



Portraits from Our Medical History: Dr. Elhan Özlüarda (1927-2013)

Tıp Tarihimizden Portreler: Dr. Elhan Özlüarda (1927-2013)

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Figure 1. Dr. Elhan Özlüarda (1927-2013)¹.

Dr. Elhan² (Özü Türk) Özlüarda (Figure 1) is one of the scientists who left her mark on virology and vaccinology

studies in Türkiye during the Republican period. She was born in İstanbul in 1927, as the third daughter of a captain from Van (Ekrem Özü Türk), who was a teacher at the İstanbul Artillery School, and a housewife mother (Hayriye Özü Türk), an immigrant from Macedonia, exactly 210 years after the famous letter of³ Lady Mary Montagu, who was another important woman in the history of smallpox vaccination, in which she reported that the Turks used a vaccine to prevent smallpox which caused massive epidemics and deaths in England during her stay in Türkiye as the wife of the British Ambassador (1716-1718), and which would lead to the spread of this method in England, and 35 years after the establishment of the Telkikhane-i Şahane (Osmani)⁴, the first official smallpox vaccine production center of the Ottoman Empire, and just only one year before the establishment of the Refik Saydam Central Institute of Hygiene⁵, one of the most important science and vaccine production centers in the history of public health and preventive medicine in the Republic of Türkiye, where she would spend 22 years of her

¹ See (1) for photographs.

² Elhân, a word of Arabic origin, is the plural form of the word "lahn" meaning "melody, tune" (2).

³ 1 April 1717 (3,4).

⁴ 27 July 1892 (5).

⁵ 27 May 1928; then known as the "Central Sanitation Centre" (6,7).

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professional life, unaware of how all these dates would affect her personal history (1,3-7). Her grandfather gave her the name "Elhan", meaning "melody, tune" (2).

When Elhan was six years old, the family lived in Kars for a while due to her father's assignment. Elhan started primary school at Kars Gazi Primary School, and one of the most memorable moments in her childhood memories is going to school with her older sisters Neriman and Kamuran in a sled carriage driven by a horse they named "Cevher" through the snow. The loss of her father when she was only 14 years old would leave a deep mark on her (1).

In the January 5, 1927 issue of the Weekly Epidemiological Record⁶, one of the World Health Organization's official publications on infectious diseases and epidemics, as well as epidemiology (9), the day Dr. Özlüarda was born, smallpox was among the diseases on the agenda, along with cholera and plague, typhus and influenza. In the same year (1927), the BCG vaccine, developed by Albert Calmette and Camille Guérin in 1921, was first used in newborns. In addition to predominantly bacterial vaccines (diphtheria toxoid, tetanus toxoid, pertussis), the world's first studies on some virus vaccines (rabies, typhoid) were conducted and put into use (10).

Following the family's return to İstanbul, Elhan (Özütürk) attends Fatih Thirteenth Primary School and graduates with a perfect grade in 1939. She starts her secondary school education in İstanbul; however, when the family moves to Ankara, she enrolls in Ankara High School for Girls, where she completes her secondary school education in 1942 and her high school education in 1945 with a perfect grade. After learning German in secondary school, she also learns English by attending courses organized by the British Cultural Delegation (1).

Dr. Elhan Özlüarda, who was torn between medicine and architecture in her choice of profession and eventually chose medicine, entered Ankara University Faculty of Medicine in 1946 and received the title of medical doctor in 1952. The same year she started her medical education, on July 15, 1947, she also completed the caregiver - nurse training given by Gülhane Military Medical Academy with a very good grade. In the same year, she worked as the Accounting Manager at the Soil Products Office for 10 months. The financial difficulties of her family led her to cover her own expenses as much as possible and to use and evaluate what she had in the most efficient and frugal way. It was reported by her family that her manual dexterity and creativity, which developed in line with the living conditions, were among the factors that rapidly shaped her achievements in this process (1).

In 1952, she completed the first two years of her specialization at the Infectious Diseases Clinic of Ankara University Faculty of Medicine and the third year at the Refik Saydam Central Institute of Hygiene and received the title of bacteriology and infectious diseases specialist in 1955 (1). In the same year, the first polio vaccine, an inactive vaccine developed by Dr. Jonas Salk, was introduced (10). During her specialty studies, Dr. Özlüarda also worked in the bacteriology and serology laboratory of Gülhane Military Medical Academy for eight months (October 1952-June 1953) and received a certificate of achievement (1).

