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CURRENT PROBLEMS IN LEPTOSPIROSIS RESEARCH

Report of a WHO Expert Group

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**WHO EXPERT GROUP ON CURRENT PROBLEMS
IN LEPTOSPIROSIS RESEARCH**

Moscow, 18-21 July 1966

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CURRENT PROBLEMS IN LEPTOSPIROSIS RESEARCH

Report of a WHO Expert Group

A group of experts met at the WHO Leptospirosis Reference Laboratory in the Gamaleja Institute of Epidemiology and Microbiology, Moscow, from 18 to 21 July, 1966, to discuss leptospirosis research. Dr Korostelev, Deputy Director of the Institute, welcomed the Group. Professor J. W. Wolff was elected Chairman, Professor V. V. Ananyin Vice-Chairman, and Dr L. H. Turner Rapporteur.

1. INTRODUCTION

In opening the meeting, Dr M. Abdussalam referred to the recent activities of WHO and FAO in the field of leptospirosis and their collaboration with the Taxonomic Subcommittee on *Leptospira* of the International Committee on Nomenclature of Bacteria in taxonomy of leptospires. He proposed that the Group review recent progress in research on leptospirosis, particularly research undertaken since the meeting of the WHO Scientific Group on Research in Leptospirosis¹ held in 1962, and make recommendations on further research and various aspects of the epidemiology and control of the infection.

The Group noted with appreciation the continued efforts of WHO, FAO, and the Taxonomic Subcommittee on *Leptospira* in promoting international collaboration² in leptospirosis research. Apart from planning, co-ordinating, and fostering collaborative research, these organizations have expanded their services to research. Two new international reference laboratories have been designated at the Gamaleja Institute of Epidemiology and Microbiology, Moscow and the Israeli Institute for Biological Research, Ness Ziona, and the provision of reference services by the Pan-American Zoonoses Centre, Azul/Buenos Aires, has been expanded. A restricted exchange of unpublished research information among laboratories in various countries has been arranged. Further

¹ This Group did not publish an official report, but a memorandum drafted by the participants and revised by correspondence in 1962 and 1965 was published in *Bull. Wld Hlth Org.*, 1965, 32, 881. The present report incorporates material from this memorandum that is still valid.

² Abdussalam, M. (1966) *Ann. Soc. belge Méd. trop.*, 46, 15.

progress in providing international reference reagents (reference sera) has been made. A world list¹ of serotype-host distribution has been compiled and will be distributed to interested workers. A list of references to first isolations of type strains of parasitic leptospire has been prepared by Professor J. W. Wolff (see Annex 2).

It is important that international organizations continue such activities, keep under review the status of known and new serotypes, and work towards the standardization of technical procedures and provision of reference reagents and type cultures through the Reference Laboratories. Current research problems suitable for support by WHO/FAO are indicated in various parts of this report and have been summarized in Section 8.

2. TAXONOMY

2.1 Species

The classification system for leptospire has not, in the past, recognized any species within the genus *Leptospira*. The basic taxon in current use — the serotype — is, in fact, infra-subspecific. However, in order to make the classification of leptospire conform to the International Code of Nomenclature of Bacteria and Viruses (1958), the WHO Scientific Group on Leptospirosis and the Taxonomic Subcommittee on *Leptospira* have recommended^{2,3} the recognition of two species: *L. biflexa* (representing saprophytic strains) and *L. interrogans* (representing parasitic strains). *L. interrogans* and *L. biflexa* strains were primarily differentiated by their ability to infect animals, their relative resistance to bivalent copper ions, their serological characteristics, and their growth in organic but serum-free media or in synthetic and semi-synthetic media. Some such strains have also been reported to differ in their relative resistance to 8-azoguanine, malachite green, and basic fuchsin; their oxidase reactions; their lipolytic activities; their susceptibility to the leptospiricidal action of serum; their salt and temperature tolerances; their ability to grow in CO₂-deficient air; and their ability to elicit cytopathogenic effects in select tissue cultures. Notwithstanding this array of proposed differential criteria it is doubtful whether there are sufficient reliable data for the circumscription of the two species at this time. The criteria by which the two species were to be differentiated from each other have either given discrepant results in different laboratories or have not been applied to a sufficient number of serotypes and strains of various serotypes. More-

¹ *Leptospiral Serotype Distribution Lists*, July 1966, US Department of Health, Education and Welfare Public Health Service.

² *Bull. Wld Hlth Org.*, 1965, **32**, 881.

³ *Int. Bull. bact. Nomencl. Taxon.*, 1963, **13**, 161.

over, it has been observed that certain strains of *Leptospira*, isolated in different areas of the world from man and domesticated and wild animals, react to the so-called differential tests (resistance to the bacteriostatic action of bivalent copper ions, the oxidase reaction, etc.) in the manner characteristic of *biflexa* strains. The Group recognizes the pertinence of the following statement by Ainsworth:¹ "For microbial taxonomy in general a major current trend is the realization that rational and stable basic classifications result only by treating pathogens and non-pathogens, parasites and saprophytes, on an equal footing and assessing their overall similarities and dissimilarities." The Group therefore recommends that the current practice of linking *interrogans* with parasitism and pathogenicity and *biflexa* with saprophytism be discontinued in the systematics of *Leptospira*.

