

BORRELIA

STRAINS, VECTORS, HUMAN AND
ANIMAL BORRELIOSIS

OSCAR FELSENFELD, M.Sc., M.D.

BORRELIA

STRAINS, VECTORS, HUMAN AND
ANIMAL BORRELIOSIS

By

OSCAR FELSENFELD, M.Sc., M.D.,

*Chief, Division of Communicable Diseases
Delta Regional Primate Research Center*

*Professor of Tropical Medicine and International Health
Tulane University School of Public Health and Tropical Medicine*

*Visiting Professor of Microbiology
Tulane University School of Medicine*

*Member, International Taxonomic
Subcommittee on Spirochaetales*



WARREN H. GREEN, INC.
St. Louis, Missouri, U.S.A.

DEDICATION

TO: Dr. M. Baltazard, Director Emeritus, Pasteur Institute, Teheran; Professor A. Rafyi, Director Emeritus, Hessarak Institute, Iran; Professor A. Geigy, Swiss Institute of Tropical Medicine, Basel; Dr. Charles M. Wheeler, Research Entomologist and the Memory of the late Professor E. Brumpt, Parasitology Institute, Paris whose patient instructions, friendly guidance, kind encouragement, competent support, and understanding criticism have made my studies of *Borrelia* possible and pleasurable during the past 35 years.

Published by

WARREN H. GREEN, INC.
10 South Brentwood Blvd.
St. Louis, Missouri 63105, U.S.A.

All rights reserved

© 2020 - LDP, with permission
© 1971, by WARREN H. GREEN, INC.

Library of Congress Catalog Card Number 72-127355

PREFACE

DESPITE PERIODIC REPORTS that tick-borne relapsing fever occurs sporadically over more than half the area of the entire Continental United States, the numerous deaths due to this disease in the drier parts of Asia and Africa including the thousands who become its victims in Ethiopia and the Sudan every year, the unknown toll in lives and suffering that the disease is still taking in Central and South America, and the ever-present danger of recurrence of epidemics should the louse-borne form burst out of its present confines if or when a disaster creates favorable conditions for such spread, only scanty notes on relapsing fever can be found in the medical literature of the United States today.

One is amazed at the confused nomenclature and the mass of misinformation concerning the transmission and vectors (some of which has managed to creep into even respectable textbooks). The considerable variations in the clinical picture during various outbreaks and in widely separated localities, and the unusual immunologic conditions that accompany the infection should be emphasized so that the medical profession can be alerted should an outbreak occur in this country.

The genus *Borrelia* that causes human relapsing fever includes some species that are of interest to the dentist (*Borrelia vincentii*), and to the veterinarian (*B. anserina*, *B. theileri*). *Borrelia* infections appear in man as relapsing fever and in animals as so-called fowl spirochetosis, or tick-transmitted spirochetosis in cattle, which are clinically defined entities. This monograph deals principally with human relapsing fever and fowl spirochetosis, while exploring other conditions in which borreliæ may play a role. The discussion of

the borreliae and their vectors, the pathology caused by them, and other features will be presented in separate chapters discussing borreliosis as human relapsing fever, cattle and fowl disease, and Vincent's angina, respectively. Each of these chapters will deal separately with the species of *Borrelia* involved, and with the consequences of the infection. Borreliae that have been isolated from vectors only, and not from man or animals, will also be enumerated.

O. F.

ACKNOWLEDGMENTS

THIS MONOGRAPH COULD NEVER HAVE GONE TO PRESS without the unselfish aid, help, and support of two persons. One of them, Dr. Addine G. Erskine, spent innumerable hours correcting, re-typing, editing, proof-reading, and indexing this volume. Busy as she was as Director of the Gradwohl School of Laboratory Technique and with numerous professional organizations, other editorial tasks, and ranching (unfortunately or fortunately, no *B. theileri* has been isolated from her stock), she has always found time to cooperate on my writing ventures, including this monograph. I am sincerely and deeply indebted to her for all her most valuable help.

The other, Dr. W. Burgdorfer, Senior Medical Entomologist of the U.S.P.H.S. Rocky Mountain Laboratories, has never hesitated to replenish my stock of *Ornithodoros* whenever my "tickorium" went out of gear. I am very much grateful to him for all support he has so kindly furnished during the years, in addition to admiring his elegant experiments and publications.

Dr. W. E. Greer, Director of Animal Resources, Gulf South Research Institute, New Iberia, La., kindly checked the chapters on animal borreliosis. Most of the entomological statements which appeared 5 years ago were reviewed by Prof. G. Anastos, University of Maryland, and Prof. A. Rafyi at that time.

I am much obligated and sincerely grateful to Dr. A. D. M. Bryceson and his colleagues for permitting me to read and to quote their outstanding clinical study of relapsing fever in Ethiopia before publication, and to Dr. H. Hoogstraal for his encouragement.

Dr. T. C. Orihel, Adj. Professor of Parasitology, Tulane University, spent much valuable time and great effort providing me

with and photographing arthropods for this book. His assistant, Mrs. B. van Duym, furnished several excellent drawings. Mrs. W. Martin of the Medical Illustration Service of this Center made additional valuable graphs. Dr. C. Jones, Smithsonian Institute, kindly selected and put at my disposal his photographs of Southeast African huts and rodent burrows. Dr. Jones also corrected and rectified the names of the mammals.

Dr. M. N. Wilderman, D.D.S., M.S., Professor and Head, Department of Periodontology, Louisiana University School of Dentistry, kindly furnished the photographs of Vincent's disease.

Mrs. M. LaCroix and Mrs. C. Bennett typed and retyped the numerous drafts as well as the final copy of the manuscript. Their diligence and help are appreciated greatly.