In 1954, she married Dr. Daver Özlüarda, an infectious diseases specialist whom she had met during her residency at the Refik Saydam Central Institute of Hygiene, who was working on BCG vaccination and was later appointed as the Chief of the Institute's Serum Control and Distribution Branch⁷, in a simple ceremony. Due to the financial difficulties they were experiencing, they started their family in a small basement apartment in Ankara, which expanded in 1964 with the addition of their daughter Bengi. This union, which continued with great mutual love and respect, would continue until Mr. Daver's death in 2011 (Figure 2-4) (1).

Dr. Elhan Özlüarda worked in the Virology and Virus Vaccines Laboratories Group of the Refik Saydam Central Institute of Hygiene between 1955 and 1977 as a specialist, laboratory chief and head of the group, respectively (Table 1). During this period, which can be called her most productive period, in addition to routine work, she took part in and led the development and production processes of a wide variety of vaccines (especially smallpox, influenza and flu vaccines, rabies vaccine and serum, and typhus vaccines) produced at the Refik Saydam Central Institute of Hygiene (1).



Figure 2. Dr. Elhan Özlüarda (seated, top right) with her husband Dr. Daver Özlüarda and colleagues (mid-1950s, Refik Saydam Central Institute of Public Health, Ankara) (1).

⁶ It was first published as "Relevé Hebdomadaire" in 1926 by a group of epidemiologists at the Geneva headquarters of the League of Nations (1920-1946). From 1946, after the signing of the founding law, it was transferred to the World Health Organization (8).

⁷ Tevzi: Distribution, allocation, separate delivery. (11)



Figure 3. Dr. Elhan Özlüarda (top left) with her husband Dr. Daver Özlüarda and their 13-month-old daughter Bengi Özlüarda (20 April 1965, Ankara) (1).



Figure 4. Dr. Elhan Özlüarda with her husband and colleague Dr. Daver Özlüarda during a reception (April, 1968) (1).

One of the most important contributions of Dr. Elhan Özlüarda to the history and literature of Turkish vaccinology is her work on glycerinated and dried (lyophilized) smallpox vaccines (Figure 5-7). Her first published studies on smallpox vaccine were on the potency and titration of calf lymph vaccines produced by the Refik Saydam Central Institute of Hygiene, comparison of laboratory methods and development

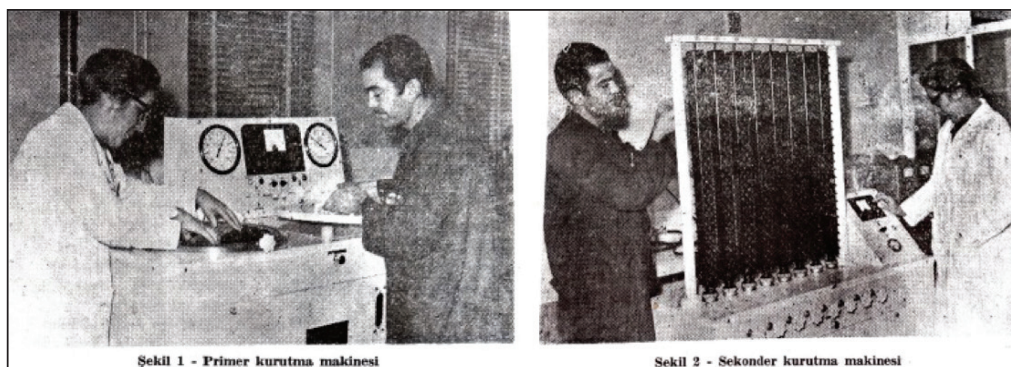
of new methods (12-15). She worked on the development of appropriate laboratory methods (determination of the most appropriate inoculation dilution, the shortest incubation period for the best counting) for the titration of the glycerinated smallpox vaccine produced at the Refik Saydam Central Institute of Hygiene, using pock counting technique in the chorio-allantoic membrane of chicken embryos instead of the method of rabbit skin intradermal test (13). Immediately after this study, Dr. Özlüarda compared this method with the standard pock counting and titration method adopted by the Lister Institute⁸, one of the UK's most established and pioneering institutions in both preventive medicine and vaccine and anti-serum production, and examined whether the current laboratory conditions were suitable for this method and what changes should be made in the method according to the characteristics of our national vaccine (14). She investigated the effects of the change in the amount of infective units in glycerinated vaccines stored under various conditions on vaccine efficacy and effectiveness. She titrated a series of glycerinated vaccines stored in deep freezer (-18 °C) with the pock counting method and showed that the number of infective units decreased within weeks (12). In a study conducted with Dr. Daver Özlüarda in the villages of Ankara Etimesgut Health Center in late 1959 (15), the success rate in primovaccination of two batches of glycerinated vaccine stored at (-) 20 °C with an infective unit level of 10^7 I.U./cc. at the time of distribution was 83.7% and 86.4%, respectively. She concluded that in order to compensate for the loss of infective units due to heat exposure during the period until administration, the vaccine preparation technique should be modified to increase the amount of infective units above 10^8 I.U./cc. at the time of distribution. Thus, the need for the production of lyophilized smallpox vaccine for remote areas where the vaccine cannot be stored and transported under cold chain conditions has been demonstrated in an evidence-based manner.