It is therefore recommended that the genus *Leptospira* be considered as monospecific until it is possible to circumscribe species with confidence. The specific epithet *interrogans* is recommended, being of earlier date than *biflexa* and *icterohaemorrhagiae*.

Nevertheless, it appears that at least two main groups of the genus *Leptospira* are discernible, corresponding more or less to the previously proposed two species. The term "complex" in the sense of a group or congeries is proposed as a provisional designation for each of these two groups of leptospire. The term "complex" has no official standing as a taxon and it would, therefore, enable further studies to proceed without the necessity for repeated approaches to the Judicial Commission of the International Committee on Nomenclature of Bacteria. The grouping of strains into these complexes would be of value in epidemiology and ecology.

Both complexes are comprised of serologically heterologous strains. Serological differences, which are based on the agglutination reaction with agglutinating sera prepared in rabbits, still form the basis of the classification of strains of *Leptospira* by serotypes, since there is no suitable alternative.

The Group recommends that WHO and FAO continue to support and collaborate with the Taxonomic Subcommittee on *Leptospira* in endeavours to formulate a stable classification of the genus *Leptospira* with the help of actively working taxonomists.

2.2 Serotype

The "serotype" is the basic taxon and is represented by a reference strain (see Annex 1).

¹ Ainsworth, G. C. (1962) *Symp. Soc. gen. Microbiol.*, **12**, 249.

In serogroups that have been studied by analysis of agglutinogenic factors by Kmety (1966),¹ it has been shown that the antigenic differences between related "sub-serotypes" are accounted for by main antigenic factors. The Group therefore favours the abolition of the category (taxon) "subserotype" and proposes² that it be included in a revised concept of the taxon serotype. Because factor analysis is not yet a routine procedure, it is proposed² that the definition of serotype be amended to read: "two strains are considered to belong to different serotypes if, after cross-absorption with adequate amounts of heterologous antigen, 10% or more of the homologous titre regularly remains in *at least one* of the two antisera in repeated tests". In practice, this definition and the technical procedures involved should be adequate to deal with the proposed change.

The term "adequate" used in the definition of serotype needs more precise definition than that given in published descriptions. It is important that the quantitative relationship between antigen and immune serum to be absorbed should be well balanced to avoid possible nonspecific absorption by excessive amounts of antigen. Further studies on standardization of typing procedure are required.

The validity of the characterization of serotypes is contingent on the stability of the agglutinogenic characteristics of leptospire. Variations in these characteristics have been observed under experimental conditions. The nature of these changes and their possible occurrence under conventional cultural and maintenance conditions needs further investigation.

2.3 Serogroup

The grouping of serotypes on the basis of major antigenic relationships as disclosed by cross-agglutination tests is retained. The Group recommends the re-adoption of the term "serogroup" to indicate the serological nature of such groups. Serogroup is not a taxonomic subdivision, as was implied previously,³ nor can leptospiral serogroups be defined or circumscribed at this time. Nevertheless, as previously stated, the concept of leptospiral serogroups has practical value for the selection of antigens and antisera for screening tests of sera and isolates, respectively — and, therefore, for diagnostic and epidemiological investigations.

The present arrangement of serogroups has limitations; for example, some strains might be allocated to either of two serogroups. Moreover,

¹ Kmety, E., (1966) *Ann. Soc. belge Méd. trop.*, **46**, 103.

² The Taxonomic Subcommittee on *Leptospira* accepted these recommendations at its meeting in Moscow on 22-29 July 1966, agreed to consider *Leptospira* a monospecific genus, and recommended that the specific epithet *interrogans* be used for the single species of this genus.

³ *Bull. Wld Hlth Org.*, 1965, **32**, 881.

some of the serogroups have become so extended over the years that they now appear to be less useful in practice; they should, therefore, be re-arranged more suitably.

2.4 List of serotypes

Annex 1 is a list of serotypes of leptospire isolates from man and animals. It represents a revision of the list compiled by the 1962 Scientific Group on Research in Leptospirosis¹ and takes account of new serotypes described since then and of further work on previously listed strains. In view of the new definition of "serotype" (section 2.2), sub-serotypes have been reclassified as serotypes. The number of serogroups has increased because of recent descriptions of distinct serotypes that could not be assigned to previously known groups and because of the inclusion of some of the so-called saprophytic leptospire isolates from man and animals.

3. DIAGNOSTIC PROCEDURES

3.1 Microscopic examination

The diagnosis of leptospiral infections in man and domestic animals by the direct microscopic examination of tissue preparations (other than kidneys) and body fluids has had limited application. The introduction of fluorescent antibody techniques for the demonstration of leptospire in fluids and tissues offers a promising method for the diagnosis of leptospirosis. Such techniques can be particularly helpful in detecting urinary shedders when the usual culture techniques are not practicable. In the present state of knowledge, however, this method is unsuitable for the identification of serotypes since too many cross reactions occur. The application of immunofluorescent techniques in the diagnosis of human and animal leptospiral infections warrants further investigation.

