activity. Preti and his collaborators mainly focused on classical occupational toxics and, in particular, on the determination of mercury and lead in body fluids. Indeed, in that period, scientists and physicians were looking for high-sensitive methods for early diagnosis of occupational poisoning. It should be also note that the

direction of the chemistry laboratory, initially managed by a physician (Preti), was given to a chemist (Lo Faso), so valuing the role of this figure in a clinical and research institute.

Finally, the first decades of the chemistry laboratory of the “Clinica del Lavoro” demonstrate that initially there were not separate laboratories dedicated to toxicology and to clinical pathology for hospitalized patients, but there was a general chemistry laboratory, in which different topics were analyzed and studied without distinctions.

Industrial Hygiene in Milan in the postwar economic boom (1950-1970)

~~The~~ War World II limited the research of the Clinica del Lavoro, which suffered significant damages as a result of the Allied bombing of Milan in 1943. In the same period, the institute changed its director after the early and unexpected death of Luigi Preti. In 1942, Enrico C. Vigliani was appointed as new director of the Clinica, but his first problem was to deal with the reconstruction of the institute, ~~which~~ ~~that~~ was completed in 1947.¹⁰⁻¹¹

In the post-war period, the Italian economy was booming, with record high growth rates and the development of new and old industries. The increase of production of Italian factories determined a rise of work-related accidents and occupational diseases, so various industries seek the medical and scientific support of the Clinica del Lavoro in preventing, identifying and treating health problems related to work.¹⁰ In that period, Montecatini was the giant of Italian industrial chemistry and its headquarter was in Milan, which was the leading industrial city of Italy. The “Società Anonima delle Miniere di Montecatini” was founded in 1888 in Tuscany, having its roots in the mining industry (copper mines). After the discovery of pyrite in Tuscany, Monecatini started to ~~produce~~ ~~product~~ sulfuric acid; it later produced ammonia, becoming known for its widely used process for fertilizer production. In 1947 Enrico Vigliani was requested by Mario Barsotti – director of Occupational Health Service of Montecatini – to conduct a study on bladder cancers among workers of an azo dye factory belonging to the big chemical industry of Montecatini.¹⁰ In 1948,

Barsotti and Vigliani showed the first results on mortality for bladder cancer by azo dye during the Conference of International Society of Occupational Health in London.¹¹⁻¹² The scientific achievements led Montecatini, together with INAIL (Italian Workers' Compensation Authority), to make funds available for establishing an industrial hygiene laboratory in Clinica del Lavoro. So in 1948 Vigliani could inaugurate the first industrial hygiene laboratory in Italy within the "Clinica del Lavoro" of Milan (Figure 2), nominating the young chemist Nicola Zurlo (1916-1990) as head of the new laboratory.¹⁰ At the same time, in 1949, Vigliani appointed Raoul Grisler (1922-2010) as director of chemistry laboratory with the aim of transforming it into a modern clinical laboratory, that could provide clinical analysis not only for the Clinica del Lavoro, but also for all the hospitals in Milan.¹⁰ The industrial hygiene laboratory of Zurlo (supported by Montecatini and INAIL) and the biochemistry laboratory of Grisler (supported by Clinica del Lavoro) were never in contrast with each other; rather they collaborated on many topics.

The first works of the new laboratory of industrial hygiene were on metal intoxications. In particular, at the ~~beginning~~beginnings of ~~the~~ 1950s Zurlo focused on lead determination in biological material and on chronic mercury poisoning in a manufacture of luxury hats in Alessandria (Northern Italy).¹³⁻¹⁴ Lead intoxication was another issue well developed in that period.¹⁵⁻¹⁸ ~~Industrial~~The industrial hygienists of the Clinica del Lavoro also developed new methods for determining silica in the environment and proposed masks and other devices to avoid or minimize exposure to dust in the workplace.¹⁹⁻²⁵ In that period, the team started to investigate on the health effects of organophosphate insecticides, which were an emerging problem in rural world.²⁶⁻²⁷ It is interesting to note that in 1950s the Clinica del Lavoro also conducted pioneering studies on air pollution, developing methods for monitoring toxic fumes and vapors in the atmosphere.²⁸⁻³¹ In the same years, the chemistry laboratory of Grisler conducted studies on biochemical alterations in workers affected by silicosis and on the intoxication by trichloroethylene.³²⁻³⁶

