REVIEW

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Epidemiology of Tuberculosis During the Period 1703–2011: Honoring the World Tuberculosis Day

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ABSTRACT

Tuberculosis (TB) is one of the oldest, the most expanded and the most lethal diseases in human history. Although Koch's discovery of the TB causative agent (1882) represented a great progress in the fight against this infectious disease, it took a significant amount of time to reduce morbidity and mortality in the world. In Bosnia and Herzegovina (B&H) it was necessary to implement actions in the form of education where the popularization of measures of recognition, treatment and preventing the disease was done. After the Annexation of B&H to Austro-Hungarian (1908) began an organized fight against TB. Dr. S. Kukric was a particularly prominent individual, putting his effort by working in clinics, through his lectures and numerous popular research papers on tuberculosis. He was followed by many colleagues working inexhaustibly while facing the high incidence of TB and the difficult social situation in B&H. Although this disease is old, at the end of the 20th century a new TB appeared, with new challenges and new, even grater problems. Significant achievement and great progress in the treatment and control of TB infection was achieved by implementing the direct observed short course treatment (DOTS from 2006.) Still, there is a too high incidence of TB that becomes again a serious threat, together with new problems and difficult economic and social situation. Nowadays in Federation of B&H the guidelines of World Health Organization on reinforcing the DOTS strategy are being daily implemented, including multidrug-resistant (MDR) TB and infection control.

Key words: epidemiology of tuberculosis, diagnostics, antiepidemic measures.

1. EPOCHAL DISCOVERY

Robert Koch's lecture on Friday, the 24th of March 1882 in Berlin, began by describing the rod-shaped bacteria *Mycobacterium tuberculosis* and represented the first big step of the modern age in the fight against TB. The lecture was published on the 10th of April in 1882 in the journal „Berliner Klinische Wochenschrift“ and soon translated in almost all the world languages. In May 1883 it was translated and published in „Lijecnicki vjesnik“ in Zagreb (1).

For a long time data on TB in B&H were scarce. Only data notations from preserved “books of medicine” in convent libraries witness how patients were treated, what were their problems and how they died from „susica“ (greek word Hektikos – consumptive). Such an example is an old but valuable paper from Necrology of Herzegovinian Franciscan Province. Herzegovinian Franciscans, the same as other monks, register all their dead members in a special book, Necrology. They register the day, the year of birth and death, as well as main features of the departed man's life.

Necrology of Herzegovinian Franciscan Province begins in 1703. Till 1844, the day when the Province was founded, in

Necrology were registered all apostolic vicars in B&H, then a lot of Franciscans, born on the territory of former Province, regardless of where they lived and died. Thus, from the year 1703 till the year 1934 in Necrology were registered 258 names, including: 10 bishops, 199 priests, 38 clerics and 11 lay-men. Of the many causes of death, the friars are given 23 most frequent diseases, the most important being “susica”¹, which represents 39,63% of death causes (2).

A method of treating TB patients is being described in details in „Kresevo book of medicine“ written by one of the first graduate doctors dr. fra Mate Nikolic (1775-1844) (3). Especially worth mentioning is the work of „Flos medicine“ - Cvit likarije – the first book printed in the Croatian language. The Latin manuscript is a famous collection of retention policies, health promotion and treatment of diseases created by the well known Salernitan medical school (from the ninth century) – mother of all medical schools in Europe. The book was translated by Fra E. Pavic in 1768 in Budapest. The Manuscript is being kept in the library of a Franciscan convent in Kresevo (R.b. 23-III-9) (4).

2. ERRORS DURING THE TREATMENT OF TUBERCULOSIS

Dubrovnik doctors in 18th century were giving to TB patients, prescriptions for different herbs, advising them to drink a lot of milk, to sunbathe, to go to the countryside and to stay in the fresh air on the hills of neighboring B&H (5).

From the 1st of January till the 30th September 1898 in the city hospital of Mostar were received 322 patients, dismissed 266, died 30, stayed 36, among them there were 32 Muslims, 200 Catholics, 97 Greco easterns, 3 Jews. In addition, a hospital doctor examined 785 patients in the clinic (6).

At that time there was still no explanation of the possibility to transmit the tuberculosis from an animal to a man, and the Provincial Government in Sarajevo passed an order in 1899 on protection against the infection by avoiding drinking milk from TB ill cows and destroying diseased cattle. According to Kobler in the period from 18th till the first half of 20th century TB has swept away millions of lives. The average mortality rate in Germany between 1882 and 1886 was 346, in Zagreb 645, in Belgrade 860 per 100.000 inhabitants.