O. F.

	<i>Page</i>
<i>Dedication</i>	vi
<i>Preface</i>	vii
<i>Acknowledgments</i>	ix
<i>Chapter</i>	
I. HUMAN BORRELIOSIS (RELAPSING FEVER).....	3
History	5
Causative Agent.....	11
Borreliae and Their Vectors.....	30
Epidemiology	77
Pathology	91
Clinical Picture.....	98
II. BORRELIOSIS IN DOMESTIC ANIMALS.....	137
Borrelia Theileri.....	137
Other Borrelia.....	138
III. AVIAN BORRELIOSIS.....	139
Borrelia Anserina and Its Transmission.....	139
Pathology	141
Course of the Disease.....	141
Treatment and Prevention.....	142

Splenic rupture may cause death. More than 90% of pregnant women abort when infected with *Borrelia* (298, 552).

Herpes labialis is frequent, especially in louse-borne infections (503) but may occur also in tick-borne borreliosis with varying frequency (335, 476, 503).

Secondary infections of the respiratory tract are common. Salmonellosis is often a fatal secondary infection (17). Epidemic typhus fever presents a grave menace (734). Latent malaria and kala azar may be activated by relapsing fever (202).

Reinfection

Kudicke *et al.* (427) called attention to the role played by treatment in the development of resistance against reinfection. If the disease has terminated abruptly, before antibodies developed, reinfection with the same strain appears a distinct possibility. Reinfection, however, is rare in louse-borne epidemics if proper hygienic measures are enforced, principally delousing and prevention of reinfestation with ectoparasites. However, reinfection may occur in 2 months according to Simmons (647), in 1½ to 6 months according to Whitmore (731), and in one year according to Más de Ayala (476). In tick-borne infections in Central Asia, Kassirsky (398) observed a shorter period of immunity against reinfections but Grothusen (326) demonstrated that the disease caused by *B. duttonii* in Africans may be as severe as in Europeans who did not have an opportunity to acquire premunity during their childhood. Childhood infection is, however, of paramount importance for the response to a later infection according to other authors (263, 303, 443, 715, 732).

Apparently, recurrence *versus* reinfection should be re-evaluated also in relapsing fever (263).

Hereditary immunity is a moot question. Nohira (546) demonstrated in rats that the offspring of the female infected with *B. recurrentis* is immune to the homologous strain for about 2 months. Women with relapsing fever usually abort and few data are available about infants delivered at term, except in studies of congenital transmission. Such instances were described in the United States (183, 283, 505); by Garnham (1936), Caldwell (1936), Kröber (1936) and Correa *et al.* (1964) in Africa (139, 203, 292, 424); and in other areas (176). Further studies of transplacental anti-

body transmission are most desirable, principally in regard to the recent concept of immunoglobulins of which only the small-sized IgG appears to be transmitted to the newborn.

Prognosis and Mortality

Sterling-Okunewski (669) demonstrated that the number of borreliae in the peripheral circulation has no bearing on the severity of the disease or on the prognosis of relapsing fever.

Mayer (482) considered continuous high fever, deep jaundice, extensive hemorrhages, and coma as bad prognostic signs. León and León (443) added to this list endocarditis and myocarditis. Bryceson *et al.* (127) called attention also to persistent Q-Tc interval changes in the ECG, disseminated intravascular coagulation, hepatic failure, cerebral edema, and shock as serious prognostic signs. Pneumonia was cause for a bad prognosis in China (176).

The disease frequently has a severe course in infants.

The case fatality rate in louse-borne relapsing fever depends on the nature of the epidemic and on the availability of treatment. The average mortality in Europe was 4 to 5%; however, in China, Indochina, and India before World War II it fluctuated between 25 and 80%, especially in untreated individuals (495, 731). The small but severe outbreaks in Darjeeling (392) and Assam (152) produced many fatalities, while in Iran few treated patients died (337). On the other hand, in Peru, in spite of the lack of intensive medical care, the case mortality rate was below 2% (164).

During World War II when arsenicals were routinely used, only 0.25% of the treated patients failed to recover, whereas in China about 40% of untreated patients died (163). In Abadan, where good medical care was available, the mortality rate was 1.1% (87). Wide variations, from 1 to 46%, were observed in Tunis, varying according to the locality and the available treatment (323).

In the epidemic following World War II, the case fatality rate was 5 to 10% in untreated individuals, 8.5% in the poor, and 3.6% in the well-to-do (298). The mortality rate among children reached 65% in some areas.

Manson and Thornton (467) calculated a case fatality rate of 0.3% in East Africa, and 4% in West Africa. Garnham *et al.* (296) encountered a 40% mortality among the untreated. Geigy (303) reported 0.7 to 70% deaths.

always a possibility (253). Proteinuria was noted (74) practically in all instances early in the disease; Pifano (573) observed it during the later course of the disease. Urinary findings resembling those of nephrosis have been recorded (176, 298, 469).

There is fluid loss (464) due to sweating and fast breathing. Blood urea nitrogen is increased. Plasma Na and K are increased but not constantly; Cl is often low in borreliosis in Abyssinia according to Bryceson *et al.* (127). These authors also noted an increase in gamma globulin, possibly changes in beta globulin, and a decrease of alpha globulins and albumin in some sera.

The "neurotropism" of borreliæ has been a constantly recurring puzzle. It may be strain-specific because reports on species-specificity list too many exceptions. The infection of the C.N.S. may be latent (133). Garnham *et al.* (296) found, in louse-borne relapsing fever of Kenya, degeneration of the ganglion cells of the cerebellum without meningovascular changes but stated that glia cell reactions may be extensive. *B. recurrentis* may remain in the C.S.F. for 65 to 69 days (582, 583). Borreliæ were found in the C.S.F., in the brain, as well as in brain tumors, in East Africa (590). Increased globulin was observed in the C.S.F. (175). Lodewyckx (454) noted lymphocytosis in the spinal fluid principally in *B. duttonii* infections. The clinical picture appears to be dominated by the consequences of the hemodynamic changes in the C.N.S., their localization, and extent.

The heart may show endocarditis (607). Other authors (17, 391) have emphasized myocardial changes seen at autopsy. Hemorrhages of various size may be found in practically every organ.

Borreliæ in the skin and the histology of the hemorrhages were studied by Taft and Pike (674) who found the organisms in the skin also between attacks, and by Judge and Perine (391) who investigated biopsy specimens.