During the 1960s, the laboratory of industrial hygiene ~~greatly expanded had a great development.~~

The European Coal and Steel Community (ECSC) and INAIL made available funds for studying pneumoconiosis and its prevention. In that period, Vigliani was able to purchase a “Siemens Elmiskop I” electron microscope – the first at the University of Milan – sponsored by INAIL.¹¹ Furthermore, the Clinica del Lavoro signed an agreement with INAM (“Istituto Nazionale di Assicurazione contro le Malattie”, National Institute for Insurance Against Sickness), the most important mutual fund in Italy at that time.¹⁰ In detail, the clinical pathology laboratory of the Clinica del Lavoro, directed by Grisler, agreed to provide laboratory analysis for all the patients of INAM in Milan, so the Clinica del Lavoro started to provide laboratory analysis for 400 patients a day, reaching over 400,000 patients in a year at the end of 1960s. Thanks to huge economic funds derived from these new incomes, in 1963 the industrial hygiene laboratory was moved in a new modern structure (“Padiglione FEAL”) built next to the old edifice of the Clinica.¹⁰ Furthermore, economic resources also allowed the recruitment of new staff: the Clinica del Lavoro were able to hire personnel: chemists, engineers, technicians and physicians. The laboratory was equipped with the most update instrumentation, such as X-ray diffractometer for the analysis of the structure of crystals in powders and fibers, gas-chromatographs with flame ionization and electron capture detector for the analysis of volatile organic compounds in air samples and industrial products, graphite furnace and flame atomic absorption spectrometry for the measurements of metals in environmental and biological samples, UV/Visible spectrometry, phase contrast microscopy for the analysis of silica particles and asbestos and glass fibers.

In that period, Gianmarco Cavagna, one of the most important Italian industrial toxicologists of that period, conducted several studies on byssinosis.³⁷⁻⁴⁰ In the same period, in the Clinica del Lavoro, Vito Foà and Carla Antonini, demonstrated the presence of endotoxins in the atmosphere of a cotton carder,⁴¹ supporting that the pathogenesis of byssinosis was based on endotoxin and anticipating studies of Rylander.⁴² Furthermore, Cavagna developed pioneering researches on health effects of insecticides and carbon disulfide.⁴³⁻⁵⁰ Zurlo, Cavagna and their team also wrote several

contributions on lead intoxications, pneumoconiosis and toxics in atmosphere and at the workplace.⁵¹⁻⁶² In this context, Zurlo invented a valuable mercury clepsydra vacuum pump to measure concentrations of atmospheric dusts by counting particles, internationally known as “Zurlo’s pump”.⁶³ The Clinica del Lavoro conducted several studies on industrial and environmental toxicology on nitroglycol and nitroglycerine (and its correlation with “Monday disease”), trichloroethylene, polytetrafluoroethylene, indene, penicillin, sodium hypochlorite (liquid bleach) and on zinc-fume fever.⁶⁴⁻⁸⁰ General papers on the development of industrial hygiene, its role and its problems were also published.⁸¹⁻⁸⁵ Works by Grisler on diagnosis and treatment of lead intoxication and on the development of other biomarkers related to occupational exposures are also noteworthy~~should be mentioned~~.⁸⁶⁻⁹⁵

In this period, the Clinica del Lavoro introduced a new approach to the problems of industrial hygiene in factories, through interventions directly agreed with the workers in the factory assemblies. It was not infrequent to see Zurlo and his collaborators talking with the workers of the factories in which they conducted their studies. The medical and technical staff of the Clinica del Lavoro could collect samples and radiological investigations on the workers directly in the workplace, also thanks to the presence of laboratory and radiology mobile units.⁹⁶ The glorious twenty-year period of industrial hygiene and toxicology in Milan reached its peak in 1969, when Zurlo founded the *Associazione Italiana Degli Igienisti Industriali* (AIDII), the first Italian association for industrial hygienists.¹⁰

The crisis and the new development (1970-2000)