She investigated the relationship between the factors those play a role in smallpox vaccine production, and with these studies, she developed various suggestions (e.g. titration level of seed, number of passages applied, comparison of the productivity of the type and breed of animals used in terms of vaccine production, etc.) on how smallpox vaccine can be produced in Türkiye under the most economical conditions and with the most appropriate methods (17,18).

⁸ It was founded as the British Institute of Preventive Medicine (1891). In 1898, it was renamed the Jenner Institute of Preventive Medicine. At the time of its foundation, the Institute aimed to carry out preventive medicine studies, especially for human and animal diseases, and to produce vaccines and antitoxins. In time, the Institute became known in the fields of microbiology, bacteriology, virology and protozoology. In the nineteenth century, the Institute pioneered the production of vaccines and antiserum for smallpox, typhoid fever, diphtheria, tetanus and gaseous gangrene, and in the twentieth century, it pioneered studies on cancer, rheumatic diseases and nutritional disorders. Since 1903, it has been known as the Institute of Preventive Medicine of the physician and researcher (Joseph) Lister (1827-1912), who was also one of its founders (16).

Table 1. Summary of some life periods of Dr. Elhan Özlüarda (1)

Birth	05.01.1927 (İstanbul)
Primary school	Fatih Thirteenth Primary School (1939)
Secondary school	Ankara High School for Girls (1942)
High school	Ankara High School for Girls (1945)
Nursing training	Gülhane Military Medical Academy (15.07.1947)
Civil service in the accounting directorate at the soil products office	1947 (For about 10 months)
Medical training	Ankara University, Faculty of Medicine (1947-1952)
Medical speciality training (Bacteriology and Infectious Diseases)	Ankara University, Faculty of Medicine (1952-1954) Gülhane Military Medical Academy Bacteriology and Serology Laboratory (October 1952-June 1953) Refik Saydam Central Institute of Hygiene (1955)
Marriage	Dr. Daver Özlüarda (1954-2011)
Childbirth	Bengi Özlüarda Hamarat (1964)
Refik Saydam Central Institute of Hygiene Period	Specialist in Virology and Virus Vaccines Laboratory Group, Laboratory Chief and Group Head (1955-1977)
Presidency of Refik Saydam Central Institute of Hygiene Period	August-September 1974
Retirement	03.05.1977
Appointment to İstanbul Regional Institute of Public Health by the Ministry of Health and Social Welfare	Head of Virology Department and Deputy Director in charge of Scientific Publications (03.10.1979-1980)
General Directorate of Borders and Coasts İstanbul Harbour and City Bacteriological Institution	December 1980-April 1981
İstanbul Rabies Treatment Centre	Chief Physician (4 May-3 June 1981)
Retirement	04.06.1981
Death	18.03.2013 (İstanbul)

**Figure 5.** Dr. Elhan Özlüarda during the production of dried (lyophilised) smallpox vaccine (1965, Refik Saydam Central Institute of Hygiene, Ankara) (25).

Since the spring of 1961, Özlüarda and her team made significant changes in the smallpox vaccine production technique in line with the production technique used by the Lister Institute (the number and preparation of animals inoculated weekly, the method used for the preparation and homogenization of pulp, titration of the vaccine, antibacterial agent used and bacteriological controls of the vaccine, incubation time required for the elimination of bacteria) and this new method improved the existing vaccine qualitatively and quantitatively (19,20).

In addition to vaccine production, Dr. Elhan Özlüarda also carried out various studies on vaccine effectiveness and vaccine safety. In the last months of 1961, when imported smallpox cases were reported in England and Germany and a small smallpox epidemic emerged in a region of Iran close to our border, a mass vaccination effort was carried out. During this mass vaccination campaign, which lasted for about three months and in which 10.616.261 doses of vaccine were administered, 315 questionnaires were sent to⁹

⁹ In the research, the total number of questionnaires sent could not be reached.



