

THE U.S. PUBLIC HEALTH SERVICE
AND
ROCKY MOUNTAIN SPOTTED FEVER

MILESTONES OF RESEARCH

Rocky Mountain Spotted Fever (RMSF) is the clinical syndrome in man caused by infection with the obligate intracellular parasite, Rickettsia rickettsia following the bite of certain ticks. The rickettsiae are perpetuated in the tick by a complex cycle of tick-wild animal transmission and transovarial passage. People are accidental victims when they intrude into the habitat of infected ticks or, in the Eastern U.S., when their dogs bring infected ticks home. It occurs in most parts of the United States but was first identified and studied in Idaho and Montana. In Montana, it gave origin to the Rocky Mountain Laboratory (RML), the largest laboratory of the National Institute of Allergy and Infectious Diseases.

Anecdotal stories trace the disease back among Indians in Montana to about 1873. The Indians recognized the seasonal and geographic influences on occurrence, related it to ticks and minimized their problem by avoiding areas such as Lolo Canyon when "evil spirits" were present in the spring. When the Indians left the Bitterroot Valley and it was settled by white men about 1890, a disease termed "black measles" began to occur among them in the spring and summer. Some settlers recognized the relation to ticks and called it "Tick Fever." Others thought it was due to drinking melted snow water that had filtered through sawdust. Many physicians who lived in Montana, Idaho and Wyoming recalled the disease and there are accounts in army reports and other writings on "Mountain Fever," "Bull Fever" or other synonyms that go back into the mid-1880's, but generally the beginning of the published record is attributed to 1899.

The following chronological listing of milestones in the history of RMSF research traces the U.S. Public Health Service interest and involvement.

- 1887 -- Hygienic Laboratory established by Dr. Joseph Kinyoun for research on infectious diseases. Moved to Washington in 1891.
- 1899 -- Dr. Edward F. Maxey of Boise, Idaho, published the first clinical description and ascribed the disease to melted snow water.
- 1901 -- Montana State Board of Health created.
- 1902 -- Dr. A. F. Longway, Secretary of the Montana State Board of Health, arranged for Drs. L. A. Wilson and W. M. Chowning of the University of Minnesota to study RMSF in the Bitterroot area. They described limitation of disease to west side of river, identified the wood tick as the probable vector and the Columbian ground squirrel as the infected animal host for ticks. Reported clinical and pathological syndromes.

- 1902 -- McCullough published on 36 cases of RMSF in Bitterroot.
- 1902 -- USPHS Surgeon General Wyman sent Surgeon J. O. Cobb to Missoula to investigate newspaper accounts. Reported mostly on work of Wilson and Chowning.
- 1903 -- Dr. John F. Anderson, Assistant Director of Hygienic Laboratory, sent to Bitterroot at request of Montana Board of Health. Published 50-page pamphlet partially based on work of Wilson and Chowning. Probably coined the name RMSF. Sent ticks to hygienic laboratory for study where the taxonomic identification as Dermacentor andersoni was assigned.
- 1904 -- Dr. Charles W. Stiles, Chief, Division of Zoology of Hygienic Laboratory, sent to Bitterroot. Published detailed report in 1905 denying finding of a piroplasma in blood as described by Wilson and Chowning and was skeptical of the tick as a vector.
- 1905 -- McCalla and Bereton, Boise, Idaho, transmitted RMSF to two volunteers by tick bite with a tick removed from a patient with the disease. Published in 1908.
- 1906 -- Dr. W. V. Ricketts, the University of Chicago, attracted by the controversy created by Stiles report, came to Missoula. Had some financial support from American Medical Association and counties in Bitterroot. Dr. W. V. King was detailed to Montana by USPHS at same time and the two worked in close collaboration. Between 1906 and 1908, Ricketts and King were able to demonstrate conclusively the tick as a vector, the transmissibility from man to guinea pigs and monkeys, as well as between these animals, and to describe the organism in microscopic sections of infected tissue. Also evidence that a man is accidental victim and suggested that control might be obtained by reducing ticks on large animals through dipping and on small animals through extermination.
- 1909 -- King was joined by Clarence Birdseye and the pair made major contributions on ecology of the tick-host cycle.
- 1909 -- Montana Legislature appropriated \$6,000 to continue Ricketts' work. Funds not released until December by which time Ricketts had gone to Mexico to study typhus. He died there of this disease in 1910.
- 1911 -- Montana Bureau of Entomology, Bureau of Survey and the Agriculture Experiment Station began coordination of studies on control of RMSF by King, Birdseye, A. H. Howell, and M. H. Spaulding.
- 1911 -- Dr. Thomas B. McClintic sent by USPHS to start a tick control program by cattle dipping of livestock and exterminating gophers. Because Montana State Board of Health bypassed Dr. R. A. Cooley, Entomologist of Montana State University who had promoted the existing efforts, there was rivalry, duplication and animosity. This led to creation of Montana Board of Entomology in 1913.