In July 1970, the Clinica del Lavoro was dismayed by the fact that Gianmarco Cavagna suddenly died during an experiment on the health effects of dibromotetrafluoroethane, a new chemical product developed by Montecanini for fire suppression systems.¹⁰ Furthermore, the researchers conducted by Cavagna himself on the effects of dichlorvos – an organophosphate, widely used as an

insecticide – on the levels of plasma and erythrocyte cholinesterase (ChE) activities in 22 newborn babies were judged inappropriate by mass media and public opinion.⁴⁷ In the meantime, student protests spread to the University of Milan and targeted Enrico Vigliani and his collaborators, accusing them of ~~colluding~~~~being colluded~~ with the employers and industry magnates.¹⁰ ~~These~~~~The~~ protests and some alleged economic scandals forced Vigliani to move away from Italy in 1971, so he decided to continue his studies in South Africa and Turkey.¹¹ The Clinica del Lavoro remained without a direction until 1977. In the first years of 1970s, the institute apparently continued the studies developed in previous decades. The works published in the period 1970-1977 were on lead intoxication, silicosis, general industrial hygiene and toxicology of cotton dusts, even if a decreasing trend in the scientific productivity was observed.⁹⁷⁻¹¹⁶

Another event that revolutionized the life of the Clinica del Lavoro was the Seveso disaster. It was an industrial accident ~~occurred~~ in July 1976 in a small chemical manufacturing plant approximately 20 kilometers north of Milan, resulting in the highest known exposure to dioxin (TCDD) in residential populations.¹¹⁷ Nicola Zurlo was ~~appointed as~~ responsible for monitoring the sampling of dioxin in Seveso, so he moved away from the Clinica del Lavoro, together with some collaborators such as Gianfranco Peruzzo and Carlo Sala.¹⁰ In the same year, Montecatini – renamed as Montedison – transferred its own personnel and equipment to other laboratories. These changes were the opportunity to create a new team of industrial hygienists and toxicologists.¹⁰

At the end of ~~the~~ 1970s, the new director of the Clinica del Lavoro, Gerolamo Chiappino (1933-2016), requested Vito Foà – ~~who was~~~~the~~ responsible ~~for the~~~~of~~ toxicology division – to reorganize the laboratory of industrial hygiene. Foà, who had started to work in the industrial hygiene laboratory of the Clinica del Lavoro since 1958, could make use of skills and experience of old and new colleagues such as Antonio Colombi, Marco Maroni (1949-2006), Gianfranco Peruzzo, Mario Patroni, Francesca Andreoletti, and Marina Buratti. In the following decade, the Clinica del Lavoro again began to develop important scientific research in the field of industrial hygiene and toxicology. In detail, the laboratory conducted studies on a large number of different substances:

carbon disulfide, aromatic amines, chromium, dimethylformamide, vinyl chloride, asbestos, and n-hexane.¹¹⁸⁻¹³¹ In this period, Foà, Colombi and Maroni proposed to use the determination of d-glucaric acid and of the pattern of urinary porphyrins as indicators of effect for exposure to chemical substances.¹³²⁻¹³⁵ The same authors, in collaboration with Marina Buratti, developed an analytical method for speciation of urinary arsenic in order to distinguish occupational and alimentary exposure.¹³⁶⁻¹³⁹ Classical metal intoxication (lead and mercury) and exposure to dusts continued to be investigated.¹⁴⁰⁻¹⁴² The team monitored workers' exposure in the production plants of 1,3-butadiene and conducted a survey on pentachlorophenol in wood industry.¹⁴³ It should be also mentioned the large number of studies on polychlorinated biphenyls, especially at the end of 1970s and the beginnings of 1980s.¹⁴⁴⁻¹⁴⁹ At the end of [the](#) 1970s, new Occupational Health Units were established in the cities around Milan, where physicians – who have studied and have worked in the Clinica del Lavoro – started to work and to conduct scientific researches. In particular, the institute of Milan collaborated with Occupational Health Units of Lecco (Sergio Zedda, Carlo Sala and Angelo Maria Cirila) and Desio (Italo Ghezzi and Franco Toffoletto). These collaborations were mainly developed by Lorenzo Alessio on intoxication from metals, in particularly lead, cadmium and other metals; in these studies the association of clinical signs and new indicators – including Zinc protoporphyrin, ZPP, recently discovered – was investigated.¹⁵⁰⁻¹⁶²