Abortion is very frequent. About 92% of pregnant women lose their children when they contract relapsing fever (552).

It is expected that the variations of the borreliæ, their particular predilection for certain localizations, the uncommon immunologic responses, together with the hemodynamic changes analyzed by Parry *et al.* (562) may assist in understanding the motley and protean clinical course of relapsing fever.

CLINICAL PICTURE

Attempts have been made to demonstrate a common denominator or to establish differential diagnostic criteria between louse-borne and tick-borne relapsing fever. Since we are confronted with one or more agents of varied pathogenicity and organotropy, with changes in the course of the illness according to epidemics and localities as well as with sick people but not diseases *per se*, this task is rather difficult if not impossible.

Clinical Course

The clinical course of relapsing fever has been described by several authors, such as Calwell (139), Selwyn-Clarke *et al.* (636), Robertson (606), Robinson (608), Davidson (215), Banwell and Kibukamusoka (67), Whitmore (731, 732), Bryceson *et al.* (127), and others to whom frequent reference will be made in this chapter.

Generally speaking, the course of human relapsing fever consists of an incubation period, the first attack, and, at intervals, of relapses. The typical "relapse course" is not always followed. There may be an irregular temperature curve (149, 345) or only one febrile attack (657). The severity of the disease often depends on circumstances which deserve further discussion even though the currently used classification (443) into severe, mild, ambulant, latent, and atypical forms, is of considerable use for recording.

Severity of the Disease

Tick-borne relapsing fever is usually more severe and more prolonged than the louse-borne type (149). There is an amazing variability, however, from outbreak to outbreak, as well as from one area to another. Individual susceptibility and residual immunity also may be important. While, for instance, in North and in East Africa *Borrelia* infections are severe in Europeans and mild in the local population (467, 642), in West Africa relapsing fever is equally severe in both Europeans and Africans. Variations in the severity of the disease according to geography are also interesting. Louse-borne relapsing fever was very severe in 1912 in Indochina (495) and in Gurkha laborers in Darjeeling (392), but it was very mild in Turkey and Egypt (139). Tick-borne infections have been de-

