

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Available online at www.sciencedirect.com





International Journal of Medical Microbiology 296 (2006) 1-4

www.elsevier.de/ijmm

EDITORIAL

Killed in action: Microbiologists and clinicians as victims of their occupation Part 4: Tick-borne Relapsing Fever, Malta Fever, Glanders, SARS

Tick-borne Relapsing Fever

A microbiologist and pathologist, who was engaged in research on African Tick-borne Relapsing Fever, Joseph Everett Dutton (Fig. 1), became a victim of this disease. He was born on 9th of September 1874 in Higher Bebington, Cheshire, as the fifth son of the chemist John Dutton, was educated from 1888 to 1892 in the King's School of Chester, and entered the Liverpool Medical School and the Royal Infirmary in the same town. In 1897 he was graduated and was appointed to the George Holt Fellowship in Pathology. One year in the Departments of Surgery followed. He undertook his first scientific expedition in 1900 as a member of the third expedition of the Liverpool School of Tropical Medicine together with H.E. Annett and J.H. Elliott. They studied malaria and filariasis. At the beginning of 1901 Dutton travelled alone in the Gambia. It was the sixth expedition of the Liverpool School. On May 10, Dr. R.M. Forde, Colonial surgeon at the hospital in Bathurst, demonstrated a patient, where he (Forde) had found in the blood "very many actively moving worm-like bodies whose nature he was unable to ascertain" (Dutton, 1902). The patient went back to England where Dutton examined him again, but he found no parasites in his blood. This patient, a 42year-old government employee, came back to the Gambia several months later. Dutton, who was also back to the colony, examined him on December 15, 1901, and "found a flagellate protozoon evidently belonging to the genus Trypanosoma" and he suggested "that the name 'Trypanosoma gambiense" [should] "be given to this trypanosoma" (Dutton, 1902). We have told earlier the whole story in this journal (Köhler, 2002). Because this patient was also ill with malaria Dutton did not realize the relation between sleeping sickness and trypanosomes. The tenth expedition of the Liverpool School led Dutton in 1902 together with J.L. Todd and C. Christy in 1903 to Belgian Congo. The King of Belgium placed a considerable amount of money at the disposal of this expedition. The researchers left Liverpool on September 23, and reached the Stanley Falls at the end of the year. Dutton's special interest was directed to tick-borne relapsing fever of the Central African type. He was able to infect monkeys by the bites of spirochaete-carrying soft ticks, Ornithodorus moubata. What he did not know, Philip Ross and Milne made the same experiment a few weeks before in Uganda. Dutton found also that Borrelia duttoni could pass into the eggs and larvae, and so confer infective potential on the tick of the succeeding generation (Manson-Bahr, 1951). Robert Koch (1906), who had no information about these results, found while he was in East Africa in 1905 that this transmission is possible up to the third generation. Christy and Dutton infected themselves with the disease, possibly at the dissection of a patient died of relapsing fever. Christy survived but Dutton died after the fourth relapse on 27th of February 1905 in Kosongo/Congo Free State. He was at the age of 31 years. The news about his death came relatively late to England because "The journey from Kosongo to the nearest telegraph station takes 2 months" (Anonymus, 1905).

Malta Fever

The "Malta Chronicle" of September 15, 1904, reported "Well known for his discovery of the microbe of Mediterranean or Malta Fever Prof. **Tito Carbone** died in Milan from a fever contracted during scientific experiments". The real story is another one, David Bruce discovered the microorganism, and Carbone is not so well-known in this respect. But, he was a victim of this disease.

Tito Carbone was born on 16th of July 1863 in Carbonara Scrivia (Alessandria). He studied medicine in Turin, Pavia and Florence and was graduated in 1886 in Turin. Working with C. Lombroso (psychiatric clinic)

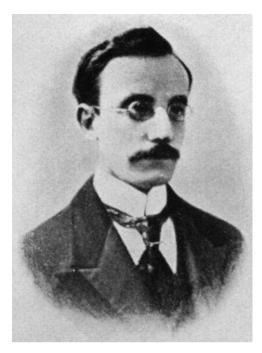


Fig. 1. Joseph Everett Dutton (from Olpp, 1932).

he was engaged in the control of a cholera epidemic in Tortona, and later worked in the pathological laboratory of G. Bizzozero. In 1888 he was assistant at the Institute of Morbid Anatomy, headed by P. Foà, and changed in 1891 to the Laboratory of Pathological Physiology at the hospital Umberto I. at Turin. He went to Buenos Aires, and back to Italy he became a coworker of S. Belfanti at the Istituto Sieroterapia Milano. Later he followed an academic career and was appointed Professor of Morbid Anatomy in Cagliari (1897), Modena (1898) and Pisa (1903). His main field of research was the aetiopathogenesis of infectious diseases, he published on bacterial toxins and immunity. In 1904 he dissected a patient died of Malta Fever and published the pathological findings (Carbone, 1904). Brucella melitensis was isolated by him and transferred to experimental animals. In order to get information about the toxin production he cultivated the microorganisms, and it seems that he infected himself by this way. Carbone died on 6th of September 1904, aged 41 years (Dizionario Biografico degli Italiani, 1976).

