

## History of Medicine

## Remembering Marcel Baltazard, Great Researcher and the French President of Pasteur Institute of Iran

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### Abstract

Dr. Marcel Baltazard (1908–1971), French scientist and former director of Pasteur Institute of Iran, is known in the international arena due to his research on the control of infectious diseases such as plague, rabies, relapsing fever, leprosy, smallpox and tuberculosis. Dr. Baltazard also played a significant role in the launch of vaccination against tuberculosis, cholera and smallpox. Dr. Baltazard's spent the first 13 years of academic life at Pasteur Institute of Casablanca, Morocco, and then 20 years at Pasteur Institute of Iran and over the last five years at Pasteur Institute of Paris.

In this paper, the activities of this important and influential researcher in the field of health and medicine are addressed.

**Keywords:** History, Iran, Pasteur institute of Iran, Marcel Baltazard

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### Introduction

Dr. Marcel Baltazard was born in a noble and scholar family on February 13, 1908 in Verdean in northeastern France. His grandfather was a physician, and his father was a military officer. He finished his secondary school in his hometown, and at obtained his diploma at the age of 15. At 20 years of age, when studying medicine in medical school at the University of Paris, he began working in the laboratory of Parasitology in the Faculty of Medicine and performed studies on murine typhus, intestinal parasites and worms. Baltazard's academic life in Morocco continued from 1932 to 1945. From 1946 to 1958, Baltazard served as the director of Pasteur Institute of Iran, and from 1958 to 1966, he served as a senior advisor of Pasteur Institute of Iran. From 1966 to 1971 when Baltazard died in Paris, he continued his scientific activity at Pasteur Institute of Paris.<sup>1</sup>

### Baltazard in Morocco

Baltazard went to Morocco in 1932, by the invitation of Prof. Georges Blanc, who had the mission of building and launching Pasteur Institute of Morocco, to conduct his medical thesis on epidemiology of schistosomiasis. At the same time, he continued his research on typhus and relapsing fever spirochete, and for the acknowledgement of his academic efforts, in 1935, he received the Desportes Prize from the French Academy of Medicine. The prize was awarded to researchers with superior researches in the field of medicine. In 1937, Baltazard and his colleagues isolated

*Borrelia* form soft ticks in southeastern Morocco.<sup>2</sup> In Morocco, Baltazard continued his research on murine typhus which had begun in Paris.

In the summer and fall of 1937, a typhus epidemic occurred in Morocco and more than 350 thousand people were vaccinated against the disease. Georges Blanc and Baltazard attempted to accelerate and standardize the vaccine and produce a new vaccine from infectious secretions of fleas against typhus whose virulence was weakened for humans.<sup>3</sup> Baltazard proved that the rickettsia responsible for murine typhus was maintained in dried dung of infected flea and in this way, passed to vertebrate host.<sup>4</sup> In 1939, Georges Blanc, director of Pasteur Institute of Casablanca, and Baltazard provided the attenuated vaccines of typhus.<sup>5</sup> In 1939, vaccination against typhus was conducted in Morocco. A year later, typhus was eradicated in Morocco and vaccination was suspended throughout the country. In 1941, coinciding with the start of the Second World War, this vaccine controlled the spread of epidemic typhus in France and North Africa, and was used until 1946 when some deaths were reported using this vaccine.<sup>6</sup> For the first time in 1944, Baltazard and Georges Blanc presented the hypothesis that there may be asymptomatic infections, which are the cause of epidemic diseases.<sup>7</sup> During 1942–1945, Baltazard served as a medical officer in Morocco.<sup>8</sup> At this time, plague was spread in the south of the country. He examined the possibility of human-to-human transmission of plague. Baltazard also attempted to produce anti-gangrene serum in Morocco.<sup>1</sup>

### Baltazard in Iran

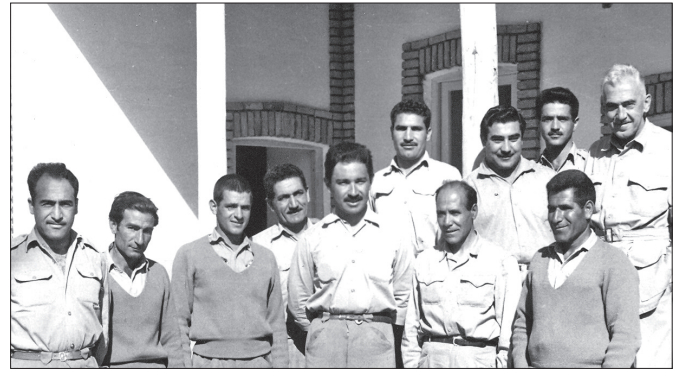
In the nineteenth century, the French physicians' influence in Iran was considerable. After Qajar Ahmad Shah's visit to Pasteur Institute of Paris and due to the deteriorating health status in Iran after the First World War, construction of a branch of Pasteur Institute in Iran was suggested.<sup>9</sup> After signing the necessary agreements, a French scientist named Dr. Joseph Mesnard came