3.2 Isolation by direct culture

The demonstration of the presence, in host tissues and fluids, of substances that inhibit the growth of leptospire serves to re-emphasize the importance of using small inocula for isolations in culture. Many workers have obtained better results in isolating leptospire from 1 in 10 or even

¹ *Bull. Wld Hld Org.*, 1965, 32, 881.

greater dilutions of tissue suspensions or body fluids than from undiluted material. A chemically defined medium without serum has been found suitable for the growth of several pathogenic strains even on primary isolation. The use of 5-fluorouracil, a pyrimidine analogue, in the culture medium has been recommended to inhibit contaminating bacteria and allow leptospire to grow.¹ For primary isolation of leptospire, media containing 5-fluorouracil should be used in conjunction with conventional media, since the pyrimidine analogue may have some growth-inhibitory action for certain leptospire. Further observations on the use of this and other pyrimidine analogues are desirable.

Plating media containing 1% agar may be used for auxiliary isolation and purification of contaminated cultures. Encouraging results have also been obtained with albumin-Tween 80 media for direct isolation of some strains and for growing leptospire for the preparation of vaccines and for biochemical studies.²

The finding of leptospire that cannot be readily cultivated in conventional media indicates the limitations of presently employed isolation techniques. Previously, many workers believed that animal inoculation procedures offered no advantage over direct cultural methods for materials that could be obtained aseptically. It is now evident that the use of laboratory animals in isolation procedures cannot be completely supplanted by direct cultural techniques even for aseptically obtained specimens. The necessity of developing a medium that readily supports the growth of all leptospire is apparent.

3.3 Microscopic agglutination test

The microscopic agglutination test is still the standard reference procedure for the serological diagnosis of leptospirosis and for the serological classification of leptospire. Two important variables in the test procedure that may have a considerable effect on the reproducibility of results, not only in different laboratories but also in the same laboratory, are antigen density and definition of the end-point. The Group recommends that the test with live antigens should be conducted with fluid cultures 4-14 days old and having an antigen density of approximately 100 million organisms³ per millilitre in the final serum-antigen mixture. The antigen density may be established by nephelometric methods or by the use of specially adapted microscope counting chambers.

¹ Johnson, R. C. & Rogers, P. (1964) *J. Bact.*, **87**, 422.

² Ellinghausen, H. C. & McCullough, W. G. (1965) *Amer. J. vet. Res.*, **26**, 39.

³ Some laboratories employ a less dense antigen containing approximately 50 million organisms per ml in the final serum-antigen mixture.

In view of the variable interpretation of the end-point reaction, it is recommended that it be defined as the highest final dilution of serum in the serum-antigen mixture in which 50% or more of the cells are agglutinated. The degree of agglutination can be assessed only by comparing the density of leptospiral cells remaining free between the clumps with density controls made up with the antigen to represent 25%, 50%, and 75% cells. In practice the end-point is determined by the presence of less than 50% of free cells. It is further recommended that this definition be clarified by the preparation of pictorial illustrations of typical gradations of reactions.

Other variables in the serological procedure are the age of the culture, the time and temperature of incubation, and the use of live or formal-treated antigens. Two hours' incubation at 22-37°C is usually preferred. The control of variations attributable to sensitivity differences in cultures of the same strain or serologically homologous strains employed as antigens requires additional study. Straightforward geometric (two-fold¹) dilution is preferable to split dilution (dilution by factors of 10 and 2-2.5). In either case, caution must be exercised to avoid errors due to the carry-over of undetermined amounts of residual serum in the pipette.

The microscopic agglutination test is only relatively serotype-specific. Agglutinins elicited by leptospire of a particular serotype often agglutinate leptospire of related serotypes (particularly those in the same serogroup) to a high level. It should also be kept in mind that the current classification by serotypes is based on agglutinins elicited in rabbits, which may differ from those of the animal species under investigation in both range (pattern) and concentration (titre). In principle, the serotype of an infecting strain can be determined with certainty only by examination of that strain. Absorption studies on serum from the infected individual can in many cases provide a serotype diagnosis of high probability, but such studies are laborious and expensive, and there is little justification for their use in routine diagnosis. The likelihood of one or more serotypes within a particular serogroup being responsible for infection is usually based on local knowledge of the incidence of such serotypes and their behaviour in the animal species under investigation. In view of the increasing recognition of the broad distribution of both recognized and new serotypes in diverse parts of the world, it is important to conduct this test with a battery of antigens encompassing the broad spectrum of cross-reactions with "parasitic" serotypes. A suggested list of serotypes for this purpose is given below. In some countries it may be expedient to delete, substitute, or add strains depending on local conditions and on the scope and purpose of tests.

¹ Some laboratories use four-fold dilution.

<i>Serotype</i>	<i>Strain</i>
<i>icterohaemorrhagiae</i>	RGA
<i>javanica</i>	Veldrat Batavia 46
<i>canicola</i>	Hond Utrecht IV
<i>castellonis</i>	Castellón 3
<i>pyrogenes</i>	Salinem
<i>butembo</i>	Butembo
<i>autumnalis</i>	Akiyami A
<i>bratislava</i>	Jež Bratislava
<i>pomona</i>	Pomona
<i>grippotyphosa</i>	Moskva V
<i>wolffii</i>	3705
<i>borincana</i>	HS 622
<i>bataviae</i>	Van Tienen
<i>tarassovi</i> ¹	Perepelicin
<i>patoc</i>	Patoc 1

¹ Previously named *hyos*, strain Mitis Johnson.

3.4 Serological procedures for screening

Microscopic agglutination tests employing multiple antigens are laborious and involve the possibility of infection and the necessity of maintaining a large number of stock cultures to provide antigens. These factors limit the usefulness of the tests for routine application in diagnostic laboratories. To circumvent these limitations, modified agglutination tests have been developed employing formol-fixed antigens in a macroscopic agglutination technique.