Figure 6. Dr. Elhan Özlüarda working on the preservation of glycerinated smallpox vaccine stocks (early 1970s, Refik Saydam Central Institute of Hygiene, Ankara) (1).



Figure 7. Public education work titled "Smallpox Disease" prepared by Dr. Elhan Özlüarda (65).

vaccine providers to collect data and feedback from them on developing "take" rate, post-vaccination adverse effects, cold chain and vaccine logistics. In the study, the average average rate of "takes" was found to be 55% for those over 25 years of age, 66% for schoolchildren and 87% for children. Post-vaccinal adverse effect rates were calculated as 14/10.000 and 1/480.000 for generalized vaccinia¹⁰ and encephalitis, respectively. This study is one of the largest field studies of the period conducted on a subject known today as "vaccine safety" (21).

While she was working on developing the production technique of glycerinated smallpox vaccine, her studies were consulted by Dr. P. D. Meers, who was the consultant of the World Health Organization on the production of lyophilized smallpox vaccine at that time, and she attended the training organized by

the World Health Organization in Bangkok, Thailand between November 6-18, 1961 with the participation of 17 experts from 14 countries (Figure 8,9) (22,23). Following this training, she was awarded a scholarship by the World Health Organization and worked on the production of lyophilized smallpox vaccine in the smallpox vaccines department of the Lister Institute between October 15 and December 15, 1962 (1).



Figure 8. Dr. Elhan Özlüarda (second row, 5th from the left; in front of him is her colleague, Dr. Masatoshi Suzuki, Chief of the Japan Lyophilisation Laboratory in Kiyosei Kitatamagun, Tokyo, with whom she would maintain a professional friendship for more than 60 years until her death), World Health Organization Inter-regional Course on Smallpox Vaccine Production (6-18 November 1961 Bangkok, Thailand) (1,23).



Figure 9. Dr. Elhan Özlüarda, World Health Organization Inter-regional Smallpox Vaccine Production Course (6-18 November 1961 Bangkok, Thailand) (1,23).

¹⁰ This finding was interpreted by Özlüarda as indicating that observers may have considered any post-vaccination skin infection (including eczema vaccinatum) as generalised vaccinia (20,21).

In 1965, Prof. Dr. Elhan Özlüarda established the national production laboratory for freeze-dried (lyophilized) smallpox vaccine, one of the most important milestones in the history of Turkish vaccinology and production, and carried out the first freeze dried (lyophilized) smallpox vaccine production in 1965, following trial studies conducted in 1964 (1,20,24). After the first production, Özlüarda and colleagues conducted comparative efficacy and stability studies of lyophilized (dried) and glycerinated vaccines on 2552 people in 8 villages of Nevşehir in the winter months of 1965 before the vaccine was introduced (20,25). In primovaccination with dried vaccine, 97% and 95% positive results were obtained with glycerinated vaccine. However, while a 92% developing “take” rate was obtained with dried vaccine kept at 37 °C for 8-10 weeks, it was found that this percentage decreased to 26% with wet vaccine kept at 37 °C for only 11 days (25,26). One year after this study (December, 1966), another study was conducted by Özlüarda and colleagues to determine the efficacy of dried vaccine in revaccination by reaching people who had undergone primovaccination in the first study. In the study, revaccination success for the dried vaccine was found to be 82% and no difference was found between people whose primovaccination was performed with glycerinated and freeze-dried vaccines in terms of their response to revaccination with dried vaccine (20,26,27). The lyophilized vaccine produced was tested by the Dutch National Institute of Public Health (Rijksinstituut voor Volksgezondheid)¹¹ on the recommendation and through the World Health Organization and found to comply with the international standards required by the World Health Organization for biological products (20,25,26,29).

Within the scope of the BCG Campaign against tuberculosis, another important disease of the period, a pilot study on the simultaneous administration of BCG and smallpox vaccines was conducted by Dr. Özlüarda and her team in late 1965. In the study, glycerinated vaccine was administered as primovaccination or revaccination dose to 1095 children aged 0-6 years in five villages of Nevşehir. BCG vaccine was administered to 703 children who had not received BCG vaccine before and the remaining 392 children were evaluated as a control group for smallpox vaccination results. As a result of the study, the success rate of smallpox vaccination administered simultaneously with BCG was higher than that of smallpox vaccination alone. The results of BCG vaccination administered simultaneously with smallpox vaccine were found to be at least as successful as BCG administered alone. No complications were reported in simultaneous vaccination (20,30). As a result of this study, smallpox vaccine was started to be admin-

istered together with the BCG vaccine as of the 5th round of the BCG Campaign started¹² in 1953 in Türkiye (31). These studies conducted by Dr. Elhan Özlüarda have taken their place in the history of vaccinology in Türkiye as important examples of evidence-based field studies in immunization services.

