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## History of Leprosy Prevention and Control in Armenia

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#### Introduction

Leprosy, also known as Hansen's disease, is one of the oldest recorded human diseases and still remains a significant public health challenge. According to the World Health Organization (WHO), leprosy is one of 20 neglected tropical diseases (NTDs). Most people lead a normal life during and after treatment. The disease is uncommon, with 72.5% of annually reported cases coming from three countries: India, Brazil and Indonesia [16]. Currently, cases diagnosed in Europe are either relapsed old cases, migrant cases or cases imported from endemic areas and are not the result of autochthonous transmission. New research provides evidence that in recent decades, leprosy transmission has ended in the Valencia region of Spain [13]. Leprosy is still being registered in our neighboring country, Iran, with 32 new cases reported in 2017 and 29 new cases reported in 2018 [14]. Russia belongs to the low endemic countries for leprosy, with sporadic cases. Endemic foci were found in the Lower Volga region, the North Caucasus, Siberia and the Far East. The most patients (2505 people) were seen in the early 1960s. About 84% of patients were registered in the southern regions [9].

Armenia is considered one of the ancient leprosy foci with the first probable case dating back to the Middle Bronze Age [15]. Around 260–270 AD, Aghvita, the wife of the Armenian feudal lord Suren Salahuni, donated her own money to build a leprosarium for 35 leprosy patients at the "Arbenut" (which means "sun bath") curative mineral water springs in the historical Armenian Derjan city. An early hospital for leprosy patients was established in Europe (Saint-Claude, France) almost 300 years later, in 560–570 [3, 4, 6]. It is assumed that the disease constantly infiltrated Armenia from Persia (nowadays Iran), particularly, due to the forced mass displacement of Armenians and the resettlement of the Persians in their place [1, 7].

Taking into account the geographical location of Armenia, as well as the historical events on its territory: mass displacements, the invasions of the Crusaders in the 13th century, and its position as a bridge between Asia and Europe, the center of the intersection of the most important trade and military routes, it can be assumed that leprosy has been present on the territory of Armenia since time immemorial, and its spread is closely related to the presence of the disease in neighboring countries [3, 5, 6, 12].

Despite the sporadic infection and the decrease in new cases globally, it is important to remember that active population movement from endemic countries, socio-economic and environmental issues, do not exclude the possibility of the transmission of infection in the region. The current narrative literature review aimed to describe the epidemiological evolution, as well as the control measures and the geographical spatial distribution of leprosy in Armenia.

#### **Material and Methods**

The literature search was carried out in an electronic database of Armenian libraries (http://armunicat.nla.am), where you can find old textbooks, collections of scientific papers for free from major libraries (Scientific medical library of NIH, Yerevan State Medical University library, National library of Armenia, Fundamental scientific library (NAS RA)) by using several keywords, such as "leprosy" or "leprosy in Armenia". There was no restriction on language (Armenian, Russian, English) or publication period. The relevant publications available on the internet (Google Scholar, PubMed) were reviewed. Inclusion criteria were: all available published materials on leprosy case studies, case series, epidemiological reports, descriptions of control measures implemented in Armenia. Russian and English guidelines, as well as old textbooks were excluded. In addition, the reporting forms available in the archive of the National Center for Disease Control and Prevention were examined, but no mention of leprosy was found. ArcGIS 10.7 software was used to generate the maps.

## **Results and Discussion**

The literature searches

Overall, 72 publications were initially identified during database searches, and 29 of them were included for full-text preview. A total of 12 publications were retrieved and included in the reference list. The available data were only published in "white" literature (books, conference proceedings): 9 nationwide and 2 Russian publications.

Situation in Armenia

Eastern Armenia joined the Russian Empire at the beginning of the 19<sup>th</sup> century (in 1828), becoming an Armenian province that was later renamed the Erivan Governorate (guberniya) in 1849. Erivan Governorate saw the opening of its first outpatient clinic in 1890 and its first hospital in 1893. During the First World War, the attempts to organize medical care were interrupted (Armenian Genocide in Western Armenia, 1915). 300–400 thousand refugees escaped to Eastern Armenia, the Caucasus, Russia [3]. Typhus, relapsing fever, typhoid fever, and dysentery epidemics were especially widespread in 1918 [6]. Armenia entered a new phase after the creation of the Soviet Union in 1920. Tropical stations and the Tropical Institute were founded in 1922 and 1923, respectively (Fig. 1) [3].