Two procedures that have been extensively applied are the plate and capillary-tube agglutination tests described by Stoenner¹ and the slide agglutination test of Galton et al.² These tests employ formolized cell antigens suspended in a diluent containing a high concentration of salt and/or glycerol.

The slide agglutination test, developed at the Communicable Disease Center, Atlanta, Ga., USA, employs four pooled antigens, each comprising three different serotypes. The antigens are relatively easy to prepare and the test is simple to perform. The pooled antigens are sensitive and have broad genus coverage. They have been used to excellent advantage for diagnosis of leptospiral infections in man and animals. By means of this test, antibodies may frequently be detected in serum earlier after onset of illness than by the microscopic agglutination test. Greater cross reactivity is observed during the acute phase of illness.

However, there is some evidence to suggest that for detection of past leptospiral infections the macroscopic test is less sensitive than the micro-

¹ Stoenner, H. G. (1954) *Amer. J. vet. Res.*, **15**, 434.

² Galton, M. M., Powers, D. K., Hale, A. D. & Cornell, R. (1958) *Amer. J. vet. Res.*, **19**, 505.

scopic agglutination test; as a serological survey method it may have limitations. The antigens are usually stable for approximately 2 years. Some commercial lots have shown clumping, reflecting perhaps the age and mode of shipment of the antigen. Some of these limitations can be avoided by closer control and standardization of antigens and vigorous shaking before use.

In recent years, the presence of genus-specific antigens in leptospire has been suggested by Chang et al.,¹ Cox,² and Rothstein & Hiatt.³ The haemolytic test, according to both Chang and Cox, is a "sensitized-erythrocyte lysis test employing complement". It can easily be performed in laboratories familiar with complement-fixation procedures. It has been extensively used in areas where many serotypes exist, such as Malaysia and Australia, and has been used with advantage to diagnose human cases of leptospirosis. It lacks sensitivity and specificity when employed with bovine and swine serum and requires modification for this purpose. Its usefulness in epidemiological studies is equivocal, and further investigation is necessary. The possible usefulness for diagnostic purposes of the genus-specific antigenic components extracted from leptospire by Rothstein & Hiatt³ also requires further study.

Some "biflexa complex" strains (e.g., Patoc 1 and São Paulo) show broad cross-reactivity in comparative agglutination and complement-fixation tests. In comparative studies on the use of Patoc 1 antigen and antigens of pathogenic strains with human sera, 80-83% correlation was obtained. It was reported that sera of persons infected with *icterohaemorrhagiae* or *copenhageni*⁴ and *pomona* strains usually reacted with Patoc 1, but poor correlation was obtained with sera from *sejroe* and *grippotyphosa* reactors. If the limitations of these "biflexa complex" antigens are recognized, they have potential usefulness for serological screening.

An indirect fluorescent antibody test using Patoc 1 antigen has been developed⁵ for the detection of leptospiral antibodies in man.

4. PATHOGENESIS

Although there is considerable descriptive literature on the pathology of leptospirosis in man and animals, there is still a paucity of basic information on mechanisms of leptospiral disease, particularly the causes of tissue

¹ Chang, R. S. & McComb, D. E. (1954) *Amer. J. trop. Med. Hyg.*, **3**, 481; Chang, R. S. et al. (1957) *Amer. J. trop. Med. Hyg.*, **6**, 90, 101.

² Cox, C. D. (1955) *Proc. Soc. exp. Biol. (N.Y.)*, **90**, 610; Cox, C. D. (1957) *J. infect. Dis.*, **101**, 203.

³ Rothstein, N. & Hiatt, C. W. (1956) *J. Immunol.*, **77**, 257.

⁴ For a redesignation of the serotype represented by strain M 20 as *copenhageni* see Kmety, E. (1966) *Ann. Soc. belge Méd. trop.*, **46**, 103.

⁵ Torten, M., Shenberg, E. & van der Hoeden, J. (1966) *J. infect. Dis.*, **116**, 537.

changes. The possible role of structural and functional factors in the production of disease, either by direct action on host cell components or through adverse immunological reactions, has not been defined.

In the past, leptospirens have been reported to produce fibrinolysin and toxic substances. In recent years, a haemolysin has been demonstrated in some strains in association with signs of anaemia and haemoglobinuria in ruminants.¹

Production of lipolytic substances by leptospirens has also been demonstrated, but the pathogenic role of such substances is unknown. More recently, the presence of endotoxin or endotoxin-like substances in leptospirens has been reported by several workers.² Further research is recommended on the characteristics of these and other factors that may be involved in the pathogenesis of leptospirosis.

5. ECOLOGY AND EPIDEMIOLOGY

5.1 Animal reservoirs

Pathogenic leptospirens are parasites of both wild and domesticated animals. In most foci of infection, one or more species of animal act as maintenance hosts. In times of epizootics other animals living in the same biocenosis are also involved in the circulation of the agent in the focus.

Rodents have been found to be the most important reservoirs, but recent studies in different parts of the world indicate that other groups of wild mammals, such as the insectivores, carnivores, and ruminants, may play an important role as animal hosts of leptospirosis. Isolation of parasitic leptospirens has also been reported from non-mammalian hosts, such as reptiles and birds, but the exact epidemiological role of non-mammalian hosts has still to be investigated.