280. Fränkel, L. (1912) *Virchow's Arch.Pathol.Anat.Physiol.*, 18:97.
281. Friedemann, V. (1942) *Physiol.Rev.*, 22:125.
282. Fry, A. G. (1920) *Indian Med.Gaz.*, 55:2.
283. Fuchs, P. C., and Oyama, A. A. (1969) *J.Amer.Med.Assoc.*, 208:690.
284. Fülleborn, F., and Mayer, M. (1908) *Arch.Schiff.Trop.Hyg.*, 12:31.
285. Fulton, J. D., and Smith, P. C. (1960) *Biochem.J.*, 76:491.
286. Gaillard, H., Lapière, J., and Coste, M. (1963) *Ann.Parasit.Hum.Compar.*, 38:1.
287. Gaillard, H., Lapière, J., and Rousset, J. J. (1960) *Pathol.Biol.*, 8:77.
288. Galloway, I. A. (1925) *C.R.Soc.Biol.*, 97:1074.
289. Galun, R., Warburg, M., and Avidi, A. (1967) *Entomol.Exp.Appl.*, 10:143.
290. Galouzo, I. G. (1957) *Argasid Ticks. Acad.Sci.Kazakh SSR, Alma-Ata,Translat. USNMUR #3.*
291. Gambles, R. M., and Coghill, N. F. (1948) *Ann.Trop.Med.Parasit.*, 42:288.
292. Garnham, P. C. C. (1936) *East Afr.Med.J.*, 13:50.
293. Garnham, P. C. C. (1947) *East Afr.Med.J.*, 24:47.
294. Garnham, P. C. C. (1950) *Parasitol.*, 40:328.
295. Garnham, P. C. C. (1958) *J.Trop.Med.Hyg.*, 61:92.
296. Garnham, P. C. C., Davies, C. W., Heisch, R. B., and Timms, G. L. (1947) *Trans. Roy.Soc.Trop.Med.Hyg.*, 41:141.
297. Gaud, M., Khalil, M. Bey, and Vaucel, M. (1947/1948) *Bull.Wld.Hlth.Org.*, 1:93.
298. Gaud, M., and Morgan, M. T. (1947/1948) *Bull.Wld.Hlth.Org.*, 1:69.
299. Gefel, A., and Rubenow, R. (1953) *Harefuah*, 44:263.
300. Geigy, R. (1951) *Atti 3o Congr.Intern.Ig.Med.Mediter,Palermo*, 56.
301. Geigy, R. (1953a) *Rev.Suisse Zool.*, 60:438.
302. Geigy, R. (1953b) *Schweiz.Ztschr.Pathol.Bakt.*, 16:821.
303. Geigy, R. (1968) *In: Infectious Diseases of Man and Animals*, 2:175.
304. Geigy, R., and Aeschlimann, A. (1957) *Ztschr.Tropenmed.Parasit.*, 8:96.
305. Geigy, R., and Aeschlimann, A. (1965) *Rev.Suisse Zool.*, 72:87.
306. Geigy, R., and Burgdorfer, W. (1949) *Rev.Suisse Zool.*, 56:334.
307. Geigy, R., and Burgdorfer, W. (1951) *Acta Trop.*, 8:151.
308. Geigy, R., and Herbig, A. (1955) *Erreger und Überträger Tropischer Krankheiten. Verlag für Recht und Gesellschaft, Basel. Acta Trop. Suppl. 6.*
309. Geigy, R., and Mooser, H. (1955) *J.Trop.Med.Hyg.*, 58:199.
310. Geigy, R., and Sarasin, G. (1960) *Pathol.Microbiol.*, 24:93.
311. Geigy, R., and Sarasin, G. (1961a) *Acta Trop.*, 18:359.
312. Geigy, R., and Sarasin, G. (1961b) *Pathol.Mikrobiol.*, 24 (Suppl.):93.
313. Geigy, R., Wagner, O., and Aeschlimann, A. (1954) *Acta Trop.*, 11:81.
314. Geiman, Q. M. (1952) *Ann.Rev.Microbiol.*, 6:299.
315. Gelman, A. C. (1961) *In: May, J. M. (Editor) Studies in Disease Ecology: Haffner Publ.Co., New York.*
316. Gill, C. A. (1922) *Indian J.Med.Res.*, 9:747.
317. Gimeno de Sande, A. (1954) *Rev.Sanid.Hig.Públ.*, 28:342.
318. Ginger, C. D. (1963) *Nature*, 199:159.
319. Goldberg, H. J. (1966) *J.Oral Ther.*, 2:451.
320. Gönner, R., and Mudrow-Reichenaw, L. (1956) *Ztschr.Tropenmed.Parasit.*, 7:369.
321. Graham, M. (1931) *Texas State J.Med.*, 27:226.
322. Gray, J. D. A. (1929) *Ann.Trop.Med.Parasit.*, 23:241.
323. Greaves, F. C., Gezon, H. M., and Alston, W. F. (1945) *U.S.Naval Med.Bull.*, 45:1029.
324. Greiner, J. (1921) *Bull.Soc.Pathol.Exot.*, 14:144.
325. Gross, W. M., and Ball, M. R. (1964) *Amer.J.Veter.Res.*, 25:1734.
326. Grothausen, J. (1920) *Arch.Schiff.Tropenhyg.*, 24:50.
327. Grün, H. (1950) *Ztschr.Hyg.Infektkr.*, 131:198.
328. Guggenheim, K., Buechler-Czaczkes, E., and Halevi, S. (1951) *J.infect.Dis.*, 89:105.
329. Guggenheim, K., and Halevi, S. (1952) *J.infect.Dis.*, 90:190.
330. Guzzon, V., and Ercoli, N. (1951) *Boll.Ist.Seroterap.Milano*, 30:543.
331. Haberkorn, A. (1963) *Ztschr.Tropenmed.Parasit.*, 14:209.
332. Haddad, C., Sheiban, A., and Budeir, R. (1946) *J.Palestine Arab Med.Assoc.*, 2:8.
333. Halawani, A. (1946) *J.Egypt.Publ.Hlth.Assoc.*, 21:183.
334. Hnllauer, C., and Kuhn, H. (1940) *Ztschr.Hyg.Infektkr.*, 222:406.
335. Hamilton, J. B. (1943) *Brit.J.Ophthalm.*, 27:68.
336. Hanson, A. W., and Cannefax, G. R. (1964) *J.Bact.*, 88:813.
337. Harold, C. T. H. (1922) *J.Roy.ArmyMed.Corps*, 38:398.
338. Hawkins, F. (1941) *J.Trop.Med.Hyg.*, 44:104.
339. Heilman, F. R. (1948) *Proc.Staff Meet.Mayo Clin.*, 23:569.
340. Heisch, R. B. (1947) *East Afr.Med.J.*, 24:3.
341. Heisch, R. B. (1949) *Brit.Med.J.*, 1:17.
342. Heisch, R. B. (1950a) *Ann.Trop.Med.Parasit.*, 44:260.
343. Heisch, R. B. (1950b) *East Afr.Med.J.*, 27:1.
344. Heisch, R. B. (1952) *East Afr.Med.J.*, 29:327.
345. Heisch, R. B. (1953) *Parasitol.*, 43:133.
346. Heisch, R. B. (1955a) *Trans.Roy.Soc.Trop.Med.Hyg.*, 49:92.
347. Heisch, R. B. (1955b) *Bull.Soc.Pathol.Exot.*, 48:322.
348. Heisch, R. B., Chamsa, M., Seydian, B., and Harvey, A. E. C. (1957) *Bull.Soc. Pathol.Exot.*, 50:735.
349. Heisch, R. B., and Garnham, P. C. C. (1948) *Parasitol.*, 38:247.
350. Heisch, R. B., and Grainiger, W. E. (1950) *Ann.Trop.Med.Parasit.*, 44:153.
351. Heisch, R. B., and Harvey, A. E. C. (1952) *East Afr.Med.J.*, 29:25.
352. Heisch, R. B., and Harvey, A. E. C. (1953) *Trans.Roy.Soc.Trop.Med.Hyg.*, 47:239.
353. Heisch, R. B., and Harvey, A. E. C. (1962a) *Parasitol.*, 52:77.
354. Heisch, R. B., and Harvey, A. E. C. (1962b) *East Afr. Med.J.*, 39:609.
355. Heisch, R. B., Sparrow, H., and Harvey, A. E. C. (1960) *Bull.Soc.Pathol.Exot.*, 53:140.
356. Hemingway, W. F., Hemingway, R. W., and Arneson, V. K. (1940) *Northwest Med.*, 39:362.
357. Hermant, D. (1912) *Bull.Soc.Méd.Chir. Indochine*, 3:418.
358. Herms, W. B., and Wheeler, C. M. (1936) *J.Parasit.*, 22:276.
359. Himmelweit, F. (1933) *Ztschr.Hyg.Infektkr.*, 115:710.
360. Hindemarsch, W. L. (1937) *New South Wales Dept.Agric.Veter.Res.Repts.*, 7:69.
361. Hindle, E. (1911) *Parasitol.*, 4:183.
362. Hindle, E. (1912) *Proc.Cambridge Philos.Soc.*, 16 (part 6):457.
363. Hindle, E. (1931a) *In: A System of Bacteriology in Relation to Medicine. Med.Res. Council.H.M.Stat.Off.London*, 8:101.
364. Hindle, E. (1931b) *In: A System of Bacteriology in Relation to Medicine. Med.Res. Council.H.M.Stat.Off.London*, 8:147.
365. Hindle, E. (1935) *Trop.Dis.Bull.*, 32:309.
366. Hirschboeck, M. M. (1954) *Amer.J.Trop.Med.Hyg.*, 3:712.
367. Hjelle, A. (1966) *Nature*, 212:856.
368. Hoffman, H. A., and Jackson, T. A. (1946) *J.Amer.Veter.Assoc.*, 109:481.
369. Hoffman, H. A., Jackson, T. A., and Rucker, J. C. (1946) *J.Amer.Veter.Assoc.*, 108:329.
370. Holmes, J. W. E. (1953) *J.Roy.Sanit.Inst.*, 73:262.
371. Hoogstraal, H. (1956) *African Ixoida. I. Ticks of the Sudan. U.S.NavyDept.Res. Rept.No.NM005050.20.07. Washington, D.C.*
372. Horrenberger, R. (1954) *Arch.Inst.Pasteur Algérie*, 32:18.
373. Horrenberger, R. (1955) *Arch.Inst.Pasteur Algérie*, 33:258.
374. Horsfall, W. R. (1962) *Medical Entomology. Ronald Press Co., New York.*
375. Huang, V. D. (1960) *Zool.Zh.*, 39:595.
376. Hungerford, T. G., and Hart, L. (1938) *Agric.Gaz.New South Wales*, 48:591.
377. Hunter, W. (1919) *Proc.Roy.Soc.Med.*, 13:129.