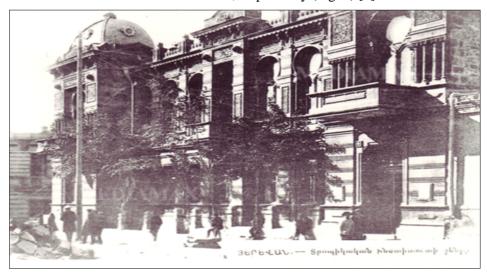


Fig. 1. The first Tropical Institute, Armenia, 1923

The official registration of leprosy patients began in 1923. The majority of cases (n=240, 65%) were diagnosed in the first two decades (1921–1940), the remaining cases (n=130, 35%) were diagnosed in the following five decades. The last case was recorded in 1982 [3, 4]. The new case detection numbers and new case detection rates per million population was high between 1921 and 1940 (Fig. 2) [3, 6].

In Armenia, patients with the lepromatous leprosy dominated (n=195, 52.5%). Due to the incomplete preservation of medical records, it was unable to identify the type of leprosy in 49 patients (13%) [4, 6, 7]. The disease mostly affected males (58%). The age ranged from 3 to 75 years old. Cases were mainly registered among children and adolescent age group (0–19, n=137, 37%). For children and adolescents, a leprosy patient in the family or close relatives were the source of infection [3, 4]. Since 1960, there was no reports of leprosy among children (0–9 years old) [3, 4, 11].

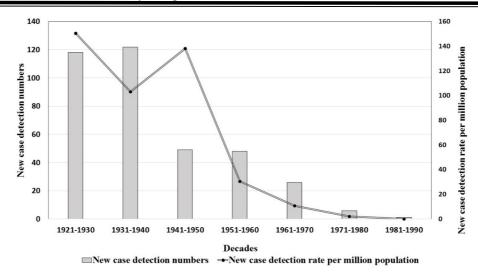


Fig. 2. New case detection numbers and new case detection rates per million population, Armenia, 1921–1990

Since the 1920s, leprosy patients were isolated in various leprosariums throughout the former USSR (("Krutie Ruchi") ("Steep Brooks") leprosarium (Saint Petersburg province of Russia, 1908–1941), Tersky leprosarium (Stavropol province of Russia), Abinski leprosarium (Krasnodar province of Russia), Astrakhan leprosarium (Astrakhan province of Russia)), because the authorities of that time did not allocate money for constructing leprosariums [1, 3, 11]. In leprosariums, patients were treated for totally at no cost and were supported financially by the state. Patients also participated in outdoor activities, acquired skills in the arts and literacy. After significant recovery, if they were no longer contagious, they were discharged from the leprosarium for outpatient care and placed under dispensary control [1, 5]. Leprosy patients must be transported in separate wagons-couchettes on the railway, according to the USSR regulations, and the patient must be accompanied by medical professionals. At each station, the sanitary staff disinfected the wagon. Patients were strictly forbidden to get out of the wagon and upon arrival, it was removed from circulation for disinfection [5]. Almost half of the patients were isolated in leprosariums in the first two decades. From the third decade (after 1941), the majority of patients were isolated in leprosarium. By 1962, regardless of the disease type, 85% of patients were already isolated (Table 1).

The average life expectancy of patients after the disease detection was 14.5 years. There were also some long-lived patients, one, for instance, had leprosy for 41 years before passing away at the age of 94. Children and adolescent patients, when they were isolated in time and received professional treatment, the disease had a benign course and the life expectancy was long. Other diseases, such as heart attack, pneumonia, tumors, etc., were the causes of death [3]. Sulfone drugs (sulfetron, solusulfone, DDS (diaminodiphenyl sulfone or dapsone)) have been used to treat leprosy [1].

Table 1
Data on isolation of leprosy patients, Armenia, 1921–1990

Decades	1921-1930			1931-1940			1941-1950			1951-1960		1961-1970			1971-1980		1981-1990			Total			Total number		
Clinical forms of Leprosy	Isolated	Not isolated	No data	Isolated	Not isolated	No data	Isolated	Not isolated	No data	Isolated	Not isolated	No data	Isolated	Not isolated	No data	of patients									
Lepromatous	18	16	11	38	9	3	40			36	1		19			3			1			155	26	14	195
Tuberculoid	13	6	6	13	4	3	4	1		3	2	2	1	2		1	1					35	16	11	62
Indeterminate	15	13		17	6		3	1		4			4			1						44	20		64
Type not specified	9	4	7	18	11																	27	15	7	49
Total		118			112			49			48			26			6			1					370