In investigating possible reservoirs among wild and domesticated animals, serological investigations may provide useful clues, but the use of serological findings alone has serious drawbacks. They may provide an erroneous or misleading index of infectivity rates, since some seronegative animals may be carriers. They provide no firm data for definitive identification of infecting serotypes. It is also possible that in certain species non-specific reactions at low titres occur for some serotypes. Efforts should, therefore, be made to isolate leptospirens from kidney and other suitable tissues and fluids. The possibility of multiple infections should also be kept in mind.

¹ Kemenes, F. (1958) *Acta vet. Acad. Sci. hung.*, **8**, 143.

² Areal, V. M., Sarasin, G. & Green, J. H. (1964) *Amer. J. vet. Res.*, **25**, 836; Sefer, M. (1965) *Arch. roum. Path. exp.*, **24**, 555; Gourley, I. M. & Low, D. G. (1962) *Amer. J. vet. Res.*, **23**, 1252; and others.

Careful ecological studies of reservoir hosts are also necessary to elucidate the more important factors involved in their role in the epidemiology of leptospirosis. Such studies should cover population dynamics, breeding cycles, diurnal movements, migrations, and the environment of the animals, with special reference to hydrology, climate, and soil conditions. These studies are particularly necessary where ecological conditions are rendered unstable by the extension of human habitation and of agriculture, and by new works such as drainage projects and the building of canals.

5.2 Transmission

Fresh water in all forms appearing in nature is a major factor in the circulation of leptospire in enzootic foci. The factors that contribute to the formation and maintenance of water foci are, however, imperfectly understood. Some of the conventional ideas of the potential infectiousness of stagnant waters and slow-moving streams in endemic foci are not necessarily valid in different ecological foci of infection. For example, the infectiousness of rapidly flowing water in jungle (and other) foci of infection has been demonstrated. Moreover, the infectiousness of these waters increases at the time of flood.

In recent years, hamster and other animal inoculation techniques for the isolation of leptospire from water have been improved. New cultural techniques, such as the use of solid plate media and 5-fluorouracil media, as well as improvement of animal inoculation methods for the isolation and study of leptospire in a natural environment, should be investigated further.

Sexual transfer of leptospire — *e.g.*, by mating of rats (*icterohaemorrhagiae*), pigs (*pomona*), and dogs (*canicola*) — has been reported,¹ although there are other types of contact and routes of infection that may be more important in a given situation.

Ticks and other blood-sucking arthropods do not seem to be important vectors, but heavy concentrations of leptospire have been found in their tissues under experimental conditions. They seem to maintain, for a long time, viable leptospire taken in with the blood-meal. The role of arthropods as possible vectors of leptospire needs further investigation, especially as it has been shown that ticks are freely carried from one region to another by migratory birds and mammals.

The blood-sucking nematode *Physaloptera clausa*, parasitic in the stomach of the hedgehog, has been found to carry leptospire, although

¹ Kallai, L., Kemenes, F. & Vizy, L. (1962-3) *Acta microbiol. Acad. Sci. hung.*, **9**, 311; Ferguson, L. C. & Powers, T. E. (1956) *Amer. J. vet. Res.*, **17**, 471; Kiktenko, V. (1962) *Z. Mikrobiol. (Mosk.)*, No. 12, 49; [Abstracts of Papers presented at the Fourth Conference on Leptospirosis, Moscow, 26-27 May 1965], 54-55.

leptospire have not been detected in the mammalian host (hedgehog), despite the presence of a highly significant serotitre for the serotype *hebdomadis*.¹ Further investigation of the epidemiological role of helminthic parasites in leptospirosis is required.

5.3 Epidemic cycles and related preventive measures

From time to time there have been reports of acute outbreaks of human leptospirosis associated with epizootics in wild or domesticated animals in special environmental conditions. Such outbreaks have occurred principally among rice-field workers, cane-cutters, butchers, field workers, and other occupationally exposed persons. The cycles of such outbreaks appear to be linked with the ecology of animal hosts and their environment; further investigation of this factor is required for accurate forecasting of epidemics.

General control measures, such as rodent control and the improvement of sanitation, are important and effective in favourable environmental conditions, but seem to be of limited value in preventing outbreaks in other situations. It is therefore proposed that systematic surveillance programmes be developed in order to follow closely the ecological and epizootiological situation in selected areas and obtain information to assist the development of measures for preventing outbreaks in man. Such programmes could be conducted in close co-operation with similar activities to control other diseases transmitted under similar conditions and could form part of a general surveillance programme in zoonosis control.

5.4 International transfer of infection in animals and animal products

Some countries have enacted legislation to prevent the importation of animals that show a prescribed agglutinin titre against certain specified serotypes. Such laws are not only of doubtful value in keeping out infected animals that may shed leptospire in the absence of a serum titre, but they also exclude vaccinated animals. Further work is required to develop more rational criteria for excluding infected animals.

6. IMMUNIZATION AND THERAPY

6.1 Vaccines in man and animals

Vaccines against human leptospirosis have been used in many countries with good results. They have a useful part to play in areas where

¹ Torten, M., Beemer, A. M. & van der Hoeden, J. (1966) *Bull. Wld Hlth Org.*, **35**, 278.

leptospirosis constitutes a hazard to certain occupational groups. The vaccine, if properly prepared and potent, is safe and gives good protection against clinical illness; it does not, however, confer total protection against infection, particularly if an insufficient number of doses are administered.