475. Maruashvili, G. M. (1945) *Med.Parazit.Parazit.Bolez.*, 14:24.
476. Más de Ayala, I. (1931) *Méd.Paises Cálidos*, 4:369.
477. Mathew, W. J. Jr., and Siddie, P. J. (1955) *J.Amer.Veter.Med.Assoc.*, 86:122.
478. Mathis, C. (1931) *Bull.Acad.Méd.Paris*, 106:188.
479. Mathis, C., and Durieux, C. (1931) *Bull.Soc.Pathol.Exot.*, 24:150.
480. Mathis, C., Durieux, C., and Advier, M. (1933) *Bull.Soc.Pathol.Exot.*, 26:1094.
481. Mathis, C., and Durieux, C. (1934) *Bull.Acad.Méd.Paris*, 111:528.
482. Mayer, A. (1922) *Ztschr.Klin.Med.*, 90:141.
483. Mazzotti, L. (1942a) *Rev.Inst.Salubr.Enferm.Trop.*, 3:213.
484. Mazzotti, L. (1942b) *Rev.Inst.Salubr.Enferm.Trop.*, 3:297.
485. Mazzotti, L. (1943) *Amer.J.Hyg.*, 38:203.
486. McKee, R. W., and Geiman, Q. M. (1950) *Feder.Proc.*, 9:201.
487. McKercher, D. G. (1950) *J.Bact.*, 59:446.
488. McNeil, E., Hinshaw, W. R., and Kissling, R. E. (1948) *J.Bact.*, 57:191.
489. Meador, C. N. (1915) *Colorado Med.*, 72:365.
490. Meleney, H. E. (1928) *J.Exp.Med.*, 48:65.
491. Merliis, R. (1952) *Med.Arts Sci.*, 6:44.
492. Mersekey, C. (1947) *Clin.Proc.Cape Town*, 6:113.
493. Meyer, P. A., and Hunter, E. F. (1967) *J.Bact.*, 39:784.
494. Miller, P. B. M. (1874/1875) *Pacific Med.Surg.J.*, 17:370.
495. Millous, J. (1913) *Bull.Soc.Méd.Chir.Indochine*, 4:14.
496. Mishchenko, N. K. (1960) *Zool.Zh.*, 39:424.
497. Moise, R. M. R. (1938) *Ann.Med.Naval Colon.*, 44:315.
498. Mölbert, E. (1956) *Ztschr.Hyg.Infektrk.*, 142:203.
499. Mooser, H. (1958a) *Ztschr.Tropenmed.Parasit.*, 9:93.
500. Mooser, H. (1958b) *Ergebn.Mikrobiol.*, 31:184.
501. Mooser, H. (1963) *Acta Trop.*, 20:369.
502. Mooser, H., and Weyer, F. (1954) *Ztschr.Tropenmed.Parasit.*, 5:28.
503. Moreno Berdugo, J., and Infante Gómez, A. (1945) *Med.Colon.*, 6:336.
504. Moroder, J. (1929) *Arch.Schiff.Trop.Hyg.*, 33:603.
505. Morrison, S. K., and Parsons, L. (1941) *J.Amer.Med.Assoc.*, 116:220.
506. Moskwin, I. A. (1929) *Ztschr.Parasit.*, 2:73.
507. Moursund, W. H. (1942) *Amer.Assoc.Adv.Sci.Symposium No. 18*, 1.
508. Mouzels, P., and Xuang Mai, N. (1912) *Bull.Sci.Méd.Chir.Indochine*, 3:427.
509. Mühlens, P. (1933) *Chinese Med.J.*, 47:1384.
510. Muñoz Cosin, F. (1953) *Med.Colon.*, 22:457.
511. Muñoz Cosin, F. (1960) *Med.Trop.*, 35:173.
512. Murrell, T. W. (1939) *Arch.Dermatol.Syphil.*, 39:667.
513. Nagano, L. (1941) *Tokyo Igakai Zasshi*, 3:21.
514. Nájera Angulo, L. (1943) *Bol.Réal Soc.Españ.Hist.Natur.*, 41:527.
515. Nájera Angulo, L. (1945) *Bol.Réal Soc.Españ.Hist.Natur.*, 43:217.
516. Narain, S., and Kalra, S. L. (1950) *Indian Med.Gaz.*, 85:87.
517. Néel, R., Payet, M., and Gonnet, C. (1949) *Bull.Soc.Pathol.Exot.*, 42:384.
518. Nevin, T. A., and Guest, W. J. (1967) *J.Bact.*, 94:1388.
519. Newcomb, C. (1920) *Indian Med.Gaz.*, 55:208.
520. Nicolle, C., and Anderson, C. (1926) *Arch.Inst.Pasteur Tunis*, 15:197.
521. Nicolle, C., and Anderson, C. (1927a) *Bull.Inst.Pasteur*, 25:657.
522. Nicolle, C., and Anderson, C. (1927b) *Arch.Inst.Pasteur Tunis*, 16:123.
523. Nicolle, C., and Anderson, C. (1929a) *C.R.Acad.Sci.*, 189:817.
524. Nicolle, C., and Anderson, C. (1929b) *Acta Med.Scandin.*, 70:392.
525. Nicolle, C., and Anderson, C. (1929c) *Arch.Inst.Pasteur Tunis*, 18:268.
526. Nicolle, C., and Anderson, C. (1930) *Arch.Inst.Pasteur Tunis*, 19:469.
527. Nicolle, C., and Anderson, C. (1932) *C.R.Acad.Sci.*, 194:333.
528. Nicolle, C., Anderson, C., and Colas-Belcours, J. (1929) *C.R.Acad.Sci.*, 189:224.
529. Nicolle, C., Anderson, C., and Colas-Belcours, J. (1930) *Arch.Inst.Pasteur Tunis*, 19:133.