Özlüarda also conducted various researches and applications on the development of methods for the production, control and dose determination of rabies vaccine in Türkiye (1). She represented Türkiye at the Interregional Rabies Seminar organized by the World Health Organization in Moscow between June 8-20, 1964 (Figure 10,11) (32). In the same year, the rabies vaccination instruction was updated in the light of new information and based on experience (33). Since the early



Figure 10. Dr. Elhan Özlüarda during the World Health Organization Interregional Rabies Seminar (8-20 June 1964, Moscow, Soviet Union) (1,32).



Figure 11. Dr. Elhan Özlüarda during the World Health Organization Interregional Rabies Seminar (different perspective) (8-20 June 1964, Moscow, Soviet Union) (1,32).

¹¹ The Netherlands National Institute of Public Health (1934), renamed the Netherlands National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu-RIVM) in 1984, was designated by the DST in 1969 as the International Reference Laboratory for the Control of Smallpox Vaccines (28).

¹² The fifth round of the National BCG Campaign was launched in January 1970 (31).

1970s, by increasing the virus titer of the seed used in vaccine production with the Semple method, it has been possible to produce rabies vaccine with a much higher potency (26-796 times) than the minimum protection value (10^3) determined and demanded by the World Health Organization and demonstrated in comparative tests conducted with the international standard vaccine. As a result of the increase in vaccine potency, it was possible to reduce the vaccine administration dose from 4 ml to 2 ml, resulting in an economic gain of approximately 50 percent in relation to vaccine production volume. Significant advances have been made, particularly with regard to inactivation and potency control methods. In rabies vaccines, potency (Habel) tests can now be performed every four batches and inactivation control tests in every two batches. Merthiolate was added to the vaccine as a preservative at a rate of 0.01%. By reducing the amount of phenol added to the vaccine by approximately 50 percent and demonstrating that this amount is sufficient and increasing the inactivation time to 75 hours, it was possible to reduce the undesirable effects of the vaccine. The Rabies Vaccine Production Laboratory has become more isolated and independent from other functions of the department to which it is attached. An increase in production volume was also achieved by switching to a uniform source in terms of the type and age of the sheep used (6-12 month old Merino sheep from State Breeding Farms) and by reducing vaccine loss due to the asepsis-antisepsis measures taken (34,35).

Under the direction of Prof. Dr. Mehmet Zühdi Berke (1897-1979), who served as the Director of the Vaccine and Serum Branch and Virology Branch, respectively, at the Refik Saydam Central Institute of Hygiene between 1949 and 1962, the Refik Saydam Central Institute of Hygiene Virology Laboratory isolated, identified and lyophilized the influenza virus circulating in Türkiye and around the world between 1950 and 1951 and sent it to the World Influenza Center in London, and the Refik Saydam Central Institute of Hygiene Virology Laboratory was recognized by the World Health Organization as an "International Regional Influenza Center" in 1950.

The first influenza vaccine was prepared by Refik Saydam Central Institute of Hygiene as a monovalent vaccine¹³ with the virus isolated during the 1950-1951 influenza epidemic and was administered to healthcare workers and military units with positive results. In addition, studies on the sensitivity of

influenza viruses to quinine chlorhydrate (and nitromine hydrochloride) were also conducted at the Institute, and quinine was recommended in addition to vitamin C for influenza cases from 1952 (36,37).

Dr. Özlüarda, who started her work on influenza in 1957, served as national influenza expert and center director at the National Influenza Center between 1962 and 1977, respectively, and carried out many sero-epidemiological studies as well as influenza vaccine production. During the Asian Flu in 1957, a monovalent influenza vaccine¹⁴ was produced and administered to healthcare workers. A mixed influenza-flu vaccine was also produced by mixing the influenza vaccine¹⁵ prepared in the bacterial vaccines service of the Refik Saydam Central Institute of Hygiene with the monovalent or polyvalent influenza vaccine prepared in the National Influenza Center (depending on the season). In a study conducted by Dr. Elhan Özlüarda and Prof. Dr. Zühdi Berke in rabbits and published in 1957 (36), it was shown that the mixed vaccine doubled the antibody level compared to the vaccine prepared with virus¹⁶. During the 1957 Asian Flu pandemic, this combination vaccine was administered to 556 people (including health workers and other occupational risk groups or applicants) with a one-week interval between the monovalent vaccine, and it was found that only six of¹⁷ the vaccinated individuals became ill. Dr. Özlüarda and Prof. Dr. Berke repeated their studies on the sensitivity of the influenza virus to quinine during the 1957 pandemic and found that the virus was sensitive to quinine. In the same period, positive results were obtained in rabbits and roosters by using aluminum hydroxide as an adjuvant in the production of influenza¹⁸ (36,37).