In the year 1905 in total 51.639 persons died in B&H of which 7.237 died (14%) from TB. Due to the small number of physicians not every death was confirmed by a doctor, and since there was no legal obligation to declare the death those data on deaths were incomplete (7, 8).

The disease mostly swept away young people, students, intellectuals, the poor and exhausted as it was described by Antun Branko Simic in his poem „Returning to the sun“ written on 2nd of May 1925 – only three days before his death.

In 1910 B&H had, in total, 89 men and 4 women physicians working in civil service, 27 in city services, 4 in rail services and 8 in factory services. In addition to those, there were private physicians and dentists, 5 with a degree and 11 without a doctoral degree and also 117 midwives. In that period every third death was caused by tuberculosis.

The station for the TB patients care and their family members has been operating in Sarajevo since 1913. Dr S. Kukric was particularly responsible for the TB patients whom he treated with tuberculin (7, 8, 9). The First World War gave its contribution by worsening the epidemiological situation in the war-affected world. From the First to the Second World War the epidemiological situation hasn't changed significantly. After the Second World War there were many health promoters in B&H who continued the fight against TB such as Prof. dr. Spiro Janovic, Prof.dr. Hisam Serdarevic, Prof.dr. Rifat Tvrtkovic, Prof. dr. Abdulah Konjicija and others across B&H. Nowadays, at the beginning of the third millennium we must not forget the contribution of physicians who were active in recent decades of the heroic period of fight against tuberculosis.

3. APPLICATION OF ANTITUBERCULOUS DRUGS

Mortality was the only indicator of TB in a specific area until the mass application of antituberculous drugs (ATD). According to vital statistics data in 1924, in the former Yugoslavia 38.882 people died from TB. Afterwards, retrospective data from 1961 indicate the total number of registered patients in Yugoslavia reached its peak of 201.729 patients and since then the number of patients has been gradually reduced.

The incidence of TB deferred from republic to republic. The

highest incidence of TB was in AP (Autonomy Province) of Vojvodina (183), followed by Serbia (155), Croatia (126), B&H (121), Montenegro (105), Macedonia (102) and Slovenia (91) per 100.000 inhabitants (10).

4. IN 21ST CENTURY PEOPLE DIE FROM TUBERCULOSIS

Antituberculous drugs were applied only from the mid 20th century. Satisfaction was soon perceived by patients and by physicians. Numerous studies (papers) give evidence about the treatment results. When the eradication and victory over tuberculosis was almost visible it came back in even more dangerous form. At the end of the 20th century TB has partnered with AIDS (Acquired Immune Deficiency Syndrome). As if not being enough, together with this malignant integration emerged very dangerous forms of multi-drug-resistant tuberculosis (MDR TB). TB germ became resistant to main ATD: isoniazid and rifampicin. Infection with multiresistant causative agents of TB is one of the biggest dangers because treatment of these patients is expensive, time-consuming and often, unsuccessful. MDR TB infection is a serious threat which makes us fear of getting to the situation which we had when being without ATD. World Health Organization experts responded urgently to exacerbated epidemiological situation with a new strategy in treating the TB (directly observed therapy–short course DOTS) implemented since 2006 (11).

5. SOURCE OF INFECTION

Data from the literature indicate that at the time when the causative agent of TB had been discovered every seventh person in the world was infected, and today, after 131 years, every third – more than two billion. The source of infection is an ill person, especially the one with pulmonary, laryngeal or bronchial TB. The most dangerous ill person for the environment is the one who in 1ml sputum excretes 10.000 germs which makes directly positive its microscopic tests results.

6. TRANSMISSION PATH

The disease is being transmitted by droplets. The risk of infection is a close contact, mostly while being together in the same room. Usually it takes 1-2 months (incubation) from the infection to the radiologically visible lesions, generally the lung ones, or to the significant cutaneous tuberculin reaction. The infection process usually does not progress but remains latent where it can persist for decades. Meanwhile, the permanent rivalry between germs on one side and body defence ability, on the other, persists. The moment the body defence is reduced due to other chronic diseases, especially HIV infection, there is a progression and emergence of manifest tuberculosis (12).

7. SPREAD OF TUBERCULOSIS

Though the TB is cosmopolitan infectious disease, it is variously distributed in the world. According to the records from 31st December, 1990 in B&H has been registered 6.871 patients with active TB, so the incidence rate was 153,6 per 100.000 inhabitants. The same year in B&H were registered 204 new patients with active extrapulmonary TB, 4,6 per 100.000 inhabitants.

In European countries during the last 15 years the number

of TB patients increased from 74,4/ 100.000 inhabitants in 1997 to 104 per 100.000 inhabitants in 2004. There is a big difference between countries of Western and Eastern European. In western European countries the incidence is up to 15 per 100.000 and in eastern European countries is higher than 50 per 100.000 inhabitants. In the third region, which consists of the central European countries, the frequency range is from 27,4 per 100.000 (Turkey), through 28,6 per 100.000 (Croatia), 60,9 per 100.000 (B&H), up to 146 per 100.000 inhabitants (Romania) (10-13).