In areas where multiple leptospirosis occurs, efforts should be made to develop multivalent vaccines containing the fewest possible serotypes and having a broad antigenic spectrum. For this purpose, further basic information on immunogenic antigens and cross-protection is required.

Vaccines for domesticated animals would be a great advantage in countries where leptospirosis is a problem of appreciable magnitude. Results to date indicate that leptospirosis vaccines in pigs, cattle, and dogs are of some value. However, some data on vaccine trials in domesticated animals have been inadequate and carefully designed trials are recommended to remedy this deficiency.

Of particular importance is the distinction between protection against clinical infection and prevention of carrier states. Both properties are desirable in an ideal vaccine. At present, animal vaccines seem to protect against clinical infection, but little is known of the protection they afford against subclinical infection and the subsequent development of a shedder state. It has been reported that vaccinated cattle incompletely protected against infection become "shedders" for a shorter time than unvaccinated controls and shed fewer leptospores in the urine.

Another topic for further study is the persistence of titres conferred by vaccines and the possibility that such titres may interfere with serological diagnostic tests that may be subsequently required for differential diagnosis or for control programmes

6.2 Therapy

Doubts have been expressed on the efficacy of penicillin and some other antibiotics in the treatment of human leptospirosis. Penicillin seems to be at least partially efficacious, if administered from the beginning of the disease in high doses (6-12 million units daily).

Specific gamma-globulins appear to be of some importance in therapy, particularly in the prevention of clinical disease.¹

Symptomatic treatment, and particularly the use of an artificial kidney, is of great benefit in severe cases.

In cattle, swine, and dogs, treatment with antibiotics sometimes results in diminution of the numbers of leptospores shed into the urine; it may even cause a temporary cessation of the shedding. There is some evidence that penicillin and dihydrostreptomycin are more effective than

¹ Varfolomeyeva, A. A., Barishev, P. M. & Strigushchenko, Y. M. (1964) *J. Hyg. Epidem. (Praha)*, **8**, 450.

tetracycline derivatives in the treatment of the subclinical carrier (and shedder) state in dogs¹ and in hamsters.²

Further research on means of preventing or curing shedder states is recommended.

7. SERVICES TO RESEARCH

7.1 Reference services

The Group noted with satisfaction the continued valuable contributions made by the WHO/FAO and WHO leptospirosis reference laboratories (see Annex 3), and the extension of the service by the designation of two more reference laboratories (Moscow and Ness Ziona) since the meeting of the Scientific Group in 1962. Consideration should be given to the designation of more laboratories as Regional or Collaborating Reference Centres.

7.2 International reference reagents

The Group examined the results of collaborative tests on homologous titres, specificity, and stability of the anti-*Leptospira* sera against certain serotypes and recommended their acceptance as international biological reference reagents.³

It is recommended that the stability test be restricted to testing against the homologous strain after storage at 56°C for two weeks. In view of past experience, tests on sera stored at 37°C can be omitted.

7.3 Exchange of information

The Group examined with appreciation the Leptospiral Serotype Distribution Lists⁴ prepared by Dr Mildred M. Galton with the collaboration of members of the Taxonomic Subcommittee on *Leptospira* and several other workers. Arrangements are being made for the distribution of these lists to interested laboratories and for bringing them up to date⁵ at suitable intervals. Another useful list is that of type strains of various serotypes compiled by Professor J. W. Wolff (see Annex 2).

¹ Hubbert, W. T. & Shott, E. B. (1966) *J. Amer. vet. med. Ass.*, **148**, 1152.

² Stalheim, O. H. V. (1966) *Amer. J. vet. Res.*, **27**, 803.

³ The recommendations have been incorporated in the list of International Reference Reagents of Anti-*Leptospira* Sera given in the nineteenth report of the WHO Expert Committee on Biological Standardization (*Wld Hlth Org. techn. Rep. Ser.*, 1967, **361**, 25) —ED.

⁴ See footnote 1, p. 6.

⁵ Information regarding new serotypes or new hosts should be sent to Dr Mildred M. Galton, Communicable Disease Center, Atlanta, Ga., USA, for continued revision of the lists.

The First Information Exchange in Leptospirosis,¹ containing unpublished research reports from laboratories in different parts of the world, has just been distributed by WHO. This is an extremely useful service that was undertaken on an experimental basis. The Group recommends that it be continued; its value would be enhanced considerably if it were to be compiled twice instead of once a year, provided contributions could be obtained.

8. SUMMARY OF RECOMMENDATIONS FOR RESEARCH

(1) Further studies on the classification of the genus *Leptospira*, based on over-all assessment of relationships and differences of strains, are required. WHO and FAO should continue to support and collaborate with the Taxonomic Subcommittee on *Leptospira* in endeavours to formulate a stable classification (section 2.1).

(2) No immunofluorescent method is yet suitable for the identification of serotypes, either for the typing of strains or for the determination of the serotype of leptospire observed in tissues or fluids. There are too many cross-reactions. The application of these techniques to the diagnosis of human and animal leptospiral infections warrants further investigation (section 3.1).