In 1956, influenza CF (complement fixation) and HI (hemagglutination inhibition) antigens were prepared in the Virology Laboratories Branch of the Refik Saydam Central Institute of Hygiene and in 1957-58, psittacosis and adenovirus CF antigens were prepared and put into practice. Only after these dates, serologic differential diagnosis of major viral and rickettsial respiratory tract diseases became possible (39). As a matter of fact, since the mid-1950s, it is understood that in the material belonging to respiratory tract infection cases sent to the Refik Saydam Central Institute of Hygiene, differential diagnosis could be made in terms of many agents including

¹³ Influenza A/England/1/51 (37).

¹⁴ Influenza A/Singapore/1/57 (Isolated by the National Influenza Centre on 16.08.1957 (38).

¹⁵ Bacteria in the flu vaccine: *Staphylococcus aureus*, *Staphylococcus albus*, *Bact. Hemophilus influenza*, *Streptococcus (polyvalent)*, *Pneumococcus I-II*, *Pneumobacillus Friedlaender*, *Micrococcus (Neiss.) catarrhalis*, *Micrococcus flavus* (36).

¹⁶ In the study, two separate monovalent vaccines prepared with two variants of influenza virus type A (A/England/1/1951 and A/England/19/1955) were used (36).

¹⁷ One immediately after the first dose, one moderately severe, 4 very mild (37).

¹⁸ It is also understood that the results of this study by Dr. Özlüarda and Dr. Berke were supported by the results of a study conducted on guinea pigs by Prof. Dr. Henneberg, who was also the Director of the Robert Koch Institute, an affiliated institution of the German Federal Institute of Public Health, and that this study was communicated to the Refik Saydam Central Institute of Hygiene by Henneberg himself (36).



Figure 12. Dr. Elhan Özlüarda (second from left), next to Prof. Dr. Mehmet Zühdi Berke, who was the first Director of the Virology Branch of the Refik Saydam Central Institute of Public Health and held this position until 1962, and Dr. Azmi Arı, who served as the Director of the Virology Laboratories Branch of the Refik Saydam Central Institute of Public Health between 1962 and 1972 and as the President of the Institute between 1974 and 1977 (early 1960s, Refik Saydam Central Institute of Hygiene, Ankara) (66).

Q-fever, psittacosis-ornithosis, adenoviruses, primary atypical pneumonia agents, myxoviruses in addition to influenza (37).

The study published by Dr. Özlüarda with Prof. Dr. Zühdi Berke and Dr. Azmi Arı¹⁹ revealed the cumulative distribution of respiratory tract agents in Türkiye (37)²⁰. During the Asian Influenza (winter 1957/58), respiratory tract samples from a school in Ankara were isolated and lyophilized in HeLa cell culture by the same team and typed as "Adenovirus type 6" by the Colindale International Virology Reference Laboratory²¹ in London (Figure 12). With this finding, the presence of adenovirus infection in Türkiye was confirmed for the first time (37). Subsequently, between 1962-1977²², Dr. Özlüarda continued to perform complement fixation tests with Q-fever, psittacosis, influenza, adenovirus antigens and complement fixation tests in sera of persons with upper respiratory tract infections sent to the Virology Branch of the Refik Saydam Central Institute of Hygiene and in sera sent to the Bacteriology Branch for the diagnosis of syphilis (41). Data on national influenza surveillance and other respiratory tract pathogens were regularly published by Dr. Elhan Özlüarda between 1958 and 1977 (42-58). In 1967, Dr. Özlüarda attended a three-month training



Figure 13. The last photograph of Dr. Elhan Özlüarda as the Head of the Virology and Virus Vaccines Laboratories Group (May 1977, Refik Saydam Central Institute of Hygiene, Ankara)

in England with a scholarship from the World Health Organization to conduct research on influenza vaccine (1).