- 1912 -- Dr. McClintic died of RMSF en route to Washington.
- 1914 -- Entomologist Dr. Ralph R. Parker left Massachusetts State College to head a fly control program in Laurel, Montana.
- 1916 -- Dr. Cooley set up tick laboratory in Powderville, Montana. Arranged for Dr. Parker to head laboratory and study RMSF.
- 1917 -- Dr. Parker reassigned by Montana Board of Entomology to Musselshell, Montana, to investigate outbreak of RMSF.
- 1917 - 1918 -- USPHS suspended support to RMSF research in Montana because of World War I and assignment of officers elsewhere.
- 1918 -- Dr. Parker moved the RMSF research laboratory to Victor in the Bitterroot Valley.
- 1919 -- Dr. S. B. Wolbach, who began investigations in 1916, published confirmation of Ricketts' observations on etiologic agent and established it as one of a new genus designated as *Rickettsiae* by Dr. Rocha Lima in 1916. Wolbach named it *Rickettsia rickettsii*.
- 1921 -- Dr. Thomas Parran (later Surgeon General) was sent to Montana at the demand of the U.S. Congress for USPHS to do something about RMSF after the death of a prominent Montana State legislator and his wife from the disease. As result, Dr. Parker was employed by USPHS and moved his laboratory into an abandoned schoolhouse in Hamilton (now owned by Dr. William Jellison, retired RML member. For several years, Dr. Jellison used it to display a number of artefacts of RMSF and RML that are now housed in a Montana Historical Society Museum at the Old County Court House in Hamilton.)
- 1922 -- Surgeon General Hugh Cumming sent Dr. Roscoe R. Spencer from the Hygienic Laboratory to join Dr. Parker for the summer. In response to rising public and political demand, began initial work on vaccine. William E. Gittinger, USPHS, and George H. Cowan, Montana Board of Entomology, died of RMSF acquired in studies.
- 1922 -- Wolbach published on cultivation of RMSF and typhus rickettsia in tissue cultures. These were explants of infected guinea pig tissues.
- 1923 -- Montana Board of Health held first conference on RMSF. Dr. Hideyo Noguchi of Rockefeller Institute described a putative vaccine. When tried on laborers it was soon abandoned because of serum sickness.
- 1924 -- Dr. F. Breinl of Czechoslovakia reported a typhus vaccine produced by phenol treatment of the gut of infected ticks.