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**Figure 1.** Injecting plaster into the nests of rodents. Meeting of the World Health Organization for plague, Akanlu Village, Hamadan Province, 1951.<sup>1</sup>



**Figure 2.** From right to left in the top row: Dr. Marcel Baltazard and from right to left in the down row, third person, Dr. Younes Karimi and other Pasteur Institute of Iran staff, The research center for emerging and reemerging infectious diseases, Akanlu, Hamadan.1961.<sup>1</sup>

to Tehran in 1920 as the first director of Pasteur Institute of Iran.<sup>10</sup> After him, Dr. Abolqasem Bahrami, Dr. Joseph Kerandel and Dr. Hussein Mashuf held the Presidency of Pasteur Institute of Iran.<sup>11-13</sup> After returning to France from Morocco in 1964, Baltazard was appointed as the third French director of Pasteur Institute of Iran following the Iranian government request from the manager of Institute Pasteur international network.<sup>14</sup>

Marcel Baltazard, known as the founder of modern Pasteur Institute of Iran, was a researcher beyond French borders, making major developments in Pasteur Institute of Iran owing to his devotion to work. For 20 years (from 1946 to 1966), Dr. Baltazard cooperated with Pasteur Institute of Iran –13 years as its director and 7 years as its director's chief scientific advisor. Baltazard's activities in Iran can be divided into fields of public health, vaccine production and launch of public vaccination, creation of new structures and performance of international activities.

### Promotion of Public Health

**Plague:** Dr. Marcel Baltazard found international fame for his work in the field of plague. His research in the field of plague with the Iranian team of Pasteur Institute, especially Dr. Younes Karimi, Dr. Mahmoud Bahmanyar, and Dr. Mansour Shamsa was remarkably widespread. Baltazard came to Iran exactly with the third wave of the plague epidemic.<sup>9</sup> He controlled plague epidemics in the west and northwest of the country, identified resistant and susceptible rodents to plague, and showed that Merinos rodents had a vital role in the preservation and transmission of plague.<sup>15,16</sup> Baltazard and the plague research team of Pasteur Institute of Iran for showed the first time that the plague bacillus could survive in soil for years after the death of infected rodents. He also wrote the first laboratory instructions for the diagnosis of plague bacillus.<sup>17</sup> In 1952, coinciding with the plague epidemic in the west of the country, Baltazard established a research center in the village of Akanlu located in the border of Zanjan, Hamadan, and Kurdistan Provinces. With the establishment of this center, specialized teams of Pasteur Institute of Iran, could control outbreaks of plague in this area by taking effective measures aimed at humans and rodents. In this research center, Dr. Baltazard and his Iranian colleagues conducted extensive research on plague and introduced the Akanlu Research Center as a global reference center of plague. One of the activities of the plague research team in this center was

studying the behavior of Merinos rodents as the main reservoirs of plague.<sup>9</sup>

**Rabies:** Dr. Baltazard considered rabies a serious public health problem. Despite the use of classic treatment at the time in the world and Iran, approximately 30% of individuals bitten by a rabid animal died due to the disease.<sup>18</sup> At that time, serum immunoglobulin injection method was performed in France and Italy to prevent rabies, but no studies were conducted to prove its effectiveness. In the summer of 1954, at the time of harvesting, a rabid wolf attacked farmers and injured 27 of them. The incident provided a good opportunity for the study and evaluation of serum therapy methods in preventing rabies. Among the injured, 18 of those with wounds in the head and face were selected and a clinical trial was performed on them to study the effects of serum and vaccine therapy. Following the successful study, using both the serum and the vaccine was regarded as the prevention and treatment instruction of WHO and the results obtained by Baltazard and his team led to a lasting effect on the treatment and prevention of rabies in the world.<sup>19</sup> From 1950 to 1956, with the classical rabies treatment among the 370 cases of rabid-bitten patients in Iran, 44 cases of death (12% treatment failure) were reported. From 1957 to 1963, despite 117 rabid bitten cases, treatment failure reached zero.<sup>1</sup> Owing to Baltazard's research conducted on rabies, he can be considered among the rescuers of humanity.