In 1980s, the intense work on biomonitoring conducted at the Clinica del Lavoro and in other European institutes prompted the Commission of the European Community to start the publication of the series on biological indicators for the assessment of human exposure to industrial chemicals. In the 1990s the researchers of the Clinica were actively involved in the works of the new born “Scientific Committee on Occupational Exposure Limits” (SCOEL) of the European Commission. In the meantime, Enea Occella (1928-2011) from Polytechnic University of Turin continued to collaborate with the Clinica del Lavoro in researches on asbestos. These works, specially developed with Mario Patroni, played a determinant role in the enactment of Italian asbestos legislation and in the identification of its limit values.¹⁶³

Among the works on general concepts of industrial hygiene and toxicology,¹⁶⁴⁻¹⁶⁷ the paper by Vito Foà published in 1989 well ~~describesevidences~~ the shift of classical industrial hygiene towards ~~an~~ occupational and environmental hygiene.¹⁶⁸ This transformation is also ~~supported~~~~testified~~ by the foundation of the International Center for Pesticide Safety by Marco Maroni in 1990.¹⁶⁹⁻¹⁷⁰ Furthermore it should be mentioned the works by Patroni on asbestos fibers and their concentration in the atmosphere.¹⁷¹⁻¹⁷³ At the beginning of the 1990s new environmental and toxicological issues associated with air pollution due to traffic emissions concerned occupational and public health. New ~~researchresearches-were~~ focused on exposure to benzene, a carcinogenic component of the mixture of aromatic hydrocarbons used to increase the gasoline anti knocking power, after the ban of leaded gasoline in Italy, using air and biological monitoring.¹⁷⁴⁻¹⁷⁸ Other pollutants arising from traffic, such as particulate matter and polycyclic aromatic hydrocarbons were also investigated, as well as the indoor air quality.¹⁷⁹⁻¹⁸⁴ Nevertheless, classic occupational toxicology issues continued to be investigated.¹⁸⁵⁻¹⁸⁷ The lowering of occupational exposure limits, and the necessity of monitoring exposure to chemicals in the general population prompted the researchers of the Clinica del Lavoro to investigate new biomarkers of exposure using very specific and sensible assays based on novel techniques such as mass spectrometry.

Conclusions

The history of laboratories of Industrial Hygiene and of Toxicology of the Clinica del Lavoro of Milan shows the development of these disciplines during the twentieth century. Luigi Devoto had the pioneering idea to establish a chemistry laboratory in his institute, since he believed that the laboratory was a valuable tool for investigating the pathogenesis and the treatment of occupational diseases. In the first decades of the century, the laboratory focused its researches towards intoxications by metals and, particularly, lead intoxication. In the period after WWII, the Italian economic boom led the Clinica del Lavoro, directed by Vigliani, to implement the laboratory activities, thanks to the support of some ~~largebig~~ chemical industries (Montecatini), INAIL and

mutual funds. In that period, the laboratory of Industrial Hygiene directed by Nicola Zurlo developed researches in different fields, such as silicosis, dusts, organophosphate insecticides, occupational toxicology, achieving relevant results. It should be mentioned the studies by Gianmarco Cavagna on pathogenesis of byssinosis based on endotoxins. Agriculture and industry appeared as the principal fields of interest for industrial hygienists and toxicologists. In the 1980s, modifications in the productive sectors in Italy, as well as in the other industrialized countries, led to a deep change also in the research of the Clinica. In detail, alongside the classic occupational issues, the laboratory began to deal with environmental toxicology, focusing on the effects of environmental toxics (e.g. benzene and polycyclic aromatic hydrocarbons arising from traffic) on general population and developed the new issue of indoor air quality. It should be also noted that the scientific works of the Clinica of that period were mostly published on “La Medicina del Lavoro”. This scientific journal – the oldest regular periodical of Environmental and Occupational Health, originally founded in December 1901 as “Il Lavoro” by Luigi Devoto and Carlo Moreschi (1876-1921)¹⁸⁸⁻¹⁸⁹ – may therefore be a precious source of information for studying the development of industrial hygiene and occupational toxicology in those years. In conclusion, the laboratories of the Clinica del Lavoro mirror the worldwide development of industrial hygiene and occupational and environmental toxicology in the last century, representing for many years an international reference point for the discipline, in Italy and worldwide in the all industrialized countries.

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Figure legends

Figure 1 – The chemistry laboratory of the Clinica del Lavoro at its foundations. A) Clinica del Lavoro side façade, the laboratory was at the first floor; B) Planimetry; C) Chemistry laboratory.