Glanders

Glanders in humans was a rare disease, even when it was common in horses. But there have been some laboratory infections because "probably no organism, with the possible exception of tularaemia bacillus, is as dangerous to work with as the glanders bacillus. In one laboratory, several members of staff became ill a few

days after the breaking of a centrifuge tube" (Parker, 1984). Without giving details Bernstein and Carling (1909) mentioned: "glanders has been assigned as the most frequent case of accidental death amongst laboratory workers". The six patients, described by these authors, were horse keepers or horse-bus drivers. Howe and Miller (1947) reported on six cases of glanders occurring within 1 year (1944/45) in Camp Detrick, Frederick, MD. In the small laboratory a research program on glanders was performed. The first two cases occurred 2 weeks after an accident, when a technician dropped a flask containing a virulent suspension of Burkholderia mallei. The technician did not infect himself but two physicians staying in the laboratory fell ill. Two technicians became infected by routine laboratory work and the route of infection of two veterinarians was possibly aerogenic. The patients were cured by sulfadiazine.

Little is known about the course of life and the death of Georg von Hofmann-Wellenhof. He was born on 14th of May 1860 in Vienna as the third child of Paul Ferdinand Hofmann von Wellenhof and his wife Klothilde, née Kraus (data from his thesis). He studied medicine in Vienna and Graz (where he was graduated), and was for some years First Assistant at the Institute of Pathology. Then he changed to the Institute of Hygiene, interrupted by some years of assistantship at the Institute of Zoology, all in Graz. As a result of his work in the Institute of Pathological Anatomy he reported on the detection of a "pseudodiphtheria bacillus" (later often cited as "Hofmann-Wellenhof'scher Bacillus"); first on 20th of September 1887 at the 66th Assembly of the "Gesellschaft Deutscher Ärzte und Naturforscher" in Wiesbaden, followed by the detailed publication (von Hofmann-Wellenhof, 1888; Köhler, 2004). Before 25th of September 1889 (he was since 1888 assistant at the Institute of Hygiene at Vienna) he performed "infection experiments with the virus of glanders". Around October 8, his temperature raised and he had pain in his left chest (pleuritic rub). For some days he improved, then he complained about "rheumatoid discomfort". Eight days later purulent blisters and abscesses developed, and on 22nd of the month he was hospitalized. The clinical picture was that of acute glanders, and the dissection confirmed the diagnosis. The source of infection was unclear; an aerogenic infection was supposed. Georg von Hofmann-Wellenhof died on 23rd of October 1889, aged 30 years (Anonymus, 1889).

Severe acute respiratory syndrome (SARS)

Deadly infections of physicians by microorganisms they were working with happened as shown in the four

Name	Born	Died	Disease
Semmelweis, Ignaz Philipp	1818, July 1	1865, August 13	Septicaemia
Plehn, Friedrich	1862, November 15	1904, August 30	Malta Fever
Schaudinn, Fritz	1871, September 19	1906, June 22	Septicaemia, rectal abscess
Gabritschewsky, Georgiy Norbertovitch	1860	1907, March 23	Pneumonia
Neisser, Albert	1855, January 22	1916, July 30	Septicaemia
Gaffky, Georg	1850, February 17	1918, September 23	Influenza-pneumonia
Kolle, Wilhelm	1868, November 2	1935, May 10	Infectious arthritis, pneumonia

Table 1. Death of microbiologists and infectious disease specialists due to infections not connected with professional duties (except tuberculosis)

parts of this article mostly at the end of the 19th up to the first quarter of the 20th century. But also recently we had to deplore the loss of a colleague who died of SARS. It was **Carlo Urbani**, born on 19th of October 1956 in Castelplanio/Italy. As to Oranski (2003) in Hanoi as a representative of the WHO he examined Jonny Chen, a Chinese-American businessman on February 28, 2003, and he was the first one who identified this "new" disease. The patient was suspected for an avian influenza infection. Urbani himself realized that he became infected on 11th of March while taking care for the patient.

About his career is known that he earned his medical degree in 1981 from the University of Ancona. For 3 years he was trained in infectious diseases at the University of Messina, and in 1990 he became deputy chief of the Department of Infectious Diseases at the General Hospital in Ancona. He worked for the WHO since 1993 and after moving to Médecins Sans Frontiérs in 1995 he became president of the Italian branch in 1999. His working places were in Vietnam, the Philippines and in Cambodia. On 29th of March 2003, 18 days after infection, Carlo Urbani died of SARS in Bangkok/Thailand.

Some well-known bacteriologists and clinicians died of infections not connected with their professional duties (Table 1; Vierordt, 1915; Köhler, 1997; Olpp, 1932; Vierhuff, 1907; Hetsch, 1935; Schloßberger, 1935).