Dr. Elhan Özlüarda, in 1960, performed early isolations and laboratory investigations of *Herpes simplex* (by passage of vesicle fluid through the chorio-allantoic membrane of chicken embryos) and mumps viruses (by inoculation of saliva material from three mumps cases into chicken embryos and HeLa cell tissue cultures) in Türkiye, and she used the water-soluble (soluble) mumps antigens they prepared in complement incorporation tests in sero-epidemiologic studies conducted in normal, healthy individuals (1,59-62).

Dr. Elhan Özlüarda was appointed as the president of Refik Saydam Central Institute of Hygiene besides her duty as the Head of Virology and Virus Vaccines Laboratories Group²³ as well as the Head of the Refik Saydam Central Institute of Hygiene on August 6, 1974 and due to the intensity of her current duties, she asked for her pardon and returned to the Group Head within a few weeks (Figure 13) (1).

In November 1976, Dr. Elhan Özlüarda established the Refik Saydam Central Institute of Hygiene Viral Hepatitis Reference Center in Türkiye to investigate the ecology and epidemiology of viral hepatitis in Türkiye, to serve as an advisory and training center for laboratories, to carry out routine controls of the products of the Blood Fractionation Department, to perform diagnostic tests of clinical cases, and to prepare and standardize test reagents (1,63). This was followed by sero-prevalence studies on hepatitis B (64).

¹⁹ Prof. Dr. Azmi Arı (1921-1999) worked as Laboratory Chief (1956-1961) and Branch Manager (1962-1972) at the Virology Laboratories of Refik Saydam Central Institute of Hygiene, and as the Head of the Institute between 1974-1977.

²⁰ This study was also presented as a report at the VIIIth Turkish Microbiological Congress (İstanbul, 1958).

²¹ This laboratory takes its name from the Colindale district of London, where it is located. During the relevant period of cooperation with the Refik Saydam Central Institute of Hygiene, it was affiliated to the "United Kingdom Public Health Laboratory Service", which was established in 1946 within the "United Kingdom National Health Service (NHS)", and since 2021, it has been working under the "United Kingdom Health Safety Authority (UKHSA) (2021)" (40).

²² At the time of the publication of Prof. Dr. Zühdi Berke's book "Medical Virology (1974)", this date was given as 1962-1967 (41). However, in the following publications of Dr. Elhan Özlüarda, it is understood that she continued her related studies until her retirement (1977) (42-58).

²³ Date of notification: 26.08.1974 (1). However, the date of the processing of her petition for resignation by the Institute could not be reached.



Figure 14. Dr. Elhan Özlüarda (at the head of the table on the right) with Prof. Dr. Mehmet Zühdi Berke, who was the first Director of the Virology Branch of the Refik Saydam Central Institute of Hygiene and held this position until 1962 and the staff of the Virology and Virus Vaccines Laboratories Group (May 1977, Refik Saydam Central Institute of Hygiene, Ankara) (1).

Dr. Elhan Özlüarda was honored with a certificate of appreciation by the Ministry of Health and Social Welfare in 1965 for her outstanding efforts and achievements in her duty (1).

Dr. Elhan Özlüarda, who produced more than 60 articles, most of which were original, during her 22 years of service at the Refik Saydam Central Institute of Hygiene and was fluent in English and German, retired voluntarily on May 3, 1977, at the age of 50 and at the peak of her career, and settled in İstanbul, where all her relatives, family friends had moved at that time (Figure 14,15) (1).

On October 3, 1979, Dr. Özlüarda was called back to work by the Ministry of Health and Social Welfare after her retirement was canceled, and she was appointed to the İstanbul



Figure 15. Dr. Elhan Özlüarda, during farewell meeting, with Dr. Azmi Ari, who served as the Director of the Virology Laboratories Branch of the Refik Saydam Central Institute of Hygiene between 1962 and 1972 and as the President of the Institute and Prof. Dr. Mehmet Zühdi Berke, who was the first Director of the Virology Branch of the Refik Saydam Central Institute of Hygiene and held this position until 1962, and Dr. Muzaffer Akyol, who was the Director of the School of Public Health between 1974 and 1982 (4 May 1977, Refik Saydam Central Institute of Hygiene, Ankara) (1).

Regional Institute of Hygiene to establish the Department of Virology. As of 1980, she also served as the deputy director responsible for the scientific studies of the Institute (1).