530. Nicolle, C., Anderson, C., and Hornus, P. (1929) *C.R.Acad.Sci.*, 188:1211.
531. Nicolle, C., and Blaizot, L. (1912a) *Bull.Soc.Pathol.Exot.*, 5:472.
532. Nicolle, C., and Blaizot, L. (1912b) *Arch.Inst.Pasteur Tunis*, 1:201.
533. Nicolle, C., and Blaizot, L. (1913) *Bull.Soc.Pathol.Exot.*, 6:107.
534. Nicolle, C., Blaizot, L., and Conseil, E. (1912a) *C.R.Acad.Sci.*, 154:1636.
535. Nicolle, C., Blaizot, L., and Conseil, E. (1912b) *C.R.Acad.Sci.*, 155:481.
536. Nicolle, C., Blaizot, L., Conseil, E. (1913) *Bull.Soc.Path.Exot.*, 6:106.
537. Nicolle, C., and Lebrailly, C. (1919) *C.R.Acad.Sci.*, 169:934.
538. Nicolle, C., and Lebrailly, C. (1920) *Arch.Inst.Pasteur Tunis*, 11:131.
539. Nieschulz, O. v., and Bos, A. (1940) *Zbl.Bakt.Abt.I.Orig.*, 145:258.
540. Nikitina, R. E. (1965a) *Sbor.Trud.Vsech.Nauch.Bolez.Pilis*, 1:164.
541. Nikitina, R. E. (1965b) *Zool.Zh.*, 44:294.
542. Nixon, A. (1921) *Lancet*, i:432.
543. Noble, R. E., and Noble, C. A. (1964) *Parasitology*, 2nd ed. Lea and Febiger, Philadelphia, Pennsylvania.
544. Noguchi, H. (1912a) *J.Exp.Med.*, 16:199.
545. Noguchi, H. (1912b) *Münch.Med.Woch.*, 59:1937.
546. Nohira, A. (1929) *Japan.Med.World*, 9:83.
547. Novy, F. G., and Knapp, R. E. (1906) *J.infect.Dis.*, 3:291.
548. Nuttall, G. H. F. (1913) *Parasitol.*, 5:262.
549. Oag, R. K. (1939) *J.Pathol.Bact.*, 49:339.
550. Oag, R. K. (1940) *J.Pathol.Bact.*, 51:127.
551. Oettinger, J., and Halbreich, J. (1922) *Münch.Med.Woch.*, 69:778.
552. Omar, M. E. S. (1946) *J.Egypt.Publ.Hlth.Assoc.*, 21:195.
553. Ombati, D. G., and Ojiambo, H. P. (1968) *East Afr.Med.J.*, 45:630.
554. Omori, N. (1939) *Taiwan Igakai Zasshi*, 38:899.
555. Ordman, D. (1939) *South Afr.Med.J.*, 13:491.
556. Ordman, D. (1955) *South Afr.Med.J.*, 29:518.
557. Ordman, D., and Jones, F. R. (1940) *South Afr.Med.J.*, 14:81.
558. Osorno Mesa, S. (1942) *Rev.Fac.Nac.Agronom.Medellin*, 16/17:1.
559. Packchianian, A. H. (1950) *Texas Repts.Biol.Med.*, 8:78.
560. Palmer, J. H., and Crawford, D. J. M. (1933) *J.Canadian Med.Assoc.*, 28:643.
561. Pampana, E. J. (1931) *Arch.Ital.Sci.Med.Colon.*, 12:257.
562. Parry, E. H. O., Bryceson, A. D. M., and Leihed, C. S. (1967) *Lancet*, i:81.
563. Pavlovskii, E. N. (1932) *Trudy Soviet.Izuch.Proizvod.Turkmenia*, 2:79.
564. Pavlovskii, E. N. (1939) *Prob.Region.Parasitol.*, 3:19.
565. Pavlovskii, E. N. (1943) *C.R.Acad.Sci.U.S.S.R.*, 39:286.
566. Pavlovskii, E. N. (1945) *Med.Parasit.Parasit.Bolez.*, 14:56.
567. Pavlovskii, E. N., and Kuzima, L. A. (1945) *Med.Parazit.Parazit.Bolez.*, 14:66.
568. Pavlovskii, E. N., and Skrynnik, A. N. (1945) *Zool.Zh.*, 24:161.
569. Pavlovskii, E. N., and Skrynnik, A. N. (1951) *Dokl.Akad.Nauk U.S.S.R.*, 78:1069.
570. Petrilla, A., and Rudnay, O. (1949) *Népegészségügy*, 30:439.
571. Petrishcheva, P. A. (1961) *Med.Parazit.Parazit.Bolez.*, 30:439.
572. Pfister, R. (1949) *Bull.Soc.Pathol.Exot.*, 42:547.
573. Pifano, F. (1941) *Rev. Sanid.Asist.Soc.Caracas*, 6:787.
574. Pillot, J. (1966) *Biol.Med.(Paris)*, 55:343.
575. Pillot, J., Dupouey, P., and Ryter, A. (1954) *Ann.Inst.Pasteur*, 107:489 and 663.
576. Pillot, J., and Ryter, A. (1965) *Ann.Inst.Pasteur*, 108:791.
577. Pino-Pou, R. (1921) *Gac.Méd.Caracas*, 28:111.
578. Pinto, M. R. (1945) *Arq.Inst.Bacteriol. Camera Pestana*, 9:224.
579. Pirot, R., and Bourgain, M. (1945a) *Bull.Soc.Pathol.Exot.*, 38:12.
580. Pirot, R., and Bourgain, M. (1945b) *Bull.Soc.Pathol.Exot.*, 38:88.
581. Pirot, R., and Bourgain, M. (1945a) *Bull.Soc.Pathol.Exot.*, 38:90.
582. Plaut, F., and Steiner, G. (1920a) *Arch.Schiff.Trop.Hyg.*, 24:33.
583. Plaut, F., and Steiner, G. (1920b) *Deutsch.Med.Woch.*, 46:1101.
584. Popow, P. P., and Achundow, I. A. (1936) *Arch.Schiff.Trop.Hyg.*, 40:289.