(3) Some improvement in culture media for the isolation of leptospire (synthetic media with chemical inhibitors for contaminants) has been reported, but there is still a great need of a medium that will readily support the growth of all leptospire (section 3.2).

(4) Genus-specific antigenic components extracted from leptospire merit further study because of their possible usefulness in diagnosis (section 3.4).

(5) Further research is necessary on the characterization of factors involved in the pathogenesis of leptospirosis (section 4).

(6) Careful studies should be made of the role of non-mammalian vertebrates and of invertebrates in the epidemiology of leptospirosis (sections 5.1 and 5.2).

(7) Further studies of the ecology of reservoir hosts are necessary, particularly in regions where environmental conditions are rendered unstable by human activity (section 5.1).

(8) Results of ecological studies should be applied to the forecasting of cycles of infection and to systematic surveillance programmes on which prevention of outbreaks in man could be based (section 5.3).

¹ Unpublished document WHO/PA/66.108.

(9) Further work is required to develop rational criteria for excluding infected animals so as to prevent international transfer of leptospirosis (section 5.4).

(10) In areas where multiple leptospirosis occurs, efforts should be made to develop multivalent vaccines containing the fewest possible serotypes and having a broad antigenic spectrum (section 6.1).

(11) Further studies of the persistence of titres conferred by vaccines are required from the point of view of possible interference with subsequent serological diagnostic tests (section 6.1).

(12) Further research is recommended on an effective means of preventing or curing shedder states (section 6.2).

(13) The following services to research should be provided or continued by WHO/FAO (section 7) :

(a) designation of more laboratories as Regional or Collaborating Reference Centres;

(b) continuation of the preparation, testing, and establishment of specific anti-*Leptospira* sera as international biological reference reagents;

(c) distribution to interested laboratories of host-serotype geographical distribution lists, and revision of such lists at suitable intervals; and

(d) continuation of the preparation of the Information Exchange in Leptospirosis, twice a year, if possible.

ACKNOWLEDGEMENTS

The Group thanks Dr L. H. Turner, Secretary of the Taxonomic Subcommittee on *Leptospira*, for facilitating close collaboration between the Group and the Subcommittee. Thanks are also extended to the following for their valuable contributions to the discussions of the Group : Professor J. W. Czekalowski, Leeds, England; Dr E. V. Karasieva, Moscow; Professor V. Kiktenko, Moscow; and Dr M. J. Lavrova, Moscow.

Annex 1

LIST OF SEROTYPES OF LEPTOSPIRES
ISOLATED FROM MAN AND ANIMALS

Serogroup ^a	Serotype	Reference Strain
Icterohaemorrhagiae	<i>icterohaemorrhagiae</i> ¹ <i>copenhageni</i> ^{1,4} <i>mankarso</i> ¹ <i>naam</i> ¹ <i>nwogolo</i> <i>dakota</i> <i>sarmin</i> ¹ <i>birkini</i> <i>smithi</i> <i>ndambari</i> <i>ndahambukuje</i> <i>budapest</i> ² <i>weaveri</i>	RGA M 20 Mankarso Naam Mwogolo Grand River Sarmin Birkin Smith Ndambari Ndahambukuje PV-1 CZ 380 U
Javanica	<i>javanica</i> ¹ <i>poi</i> ¹ <i>sorex-jalna</i> <i>coxi</i> <i>sofia</i>	Veldrat Batavia 46 Poi Sorex Jalna Cox Sofia 874
Celledoni	<i>celledoni</i> <i>whitcombi</i>	Celledoni Whitcomb
Canicola	<i>canicola</i> ¹ <i>bafani</i> <i>kamituga</i> <i>jonsis</i> <i>sumneri</i> <i>braomi</i> <i>bindjei</i> <i>schueffneri</i> ¹ <i>benjamin</i> ¹ <i>malaya</i>	Hond Utrecht IV Bafani Kamituga Jones Sumner Patane Bindjei Vleermuis 90 C Benjamin H 6
Ballum	<i>ballum</i> <i>castellonis</i> ¹ <i>arborea</i> ²	Mus 127 Castellón 3 Arborea
Pyrogenes	<i>pyrogenes</i> ¹ <i>zanoni</i> ¹ <i>myocastoris</i> <i>abramis</i> <i>biggis</i> <i>hamptoni</i> <i>alexi</i> <i>robinsoni</i> <i>manilae</i>	Salinem Zanoni LSU 1551 Abraham Biggs Hampton HS 616 Robinson LT 398
Cynopteri	<i>cynopteri</i> ¹ <i>canalzonae</i> <i>butembo</i>	3522 C CZ 188 K Butembo