- 1924 -- Dr. Spencer at Hygienic Laboratory used Breinl method to prepare RMSF vaccine that protected guinea pigs. In summer at Hamilton, he and Parker further perfected vaccine. Spencer took first dose and showed that his post vaccination serum could protect guinea pigs while his pre-vaccination could not. Parker and Cooley took vaccine.
- 1925 -- Laboratory produced two quarts of vaccine at estimated cost of \$20 per dose. Immunized 34 persons.
- 1926 -- Vaccination program in Bitterroot Valley and Idaho. Reports were that in Bitterroot, vaccine did not reduce number of cases but did reduce severity and mortality. In Idaho, where disease was milder, reduced number of cases. Annual immunization necessary.
- 1927 -- Increasing demand for vaccine led Montana Board of Entomology to request funds from legislature for a new building. State appropriated \$60,000.
- 1928 -- "Montana Research Laboratory" completed at Hamilton. Hamilton citizens demanded it be enclosed in moat to protect town from infected ticks or animals. USPHS leased the building from State. Laboratory produced 4,000 doses of vaccine. Dr. Spencer was recalled to Hygienic Laboratory, leaving Parker in charge. Arthur L. Kerlee, USPHS, died of RMSF.
- 1930 -- Ransdell Act creating the National Institute of Health signed by President Hoover. Engineered by the then Director of Scientific Research at the Hygienic Laboratory, Assistant Surgeon General Lewis R. (Jimmy) Thompson, the Act authorized new funds and buildings.
- Dr. Spencer appeared before Montana Board of Entomology stating that the Ransdell Act made it possible for the USPHS to enlarge the work on RMSF and take over the Laboratory. The Board, on the basis that several states were in need of vaccine and Montana should not have to bear all costs, adopted a resolution calling for the purchase of building by the U.S. Government and assumption of the work.
- 1931 -- U.S. Congress appropriated \$75,000 to purchase Laboratory and \$75,000 to build a new wing to increase vaccine production.
- 1932 -- The Federal Government paid the State of Montana \$68,757 and the Hamilton Laboratory became a field station of the National Institute of Health. Was renamed Rocky Mountain Research Laboratory. Additional building for vaccine manufacture begun.
- 1935 -- Bengston and Dyer published report on cultivation of RMSF rickettsia in developing chick embryo. This followed earlier reports by Goodpasture and others on use of technique for growth of viruses.

- 1936 -- Dr. Herald R. Cox employed by RML to find a simple method to produce vaccine. Perfected methods for use of embryonated chick egg and published on this in 1938. One bacteriologist and two technicians could now prepare 40 to 50 liters a week. Technique also useful in growing other rickettsiae for preparation of antigens and was used to produce an attenuated strain for possible vaccine use.
- 1937 -- RML became a part of the Division of Infectious Diseases, NIH.
- 1942 -- Cox further developed growth methods for vaccine production.
- 1942 - 1948 -- RML produced RMSF, typhus and yellow fever vaccines for use by the U.S. military forces. Additional buildings built to enable this effort.
- 1948 -- Former Division of Infectious Diseases of NIH became National Microbiological Institute (NMI), and the RML became a part of its intramural research program. NMI staff moved to RML were Dr. Carl L. Larson, who followed Dr. Parker as Director in 1949; and Drs. John F. Bell, Edgar E. Ribic, Samuel Salvin, William Hoyer, and Charles Sheperd (now at CDC).
- 1949 -- RML discontinued RMSF vaccine production.
- 1955 -- The name of the National Microbiological Institute became National Institute of Allergy and Infectious Diseases (NIAID). RML continued as a part of the intramural program.
- 1960 -- Dr. Cornelius B. Philip succeeded Dr. Larson as Acting Director, then Director, RML.
- 1964 -- Dr. Herbert G. Stoenner succeeded Dr. Philip as Director, RML.
- 1971 -- NIAID sponsored a conference on the status of rickettsial diseases research. Data presented showed a decline in man-years devoted to research in the Department of Health, Education, and Welfare and in the U.S. Government as a whole; the aging of competent investigators without new replacement being developed; the loss of commercially produced diagnostic reagents; and the still rising incidence of RMSF in the eastern U.S.
- 1973 -- AFEB Commission on Rickettsial Diseases terminated.
- 1973 -- DuPont et al. published a report on comparative efficacy of licensed vaccine in volunteers challenged with RMSF rickettsia that showed little or no protective ability. The study included a vaccine made from ticks.
- 1975 -- Kenyon and Pederson published on a chick embryo tissue culture prepared vaccine.