585. Popow, P. P., and Achundow, I. A. (1940) *Med.Parazit.Parazit.Bolez.*, 9:255.
586. Pospelova-Shtrom, M. V. (1940) *Med.Parazit.Parazit.Bolez.*, 9:618.
587. Pospelova-Shtrom, M. V. (1968) *Proc.8th Internat.Congr.Trop.Med.Malar.*, 888.
588. Prado, E. del (1919) *Crónica Méd.Lima*, 36:408.
589. Prado, E. del (1920) *Ann.Fac.Méd.Lima*, 3:26 and 134.
590. Quinn, C. E., and Perkins, E. S. (1946) *J.Trop.Med.Hyg.*, 49:30.
591. Rafiyi, A. (1946a) *Arch.Inst.Hessarek*, 2:37.
592. Rafiyi, A. (1946b) *Arch.Inst.Hessarek*, 4:49 and *Sem. Hôp.Paris*, 23:76.
593. Rafiyi, A., Felsenfeld, O., Dupont, J. R., and Maghami, G. (1965) *Ann.Parasit.Hum. Compar.*, 40:631.
594. Rafiyi, A., and Maghami, G. R. (1949) *Bull.Soc.Pathol.Exot.*, 42:215.
595. Rahaman, A. H. (1946) *J.Egypt.Publ.Hlth.Assoc.*, 21:125.
596. Ranque, J. (1963) *Transfusion (Paris)*, 6:163.
597. Ranque, J. (1968) *Méd.Trop.(Marseille)*, 27:519.
598. Ranque, J., Depieds, R., and Fauré, A. (1957) *Bull.Soc.Pathol.Exot.*, 50:360.
599. Ranque, J., Quilici, M., and Assadourian, Y. (1968) *Proc.8th Internat.Congr.Trop. Med.Malar.*, 2:893.
600. Rao, K. N. A., and Kalra, S. L. (1949) *Indian J.Med.Res.*, 37:385.
601. Reddy, V. M., Ramachandran, P. K., and Ramachandran, S. (1966) *Indian J.Veter. Sci.Anim.Husb.*, 36:1.
602. Remlinger, P., and Bailly, J. (1929) *C.R.Soc.Biol.*, 102:741.
603. Riding, D., and McDowell, T. W. (1927) *Trans.Roy.Soc.Trop.Med.Hyg.*, 20:524.
604. Roaf, H. E. (1922) *Brit.J.Exp.Pathol.*, 3:59.
605. Robertson, A. (1935) *J.Trop.Med.Hyg.*, 38:237.
606. Robertson, R. C. (1932) *Chinese Med.J.*, 20:524.
607. Robinson, P. (1942) *Brit.Med.J.*, ii:216.
608. Robinson, S. P. (1943) *Ann.Trop.Med.Parasit.*, 37:38.
609. Rodhain, J., and Bergh, L. van den (1943) *Ann.Soc.Belge Méd.Trop.*, 23:141.
610. Rodino, N. (1922) *Giorn.Med.Milit.*, 70:90.
611. Rosenholz, H. P. (1927) *Cbl.Bact.Abt.I.Orig.*, 102:179.
612. Ross, P. H. (1912) *Nairobi Lab.Publ.Hlth.Repts.*, 2(part 2):6.
613. Ross, P. H., and Milne, A. D. (1904) *Brit.Med.J.*, ii:1453.
614. Roy, S. C. (1920) *Indian Med.Gaz.*, 56:320.
615. Rubinstein, P. L., and Kapusto, M. L. (1931) *Ztschr.Immunforsch.Exp.Ther.*, 72:309.
617. Russell, H. (1932) *Trans.Roy.Soc.Trop.Med.Hyg.*, 26:259.
618. Russell, H. (1933) *West Afr.Med.J.*, 6:36.
619. Russell, H. (1936) *Trans.Roy.Soc.Trop.Med.Hyg.*, 30:179.
620. Sabalette, R., Dominguez, M., and Iglesias, R. (1947) *Med.Colon.(Madrid)*, 9:207.
621. Saglam, T. (1947) *Türk Tip Cemiyeti Mekmuası*, 13:36.
622. Sarasin, G. (1959) *Acta Trop.*, 16:218.
623. Saurinov, V. R., and Delamater, E. D. (1952) *Am.J.Syph.*, 36:352.
624. Sautet, J. (1937) *Marseille Méd.*, 74:273.
625. Sautet, J. (1941) *Arch.Inst.Pasteur Algérie*, 19:240.
626. Scheff, G. (1935) *Zbl.Bakt.Parasit.Abt.I.Orig.*, 134:35.
627. Scheff, G. J., and Kutner, F. R. (1959) *Experientia*, 15:342.
628. Schilling, V. (1921) *Beihft.Arch.Schiff.Trop.Hyg.*, 25:5.
629. Schofield, T. P. C., Talbot, J. M., Bryceson, A. D. M., and Parry, E. H. O. (1968) *Lancet* ii:58.
630. Schuhardt, V. T. (1942) *Amer.Assoc.Adv.Sci.Symposium No. 18*, 58.
631. Schuhardt, V. T. (1952) *Ann.New York Acad.Sci.*, 55:1209.
632. Schuhardt, V. T., and Wilkerson, M. (1951) *J.Bact.*, 62:215.
633. Schwetz, J. (1943) *Ann.Soc.Belge Méd.Trop.*, 23:219.
634. Scott, H. H. (1942) *A History of Tropical Medicine*, 2:781. The Williams and Wilkins Co., Baltimore, Maryland.
635. Scott, R. B. (1944) *Lancet*, ii:436.