Selective mass population screenings in communities with repeated cases were conducted on a regular basis (every 2–3 years), for example, in 1962, 13289 out of 13332 residents of Amasia region were examined during the population screening [3, 7]. The number of contacts per index case ranged from 3 to 20, sometimes more. All contacts were registered and monitored 2–3 times a year for 5–10 years, occasionally up to 20 years. From 1951, 653 contacts were monitored, 36 of them were discovered to be infected: in 1954–3, in 1955–6, in 1956–6, in 1957–3, in 1958–1, in 1959–4, in 1960–7, in 1962–7. The number of contacts fell year by year as the number of main patients declined: 541 contacts in 1965, 394 in 1970, and 177 in 1972 [3]. The geographical distribution of the cases showed that leprosy was more prevalent in the Lake Sevan (Vardenis, Gavar), Shirak highlands (Amasia, Artik), Aragatsotn region (Aparan, Talin), Vayots Dzor region, Ararat valley (Artashat) (Fig. 3) [3, 6]. Martiros village of Vayk had the shortest active foci, lasting 39 years (1899–1938). The longest 140-year active foci were found in the Artsvanist village of Martuni (1825–1965) (Table 2) [3].

Duration of leprosy active foci in Armenia

Table 2

Name of settlements/villages	City	Year of re	Duration of foci (in years)			
Martiros	Vayk	1899	1938	39		
Lusagyugh	Aparan	1870	1966	96		
Etchmiadzin	Etchmiadzin	1870	1966	96		
Dashkend	Vardenis	1890	1940	50		
Dalarik	Talin	1899	1938	39		
Gyumri	Gyumri	1895	1969	74		
Martuni	Martuni	1899	1939	40		
Verin Getashen	Martuni	1885	1941	56		
Lichk	Martuni	1900	1963	63		
Artsvanist	Martuni	1825	1965	140		
Vardenik	Martuni	1900	1958	58		

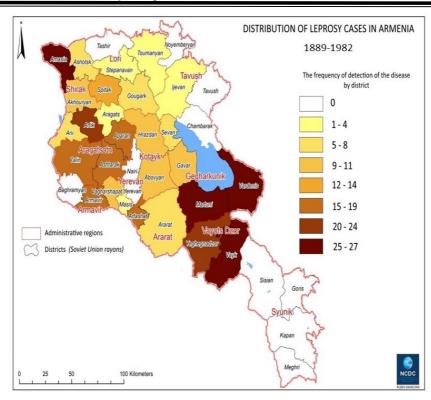


Fig. 3. Geographical distribution of leprosy cases, Armenia, 1889–1982

Hundreds of cases were identified in Armenia prior to the creation of the Soviet Union, but no preventive measures were implemented. The patients were neither treated or isolated and were left at home. Along with poverty and malnutrition, the unsanitary living conditions of the population were a significant factor. The majority of cases in Armenia were registered during 1887–1905 and 1921–1940: the first increase occurred between 1887 and 1905, due to the presence of local outbreaks, the lack of control measures, and the imported cases from Iran and Turkey, the second increase occurred between 1920 and 1940, which was due to the mass movement of people from Turkey to Armenia (migration in 1915–1920) [3, 6, 11]. From 1950, there was a considerable decrease in the frequency of new cases, with the last known case being recognized in 1982.

During 7 decades, the reduction was due to the implementation of suitable preventive measures (mass and selective population screening, active case finding, isolation and monitoring of contacts, health education) as well as an increase in social factors and hygienic level of the population [2, 11]. Isolation of patients was considered the best strategy to prevent the disease and was carried out in the absence of a leprosarium in the country. In the settlements where new leprosy cases were often registered, mass preventive examinations of the whole population were conducted [1].

This review has several limitations that should be considered. In regard to data quality, there was no information about laboratory diagnoses, relapses, the proportion of patients with deformities, the role of family or community contacts in the disease epidemiology or the introduction of the BCG vaccination in Armenia. On the other hand, there is no information about leprosy among refugees and migrants. The presented data was mainly based on the information from the book of dermatovenerologist, Professor Mira Mirakyan (December 18, 1929). She is the daughter of Yenok Mirakyan, one of the founders of the dermatovenereology service in the Soviet Armenia. He actively participated in the detection and control of skin diseases. The book is designed for dermatologists, mycologists, epidemiologists, general practitioners and medical students [3].