**Relapsing Fever:** Dr. Baltazard was acquainted with spirochetes that cause relapsing fever at Pasteur Institute of Casablanca. In 1947, Baltazard attempted to prevent relapsing fever, which was then highly prevalent in Iran. Until this time, all the work of researchers conducted in the area of the tick bite and blood seeking of laboratory animals failed and no good laboratory animal model existed for research. Baltazard and his colleagues showed that the infant of white and gray house mice (*Mus musculus*) and the infant rabbits were extremely sensitive to tick bites infected with *Borrelia*.<sup>20</sup>

Baltazard showed that three species of spirochete were involved in the spread of relapsing fever in Iran.<sup>21</sup>

**Smallpox:** Baltazard and his colleagues studied variola virus culture in the cells of various tissues, and for the first time,



**Figure 3.** Dr. Baltazard (first person from the right) is monitoring the construction of Pasteur Institute of Iran. 1959.<sup>1</sup>

they cultured the variola virus in the kidney tissue of rabbit. The cytopathic effect of this culture reached 6–7 days for early passages and 2–3 days in subsequent passages (22).

**Study of Other Infectious Diseases:** As an epidemiologist physician, Baltazard conducted studies on other infectious diseases common in Iran, such as typhoid, tuberculosis and cholera.

### Vaccine Production and Launch of Public Vaccination

**BCG Vaccine:** At the end of the Second World War in 1946 and with the presence of scientists of Pasteur Institute of Paris in Iran and by of Dr. Baltazard's suggestion, it was decided that Bacillus Calmette–Guérin (BCG) vaccine production sector be established in Iran. The first BCG strain was brought to Iran in the spring of 1947, and the BCG vaccine was produced; the first BCG vaccination operation started in 1947 in Tehran.<sup>23</sup>

**Smallpox Vaccine:** After the mass production of BCG vaccine, since 1953, Baltazard and his Iranian team in Pasteur Institute of Iran attempted to produce vaccines against smallpox. With the establishment of the national committee for rapid response to eradicate smallpox, 120 health teams went to various regions throughout the country in Jeeps. Two years later, the World Health Organization implemented this model as a template in neighboring countries.<sup>1</sup>

**Cholera Vaccine:** Owing to Dr. Baltazard's efforts, at the time of the cholera outbreak in Iran and eastern neighboring countries, approximately 400 thousand doses of vaccine in Pasteur Institute of Iran were prepared daily and in a limited time, approximately 24 million doses of cholera vaccine were produced.<sup>1,9</sup>

**Other Vaccines:** Baltazard was also highly active in massive vaccination against typhoid in Iran.

### Creation of New Structures

**Construction of the New Building of Pasteur Institute of Iran:** Pasteur Institute of Iran was first established in the Estakhr Street of Hassan Abad area. Using the land donated by the late Abdul Mirza Farman Farmaian, the construction of a new building started in the current Pasteur Street at the time of Baltazard and continued for 10 years. Baltazard was a serious designer and constantly monitored all stages of the design and building of Pasteur Institute of Iran.

**A Great Inventor:** Dr. Baltazard was deeply interested in creativity and innovation, and in this regard, he formed an association for the protection of inventions in Morocco and Iran. Baltazard's first invention in Morocco was relevant to producing a specific type of toilet bowl with quite slippery walls in order to prevent the escape of infected fleas of typhus and dispersion of dust and their dung. By collecting these fleas, he succeeded in producing typhus vaccine.<sup>1,4</sup>

In Iran, the cages that were used for capturing the rodents in plague studies were large wire baskets and since there were not enough trucks to carry the cages, Baltazard decided to change the shape and size of cages. The small and fully closed wooden cage proposed by Baltazard was heat-resistant and had a grid door of steel. This type of basket is still used in the studies of plague research teams in Pasteur Institute of Iran.

Baltazard's innovations were not limited to scientific works of Pasteur Institute. On the roof of his house located at Pasteur Institute of Iran, he launched and installed the first solar panel setup of Iran. The black curved surface with water moving on its surface, warmed by heat and sunlight, was protected by glass. He read the description of this production system of solar energy in a



magazine and then designed and implemented it.

**Tehran Water Disinfection:** The establishment of water piping network and disinfecting of water in Tehran can be noted among Baltazard's most important and effective activities. Until 1950, the aqueduct was used as a source of drinking water, causing transmission of diseases such as typhoid and cholera through drinking water. Pasteur Institute of Iran headed by Dr. Baltazard, for the first time conducted monitoring and chlorination of Tehran drinking water.<sup>1</sup> This activity was highly effective. High-quality water was provided to the public for four years, and following that through a French company, water treatment plants were established in Tehran.