In 1997 there were 8 million patients having active TB in the world—95% in African countries, Southeast Asia and South America. Each year about 2,5 to 3 million people die from TB. During the last decade there has been registered the significant increase of incidence in Russia, especially a large number of MDR patients. This represents a huge danger and threat for nowadays generations and generations to come. In those countries there are more than 11% TB and HIV patients registered, while in Sub-Saharan Africa there are about 38 % at the same time TB and HIV positive ones. In the period from 1996 to 2011 in the Federation of B&H TB incidence ranged from 44 to 91 per 100.000 inhabitants (14).

8. EPIDEMIC CONTROL MEASURES

One of the best measures of primary prevention is a vaccination against TB with the Vaccine Bacil Calmette Guérin (BCG) immediately after birth.

The vaccine was administered to a child (in 1921) whose mother and grandmother died from TB, and the child survived. In 1929 in Lübeck 290 children were vaccinated and 70 of them died. The children instead of apathogenic were vaccinated by live TB germs. It took a long time to gain confidence in, up to date, the safest vaccine. Our vaccination rate is about 98%, and as a result the disseminated forms of TB and tuberculous meningitis between children are eliminated. This vaccine insures the protection during the period of about 15 years. The resulting papule on the skin at the application of the vaccine indicates that the vaccine was properly administered intradermally and on that place remains a scar. In B&H BCG vaccination is administered at birth of a child according to World Health Organization instructions, and since 1998 the booster shot is not implemented. New vaccine is expected to be derived from the existing one, it will be in use already in next 5-10 years and it will have an extended protection (15).

9. RECOGNITION AND DIAGNOSIS OF TUBERCULOSIS

Each examination begins by taking a medical history, the symptoms, duration, intensity and frequency with a special accent on family history and epidemiology.

The clinical evaluation starting with accurate physical examination and laboratory analysis of a biological material, functional tests and radiological results, is of extreme importance. X-ray PA and profile picture, and CT scan can be of use when minimal pulmonary changes are existent. Mass population fluorography contributed significantly to the early detection of TB. Besides TB this method helped in discovering other pulmonary, cardiovascular and malignant diseases. World Health Organization experts on the ninth session in 1973 concluded

that the method of mass population photography should be abandoned, because of medical and economic reasons (16, 17).

10. BRONCHOSCOPY IS COMMONLY USED IN DIFFERENTIAL DIAGNOSIS

Microbiological procedures – direct sputum smear, done immediately and the results are positive when there are 10.000 to 100.000 germs in 1ml of sputum. Smaller number is proved by seeding the culture medium (10 germs in 1ml). After TB germ isolation the sensitivity to drugs is being determined.

The polymerase chain reaction test (PCR) is a fast method, used in diagnostics of pulmonary and extrapulmonary TB.

Tuberculin test–PPD (Purificated Proteine Derivat) indicates that person has been in contact with any BK through inhalation or by BCG vaccination.

Quantiferon test – based on the release of interferon–gamma. It is conducted on people who were in close contact with those with active tuberculosis changes detected. The specificity is higher than in the tuberculin test.

11. CHEMOPROPHYLAXIS

Chemoprophylaxis is being applied on highly reactive people, younger than 35 and whose tuberculin or Quantiferon test had been negative but they had contacts with TB infected person. HIV positive patients who were in contact with TB infected person. Children under 16 with high reactive tuberculin test, who did not receive the BCG vaccine.

Regardless of the age of a person chemoprophylaxis is indicated for latent TB infection, if longer treatment with glucocorticoids is required.

12. THE BEST EPIDEMIC CONTROL MEASURE IS TREATMENT OF AN ILL PERSON

The DOTS strategy is implemented, which includes 5 basic elements:

- Political support for the program,
- Passive detection with mandatory sputum analysis,
- DOTS *directly observed therapy* – *short* course of the TB infected person,
- Regular supply with main ATD,
- Detection and reporting of patients, treatment follow-up, reporting to a higher level.

DOTS plus is a program of treatment for multi-drug-resistant (MDR) TB, representing a big problem in the world nowadays, especially in countries with high AIDS morbidity rate (18, 19).