Armenia has seen no leprosy cases in recent years, which might lead to information gaps among health care workers (HCWs). The deterioration of population living standards as a result of social, political, and economic challenges must also be considered. Currently leprosy is a notifiable disease and there is a room for the leprosy patients in the National Center for Dermatology. Additionally, there is no information on whether the contacts of leprosy patients are still alive. The last attempt to active case finding was conducted in 2008, when the grandson of leprosy patient was examined with a negative result. In June 2017, a suspected case was detected in a 57-year-old male who lives on Lake Sevan's southern coast. The Republican Anti-Tuberculosis Dispensary Center performed the laboratory analysis. The patient was eventually diagnosed with skin cancer and passed away.

To summarize, leprosy is a forgotten and neglected issue in Armenia. To guarantee the detection and management of any probable imported leprosy case, the creation of national guidelines in accordance with the WHO's most recent recommendations on leprosy diagnosis, treatment, and prevention should be prioritized. Building capacity and education are required to enhance the surveillance system and raise awareness among HCWs and the general public. To gain technical assistance, collaboration with WHO reference centers is essential.

#### Conflicts of Interest

The authors have no conflicts of interest. No funding was obtained for this project.

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## Ethical approval

Approval was not required.

### История профилактики и борьбы с проказой в Армении

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Проказа присутствовала на территории Армении с незапамятных времен. Текущий обзор литературы направлен на описание эпидемиологической эволюции, а также мер борьбы и географического распределения лепры в Армении. Поиск литературы осуществлялся в электронной базе данных библиотек Армении по нескольким ключевым словам, например, «проказа» или «проказа в Армении». Кроме того, были рассмотрены соответствующие статьи, доступные в интернете. Снижение случаев заболевания за 7 десятилетий произошло за счет реализации соответствующих профилактических мер (скрининг населения, активное выявление случаев заболевания, изоляция и мониторинг контактов, санитарное просвещение), а также увеличения социальных факторов и гигиенического уровня населения. Изоляция больных считалась лучшей стратегией профилактики заболевания и проводилась при отсутствии в стране лепрозория. В населенных пунктах, где часто регистрировались новые случаи лепры, проводились массовые профилактические осмотры всего населения.

# Քորոտության կանխարգելման և վերահսկման պատմությունը Հայաստանում

# Ա.Հ. Մանուկյան, Ռ.Ռ. Դանիելյան, Լ.Վ. Պարոնյան, Գ.Ֆ. Սահակյան, Ա.Վ. Վանյան, Հ.Ա. Հովհաննիսյան, Գ.Գ. Մելիք-Անդրեասյան

Բորոտությունը Հայաստանի տարածքում տարածված է եղել անհիշելի ժամանակներից։ Ներկայիս գրականության ուսումնասիրությունը նպատակ ուներ նկարագրելու համաձարակաբանական էվոլյուցիան, ինչպես նաև Հայաստանում բորոտության դեմ պայքարի միջոցառումները և աշխարհագրական տարածումը։ Գրականության որոնումն իրականացվել է հայաստանյան գրադարանների էլեկտրոնային բազայում՝ օգտագործելով որոշ բանալի բառեր, ինչպիսիք են՝ «բորոտություն» կամ «բորոտությունը Հայաստանում»։ Բացի այդ, վերանայվել են համացանցում առկա համապատասխան հոդվածները։ Յոթ տասնամյակների ընթացքում հիվանդության նվազումը պայմանավորված է համապատասխան կանխարգելիչ միջոցառումների իրականացմամբ (բնակչության կանխարգելիչ հետազոտություն, դեպքերի ակտիվ հայտնաբերում, կոնտակտավորների մեկուսացում և մոնիթորինգ, առողջապահական կրթություն), ինչպես նաև սոցիալական գործոնների և բնակչության հիգիենիկ մակարդակի բարձրացմամբ։ Պացիենտների մեկուսացումը համարվում էր հիվանդության կանխարգելման լավագույն ռազմավարութ

յունը և իրականացվում էր երկրում բորոտանոցի (լեպրոզորիա) բացակայության պայմաններում։ Այն բնակավայրերում, որտեղ հաձախ են գրանցվել բորոտության նոր դեպքեր, զանգվածային կանխարգելիչ հետազոտություններ են անցկացվել ողջ բնակչության շրջանում։

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