Dr. Özlüarda was then appointed (at her own request) as General Directorate of Borders and Coasts, Director of the İstanbul Port and City Bacteriology Facility (Laboratory) and then as Chief Physician of the İstanbul Rabies Treatment Facility (May 4, 1981) and retired for the second time on June 4, 1981 (1).

Despite this intense work schedule, Dr. Elhan Özlüarda, who had been interested in many subjects throughout her life, had a wide range of interests such as poetry, charcoal portraits, story essays, classical music, travel, dance, swimming, theater, opera, ballet, nature, animals, sewing, and clothing design (Figure 16,17) (1). Her parents' interest in classical music would result in their daughter Bengi -receiving music education- in the period following the introduction of a huge piano to the house one day while she was lying sick in the living room. During the period when they lived in the lodging house in the garden of the Institute, Bengi's childhood memories of returning from school would include long hours of playing games with the laborers while waiting for her mother, who left home in the morning and returned from work around

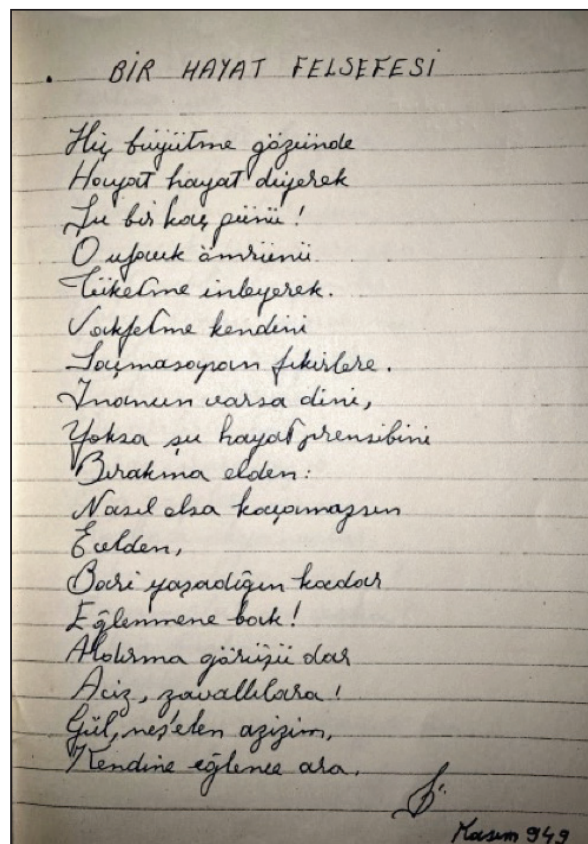


Figure 16. Among Dr. Elhan Özlüarda's personal poetry collection; a work described by her daughter as one of the poems that best defines her (1949, Ankara) (1).



Figure 17. Among Dr. Elhan Özlüarda's personal charcoal works; charcoal self-portraits reflecting herself in the period between 1955 and 1977 respectively (1).

midnight. She would also be accompanied by the feeling of privilege of standing outside the line at school, while all her friends were lining up for their vaccinations since her mother administered her own vaccinations, as a memory from her past (1).

In the eyes of her colleagues at the institute, she was modest, of strong character, with an invisible authority, uncompromising yet friendly, a warrior who, like the other professors of her generation, persisted and obstinately, obdurately continued to work (59). Dr. Özlüarda was described by her family as a mother, wife and aunt who was full of life, loved to laugh and was witty, and these lines were heard almost every day from her: "Life is about the moment." (1).

On March 18, 2013, Dr. Elhan Özlüarda, who had been struggling with her disease for a long time after her diagnosis of lymphoma in 2003 but was very shaken after the loss of her husband in 2011 and could no longer hide her loneliness despite all the support of her family, passed away in İstanbul (1).

We commemorate and express our gratitude to Dr. Elhan Özlüarda for her contribution in the prevention, diagnosis, surveillance and eradication of smallpox, the production of some other virus vaccines (smallpox, influenza, rabies), the isolation of many viruses (*H. simplex*, mumps, adenovirus, etc.), the establishment of important national reference laboratories (influenza, hepatitis) and the establishment of vaccine-preventable disease (smallpox, influenza, hepatitis) surveillance systems in Türkiye.

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This article has been prepared to ensure that Dr. Elhan Özlüarda's unique contribution to the development of

virology, vaccine production and vaccine-preventable disease surveillance in Türkiye will be remembered for generations to come and to shed light for young scientists. We would like to thank Mrs. Bengi Özlüarda Hamarat for her kind attention and generous sharing of various information and documents from her mother's personal archive and her personal memories during the preparation of this article.

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