Figure 2 – The industrial hygiene laboratory in the 1960s. A) Chemistry laboratory; B) the sample preparation for the determination of Pb in blood; C) two members of the team performing measurements at the workplace using the mobile unit. Source: Archivio Edison, Centro per la cultura d'impresa.

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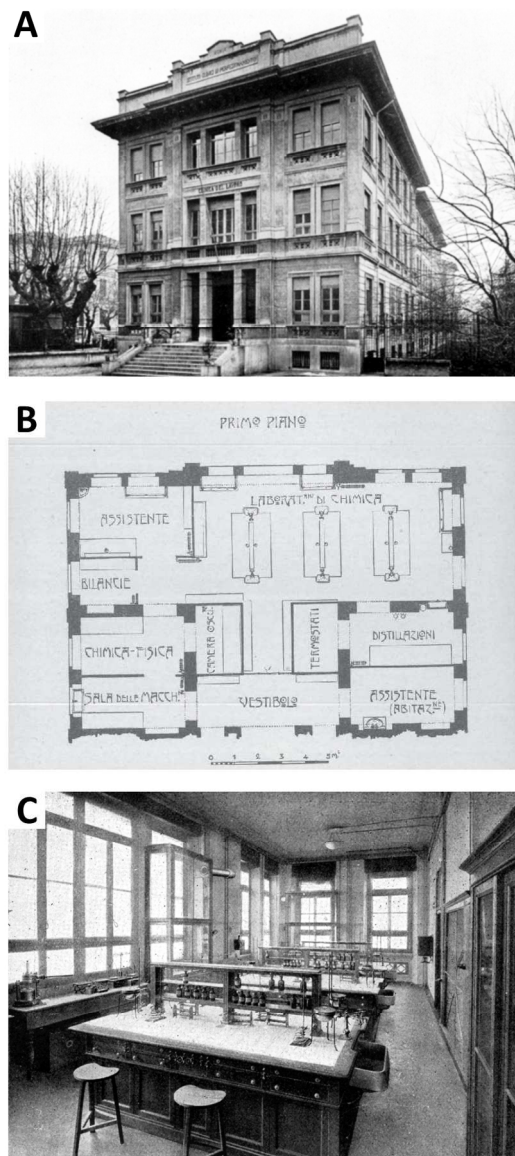


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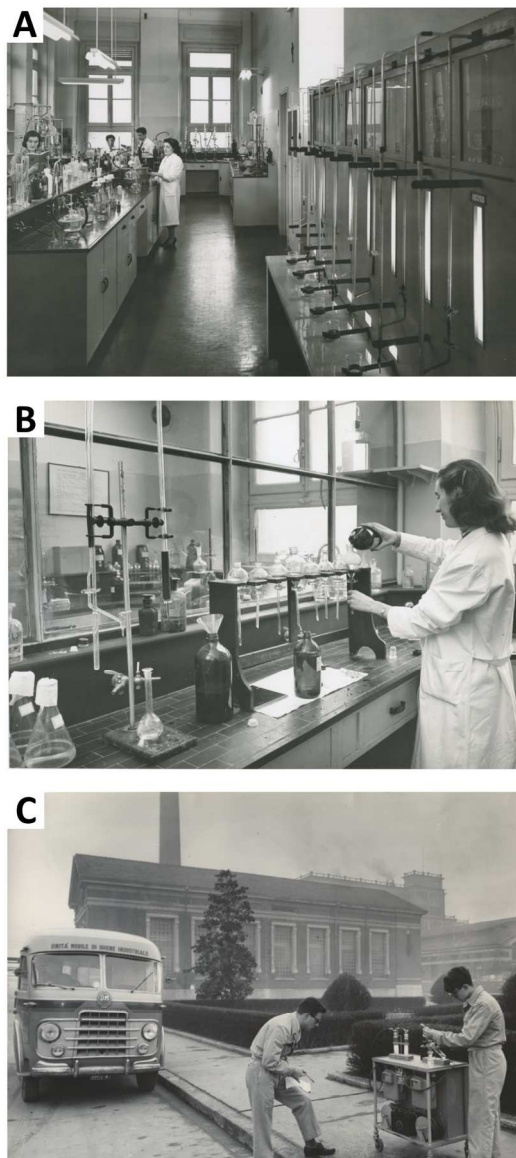


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