636. Selwyn-Clarge, P. S., LeFam, G. H., and Ingram, A. (1923) *Ann.Trop.Med.Parasit.*, 17:389.
637. Sergeant, A. (1933) *C.R.Acad.Sci.*, 197:717.
638. Sergeant, A. (1936) *C.R.Soc.Biol.*, 14:1520.
639. Sergeant, A. (1938) *Arch.Inst.Pasteur*, 61:217.
640. Sergeant, E. (1945) *Ann.Inst.Pasteur Algerie*, 23:245.
- 640a. Sergeant, E. (1957) *Ztschr.Tropenmed.Parasit.*, 3:242.
641. Sergeant, E., and Foley, H. (1908) *Bull.Soc.Pathol.Exot.*, 1:174.
642. Sergeant, E., and Foley, H. (1921) *Bull.Soc.Pathol.Exot.*, 14:632.
643. Sergeant, E., and Poncet, A. (1961) *Arch.Inst.Pasteur Algerie*, 39:109.
644. Serstnev, E. (1953) *Higijena*, 5:106.
645. Shrimpton, E. A. G. (1936) *Chinese Med.J.Suppl.I*, 312.
646. Sibilia, D. (1937) *Policlinico*, 44:722.
647. Simmons, J. S. (1955) *In: Cecil, R. L.: Textbook of Medicine*, 9th ed. Saunders & Co., New York.
648. Simons, H. (1939) *Ann.Parasitol.Hum.Compar.*, 17:62.
649. Skinner, J. E., Trimble, C. G., and Cheng, C. G. (1919) *Chinese Med.J.*, 33:210.
650. Skrynnik, A. N. (1968) *Parazitologiya*, 2:3.
651. Slavina, N. S. (1944) *Med.Parazit.Parazit.Bolez.*, 13:85.
652. Smith, L., and Brown, T. G. (1969) *California Med.*, 101:322.
653. Smith, P. J. C. (1960a) *Biochem.J.*, 76:500.
654. Smith, P. J. C. (1960b) *Biochem.J.*, 76:508.
655. Sofiev, M. S. (1941) *Med.Parazit.Parazit.Bolez.*, 10:267.
656. Sofiev, M. S., and Leitman, M. Z. (1946) *Med.Parazit.Parazit.Bolez.*, 15:81.
657. Sofiev, M. S., and Leonova, N. A., (1945) *Med.Parazit.Bolez.*, 14:60.
658. Soule, M. H. (1942) *Amer.Assoc.Adv.Sci.Symposium No. 18*, 53.
659. Southern, P. M. Jr., and Sanford, J. P. (1968) *Medicine*, 48:129.
660. Sparrow, H. (1955a) *Arch.Inst.Pasteur Tunis*, 32:25.
661. Sparrow, H. (1955b) *C.R.Acad.Sci.*, 241:1636.
662. Sparrow, H. (1956a) *Bull.Soc.Pathol.Exot.*, 49:630.
663. Sparrow, H. (1956b) *Arch.Inst.Pasteur Tunis*, 33:163.
664. Sparrow, H. (1958) *Bull.Wild.Hlth.Org.*, 19:673.
665. Sparrow, H. (1959) *Proc.6th Internat.Congr.Trop.Med.Malar.*, 4:484.
666. Sreenivasan, M. K., and Sankaranarayan, N. S. (1945) *Indian Veter.J.*, 21:325.
667. Stavitsky, A. B. (1948) *Bact.Rev.*, 12:203.
668. Stein, G. J. (1944) *J.Exp.Med.*, 79:115.
669. Sterling-Okunewski, S. (1919) *Cbl.Bact.Abt.I.Orig.*, 82:456.
670. Stuart, G. (1945) *Epidem.Inform.Bull.U.N.R.R.A.*, 1:453.
671. Suchanek, J., Cieciorski, L., and Lawrynowycz, R. (1957) *Polski Tygod.Lek.*, 22:1103.
672. Sudley, E. W. (1920) *Bull.Soc.Pathol.Exot.*, 13:63.
673. Swain, R. H. A. (1955) *J.Pathol.Bact.*, 69:117.
674. Taft, W. C., and Pike, J. B. (1945) *J.Amer.Med.Assoc.*, 129:1002.
675. Talice, R. V. (1929) *Ann.Parasit.Hum.Compar.*, 7:177.
677. Tesdale, C. (1952) *East Afr.Med.J.*, 29:138.
678. Tesdale, C. (1965) *East Afr.Med.J.*, 52:529.
679. Teravskii, I. K. (1966) *Zool.Zh.*, 45:371.
680. Thayer, K. H. (1940) *Southwest.Med.*, 24:125.
681. Theiler, A. (1902) *J.Compar.Pathol.Ther.*, 17:47.
682. Thiel, P. H. van (1960) *Acta Leidensia*, 30:123.
683. Toda, T., and Hiroki, H. (1934) *Ztschr.Immunforsch.Exp.Ther.*, 82:1.
684. Todd, J. L. (1913) *Proc.Soc.Exp.Biol.*, 10:134.
685. Todd, J. L. (1919) *Bull.Soc.Pathol.Exot.*, 12:1290.
686. Tongeren, H. A. E. van, and Koetsier, J. C. (1968) *Nederl.Tijd.Geneesk.*, 112:1778.
687. Toyoda, H. (1919) *Kitsato Arch.Exp.Med.*, 3:42.