13. APPLICATION OF BIOMARKERS IN TUBERCULOSIS

Biomarkers are measurable biological parameters used both in diagnostics and individualized treatment of patients with tuberculosis. Biomarkers can be used as disease intensity indicators. Never before in the world were so many persons infected by TB. Nowadays, there are more and more patients, more persons with immunodeficiency and more persons with multi-drug-resistant tuberculosis and that can take us back in time when ATD did not exist. Therefore biomarkers, both in

scientific research and clinical practice, are being more and more relevant. Biomarkers are expected not only to provide early diagnosis but to assess severity of the disease. Rapid information is important before the disease manifests itself, it gives a possibility to individualize and include the appropriate therapy. While skin-tuberculin test cannot show whether there is an active TB process or not, this information is provided by biomarkers whether obtained in invasive (through serum – leukocytes) or non-invasive way (through exhaled breath or urine). The price issue is also important. Therefore, direct sputum smear, culture on solid or liquid medium is the cheapest way.

Today there are rapid molecular methods which cost about 16 dollars where contemporaneously the result on rifampicin resistance is obtained in two hours (20).

14. CONCLUSION

Statistical data on tuberculosis long past indicate the extremely poor epidemiological situation in many countries especially in Bosnia and Herzegovina.

Even today the incidence of TB and its complications as well as associated diseases threat and worry. In 5–10 years the range of new powerful antituberculous drugs, application of a new vaccine and mass use of bio records, is expected.

Nowadays, the Federation of B&H is implementing the World Health Organization guidelines to strengthen the DOTS strategy, infection control, to repress the resistance on antituberculous drugs and also the lethal KB and HIV integrations. The organization and work to protect the population and to treat ill persons give hope and real opportunity to catch up with the modern trends in the world.

REFERENCES

1. Koch R. Aetiologija tuberkuloze. Liječ vjesn. 1883; 6: 9–11; 20–26; 40–44; 53–60.
2. Šantić Ž. Epidemiološki i preventivno klinički aspekti tuberkuloze u širokom Brijegu. Mostariensia, Mostar, 1997; 7: 33–42.
3. Šantić Ž. Kreševska ljekaruša fra Mate Nikolića (1775.–1844.). Mostariensia, Mostar, 1999; 10: 91–108.
4. Flos medicinae- Cvit likarije. Budimpešta, 1768.
5. Ferri R. Liječenje tuberkuloze u starom Dubrovniku. Tuberkuloza, 1956; 8: 176–180.
6. Osvit. 1898; 1/42/:4–2, sub 17.12. 1898.
7. Hrisafović B. Početak organizirane borbe protiv tuberkuloze u Bosni i Hercegovini. Radnička zaštita. 1939; 20: 146–152.
8. Grujić M. Rasprostranjenost tuberkuloze kod nas i u svijetu. U: Tuberkuloza pluća, Beograd, Naučna knjiga, 1967; 383–406.
9. Vučak I. Borba protiv tuberkuloze, kao svojevrsne socijalne bolesti, u Hrvatskoj i Bosni i Hercegovini u razdoblju 1880.–1920. Mostariensia, Mostar, 2003; 17: 79–89.
10. Kaleta J. Epidemiološka situacija tuberkuloze u Jugoslaviji. Tuberkuloza I, 1969; XXI, 22–35.
11. World Health Organization: Global tuberculosis control 2009: Epidemiology, strategy, finncig (WHO/HTM/TB/2009;411). Geneva: World Health Organiztion, 2009.
12. Popović-Grle S. Tuberkuloza dijagnostika i terapija. Priručnik, Zagreb, 2004.
13. Walls T, Shingadia D. The epidemiology of tubrculosis in Europe. Arch Dis Child. 2007; 92: 726–729.
14. Dizdarević Z, Imamović S, Prnjavorac B. Tuberkuloza U: Plućne bolesti. Tuzla, 2012; 243–269.
15. Andersen P. TB vaccines: progress and problems, Trends in Immunology. 2001; 22 (3):160–168.
16. Crofton J, Horne N, Miller F. Klinička tuberkuloza, 2.izd. IBIS grafika, Zagreb, 2001.
17. Dizdarević Z, Žutić H, Mehić B, Hošić M, Šantić Ž, Agić S. et al. Dijagnostičko terapijski vodič za tuberkulozu. Sarajevo, 1995; 9–22.
18. Miller N, Hernandez SG, Cleary TJ. Evalvation Gen-Probe amplified Mycobacterium tuberculosis in clinical specimens. J Clin Microbiol. 1994; 32: 393–397.
19. Šantić Ž. Bogut S. Izvanplućna tuberkuloza.U: Bolesti sluznica. Medicinska naklada, Zagreb, 2012; 74–79.
20. Wallis RS, Pai M, Menzies D, Doherty TM, Walzl G, Perkins MD, Zumla. Biomarkers and diagnostics for tuberculosis: progress needs, and translation into practice Lancet. 2010; 375 (9729): 1920–1937.