Many microbiologists and physicians lost their life in the battle against the disease they wanted to explore and to overcome for the welfare of mankind. A few of them were honoured by a monument of memory like Ricketts, Lazear, Noguchi, Thuillier or da Camara Pestana, others were mentioned only in a short obituary in scientific journals, or are remembered among microbiologists like E. Hailer of the Robert-Koch-Institute (Berlin) who died after a laboratory infection with anthrax bacilli in 1939 (Stefan Winkle, personal communication; Robert-Koch-Institut, 1991). Many are unnamed like those plague doctors in the Middle Ages who did not leave their patients, or the many army surgeons who died of typhus, variola or other infectious diseases. These men are shining examples and we should

stand in awe of them. – This is the bright side, but there was (and is?) also a dark one. Microbiologists and so-called "physicians" used their knowledge and medical skills to kill people by application of virulent microorganisms in order to prove the efficacy of bacteriological weapons (e.g. see Geißler, 2003). We should treat them with scorn.

Acknowledgements

Some unpublished data were obtained from colleagues and institutions. I am indebted to Prof. Stefan Winkle, Hamburg, to my dear colleague Prof. Heinz Flamm, Klosterneuburg, and to Hofrat Dr. Kurt Mühlberger, Archives of the University at Vienna, as well as to the head of the library of the Deutsche Akademie der Wissenschaften Leopoldina, Halle, Dipl.-Math. Jochen Thamm, and Dr. Eva Kotzurek, library of the University at Graz. I also thank Dr. Dagmar Gebauer (Elsevier GmbH, Jena) for her careful linguistic revision of the text.

References

Anonymus, 1889. Dr. Georg von Hofmann-Wellenhof †. Wien. Klin. Wochenschr 2, 855.

Anonymus, 1905. Joseph Everett Dutton. Lancet i, 1020–1021. Bernstein, J.M., Carling, E.R., 1909. Observations on human glanders with a study of six cases and a discussion of the methods of diagnosis. Br. Med. J. i, 319–325.

Carbone, T., 1904. Un caso di febbre di Malta. Arch. Sci. Med. 28, 273–299.

Dizionario Biografico degli Italiani, 1976. Ist. Enciclop. Ital., Roma.

Dutton, J.E., 1902. Note on a trypanosoma occurring in the blood of man. Br. Med. J. ii, 881–884.

Geißler, E., 2003. Anthrax und das Versagen der Geheimdienste. Kai Homilius Verlag, Berlin.

Hetsch, H., 1935. Wilhelm Kolle †. Dtsch. Med. Wochenschr. 61, 849–850.

Howe, C., Miller, W.R., 1947. Human glanders: report of six cases. Ann. Intern. Med. 26, 93–115.

- Koch, R., 1906. Über afrikanischen Recurrrens. Berl. Klin. Wochenschr. 43, 185–194.
- Köhler, W., 1997. Vor 150 Jahren: Ignaz Philipp Semmelweis führt die Händedesinfektion ein. Immun. Infekt. 1, 219–222.
- Köhler, W., 2002. Zentralblatt für Bakteriologie 100 years ago. Sleeping sickness – intoxication or infectious disease? Int. J. Med. Microbiol. 292, 141–147.
- Köhler, W., 2004. Zentralblatt für Bakteriologie 100 years ago. The controversy diphtheria and pseudodiphtheria bacilli versus virulent and avirulent diphtheria bacilli. Int. J. Med. Microbiol. 294, 355–361.
- Manson-Bahr, P., 1951. Manson's Tropical Diseases, 13th ed. Cassel and Comp., London.
- Olpp, G., 1932. Hervorragende Tropenärzte in Wort und Bild. Verlag d. ärztl. Rundschau. Otto Gmelin, München.
- Oranski, I., 2003. Obituary Carlo Urbani. Lancet 361, 1481.
- Parker, M.T., 1984. Septic infections due to Gram-negative aerobic bacilli. In: Smith, G.R. (Ed.), Topley and Wilson's

- Principles of Bacteriology, Virology and Immunology, vol. 3. Edward Arnold, London, p. 290.
- Robert-Koch-Institut, 1991. 100 Jahre Robert Koch Institut, 1. Juli 1991. Berlin, p. 64.
- Schloßberger, H., 1935. Wilhem Kolle †. Klin. Wochenschr. 14, 806–807.
- Vierhuff, W., 1907. Moskauer Brief (Obituary Gabritschewsky). Dtsch. Med. Wochenschr. 33, 1501–1502.
- Vierordt, H., 1915. Todesursachen bei namhaften Medizinern. Med. Klin. 11, 499–500; 525–526; 549–551.
- von Hofmann-Wellenhof, G., 1888. Untersuchungen über den Klebs-Löffler'schen Bacillus der Diphtherie und seine pathogene Bedeutung. Wien. Klin. Wochenschr. 38 (65–68), 108–110.

Werner Köhler Adolf-Reichwein-Str. 26, D-07745 Jena, Germany