**Establishment of the Village of Lepers:** With the help of leading research institutes in France, the USA and Russia, Baltazard established centers for reception and treatment of leprosy patients in Mashhad, Tabriz and Tehran.<sup>8</sup>

**Use of GIS in Field Studies:** By starting the systematic studies of plague in Akanlu center of Pasteur Institute of Iran since 1952, Baltazard developed aerial maps of western regions of the country, and in this way, the first studies using the Geographic Information System (GIS) were implemented in the country.<sup>24</sup>

## International Activities

As an expert of the World Health Organization (WHO) in the field of plague, rabies and relapsing fever, Baltazard was asked for outbreak investigation and control of these diseases around the world. He studied the animal reservoirs of plague and the disease control in different countries. In 1960, with the support of the WHO, he was responsible for research on the cause of the maintenance of plague in India and showed that the resistance of a species of rodent named Indian gerbil (*Tatera indica*) to plague was the cause of the persistence of the disease in this country and domestic mice were the link between these rodents and human.<sup>25</sup> He conducted the same study in Indonesia and found that the resistance of a rodent named "*Rattus exulans*" to the plague was the cause of the maintenance and spread of the disease in this country.<sup>26</sup> In 1960, he also performed a joint project with research groups from Turkey, Iraq and Syria and showed that plague infection circulates in these three countries, the plague bacillus was present with the same biochemical characteristics and exclusively in Meriones.<sup>27</sup> In 1966, Baltazard studied the presence of wild rodents in different ecological conditions and their role in the outbreaks of plague in Brazil and found that the plague was limited to areas in the northeast and southeast of this country. In 1966, the research center for the study of plague was established in Brazil by Baltazard.<sup>13,28</sup> Baltazard also performed different studies during the years 1967–1970 in Myanmar, Peru, Mauritania, Nepal, Congo, Yemen and Saudi Arabia in the field of plague.<sup>29–33</sup> He also fulfilled the project of fighting against relapsing fever disease in Ethiopia.<sup>34</sup> Over the years 1948–1954, Baltazard and his colleagues showed that people who were infected by *Borrelia crocidurae* catch a mild relapsing fever in North and West Africa and Turkey by studying in the desert and arid and semi-arid areas.<sup>35,36</sup>

Attendance in international scientific meetings and congress to present the scientific achievements of Pasteur Institute of Iran

can be regarded as Baltazard's other activities during his service. In 1967, Baltazard presented Iran's findings regarding plague in the seminar of the WHO addressed to the measures in the control of plague<sup>37</sup> and in 1969 at an international meeting in Geneva.<sup>38</sup> Other results of Iran's research, particularly in the field of rabies and relapsing fever were also presented by Baltazard at several international forums.

Holding international courses regarding relapsing fever and plague in Iran was among Baltazard's other activities. At the time of Dr. Baltazard's presidency in Pasteur Institute of Iran, the sphere of consumption of Iran's produced vaccines was much further than the borders of the country. Smallpox vaccines produced in Pasteur Institute of Iran also covered Iraq, Afghanistan and Egypt. Under the auspices of the United Nations Children's Fund (UNICEF), 238 million children in 22 countries used BCG vaccine produced in Pasteur institute of Iran.

Using the vaccine produced by Baltazard and his Iranian colleagues, the deficiency of vaccine in Pasteur Institute of Paris was also compensated. Referring of developed countries such as France for cholera vaccine to Pasteur Institute of Iran was a major success for Iran vaccine industry.<sup>8</sup>

At the time of Dr. Baltazard, Afghanistan suffered from numerous health problems. Accordingly, Baltazard decided to establish a Pasteur Institute in the capital Kabul. In 1964, three Afghan physicians came to Tehran for training to promote the Kabul Vaccine Institute to the center of the production of vaccines and biological products. In this year, in order to establish the Pasteur Institute of Kabul, Baltazard studied all aspects necessary to implement the project with the French Ambassador and the Afghanistan Minister of Health. However, the Russian invasion and sudden change of government made the implementation of the project impossible.<sup>1</sup>

## Baltazard in France

While in France, Baltazard did not cut ties with Pasteur Institute of Iran and at the same time continued his international connections. In 1969, Baltazard founded the research department for epidemiological studies at Pasteur Institute of Paris.<sup>39</sup> In 1970, the first course of field epidemiology was formed by him. The aim of the course was training the field studies of communicable diseases.<sup>1</sup>

In September 1971, after a long battle with lung cancer, Dr. Baltazard died in Paris. Due to the valuable services of this distinguished scientist, two buildings in Pasteur Institute of Iran in Tehran and Akanlu in 2005 and 2013 and a boulevard in the Akanlu village in 2016 were named Baltazard.

In conclusion, Dr. Marcel Baltazard was a distinguished French scientist who came to Iran in 1946 after finishing his medical studies in Paris and learning from great masters in France and Morocco. During his 20 years of activity in Pasteur Institute of Iran, he made great developments in the field of medical and health in the country. Among his valuable services at Pasteur Institute of Iran, creation of new structures, study and control of infectious diseases, especially the plague, rabies and relapsing fever, launch of vaccination systems and development of international relations of Pasteur Institute of Iran, can be mentioned.

Iranians and the staff of Pasteur Institute of Iran will never forget his attempts in Iran.

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