Serogroup ^a	Serotype	Reference Strain
Autumnalis	<i>autumnalis</i> ¹ <i>rachmati</i> ¹ <i>fort-bragg</i> <i>sumatrana</i> ² <i>bulgarica</i> <i>bangkinang</i> <i>erinacei-auriti</i> <i>mooris</i> <i>sentot</i> <i>louisiana</i> <i>orleans</i> <i>djasiman</i> <i>gurungi</i>	Akiyami A Rachmat Fort Bragg Sapulette Nikolaev Bangkinang I Erinaceus auritus 670 Moores Sentot LSU 1945 LSU 2580 Djasiman Gurung
Australis	<i>australis</i> ¹ <i>lora</i> <i>muenchen</i> ¹ <i>jalna</i> <i>bratislava</i> ⁵ <i>fugis</i> <i>bangkok</i> <i>peruviana</i> ² <i>pina</i> ² <i>nicaragua</i> ²	Ballico Lora München C 90 Jalna Jež Bratislava Fudge Bangkok-D 92 LT 941 LT 932 LT 990
Pomona	<i>pomona</i> ¹ <i>kennewicki</i> ² <i>monjakov</i> <i>mazdok</i> ² <i>trapica</i> <i>proechimys</i> ²	Pomona LT 1026 Monjakov 5621 CZ 299 U LT 796
Grippotyphosa	<i>grippotyphosa</i> <i>valbuzzi</i> ²	Moskva V Valbuzzi
Hebdomadis	<i>hebdomadis</i> ¹ <i>nona</i> <i>kambale</i> <i>kremastos</i> ¹ <i>worsfoldi</i> <i>jules</i> <i>maru</i> <i>borincana</i> <i>kabura</i> <i>mini</i> ¹ <i>szwajizak</i> <i>georgia</i> <i>perameles</i> <i>hardjo</i> ¹ <i>recreo</i> ² <i>medanensis</i> ¹ <i>wolffi</i> ¹ <i>trinidad</i> ² <i>sejroe</i> ¹ <i>balcanica</i> <i>polonica</i> <i>saxkoebing</i> ¹ <i>nero</i> <i>haemolytica</i> <i>ricardi</i>	Hebdomadis Nona Kambale Kremastos Worsfold Jules CZ 285 D HS-622 Kabura Sari Szwajizak LT 117 Bandicoot 343 Hardjoprajitno LT 957 Hond HC 3705 LT 1098 M 84 1627 Burgas 493 Poland Mus 24 Gamsulin Marsh Richardson
Bataviae	<i>bataviae</i> ¹ <i>paidjan</i> ¹ <i>djatzi</i> <i>kabbe</i> <i>balboa</i> <i>claytoni</i> ² <i>brasiliensis</i> ²	Van Tienen Paidjan HS 26 CZ 320 K LT 761 LT 818 LT 966

Serogroup ^a	Serotype	Reference Strain
Tarassovi	<i>tarassovi</i> ³ <i>bakeri</i> <i>atlantae</i> <i>guidae</i> <i>kisuba</i> <i>bravo</i> <i>atchafalaya</i> <i>chagres</i> ² <i>rama</i> ² <i>galuni</i> ²	Perepelicin LT 79 LT 81 RP 29 Kisuba Bravo LSU 1013 LT 924 LT 955 LT 839
Panama	<i>panama</i>	CZ 214 K
Shermani	<i>shermani</i> ²	LT 821
Semarang	<i>semaranga</i> <i>patoc</i> <i>sao-paulo</i>	Veldrat Semarang 173 Patoc I Sao Paulo
Andamana	<i>andamana</i>	CH 11

^a It should be noted that "serogroup" is not a taxon (see section 2.3) and some of the present serogroups may be subdivided in the future. In the present list an incomplete effort has been made to place related serotypes in proximity, but in most cases further work is required to establish these relationships and the consequent subdivision of serogroups.

¹ International Reference Preparation of Anti-*Leptospira* serum and homologous culture/reference strain available to national laboratories on request from one of the leptospirosis reference laboratories (see Annex 3).

² Provisional classification pending further work.

³ Previously named *hyos*, strain Mitis Johnson.

⁴ For a redesignation of the serotype represented by strain M20 as *copenhageni* see Kmety, E. (1966)

Ann. Soc. belge Méd. trop., 46, 103.

⁵ The nomenclature of this serotype is being examined further.

Annex 2

**REFERENCE STRAINS OF LEPTOSPIRES
WITH REFERENCES TO ISOLATION AND TYPING ***

Group and reference strain	Serotype	Origin	References
Icterohaemorrhagiae			
RGA	<i>icterohaemorrhagiae</i>	Man, France, 1915	99; 25; 49
M 20	<i>copenhageni</i>	Man, Denmark, 1935	25; 49
Mankarso	<i>mankarso</i>	Man, Indonesia, 1938	110
Naam	<i>naam</i>	Man, Indonesia, 1936	108
Mwogolo	<i>mwogolo</i>	Man, Congo, 1938	77
Grand River	<i>naam</i>	surface water, USA, 1958	8
Sarmin	<i>sarmin</i>	Man, Indonesia, 1930	68; 88
Birkin	<i>birkini</i>	Man, Malaya	6
Smith	<i>smithi</i>	Man, Malaya	6
Ndambari	<i>ndambari</i>	Man, Congo	77
Ndahambukuje	<i>ndahambukuje</i>	Man, Congo, 1938	77
PV-1	<i>budapest</i>	White rat colony, Hungary	41; 44; 18
CZ 390 U	<i>weaveri</i>	Man, Panama Canal Zone	45
Javanica			
Veldrat Batavia 46	<i>javanica</i>	<i>Rattus brevicaudatus</i> , Indonesia, 1938	39; 64
Poi	<i>poi</i>	Man, Italy, 1941	73; 74; 64
Sorex Jalná	<i>sorex-jalna</i>	<i>Sorex araneus</i> , Czechoslovakia, 1953	16; 59; 60; 61; 65; 103
Cox	<i>coxi</i>	Man, Malaya	6; 64
Sofia 874	<i>sofia</i>	Man, Bulgaria	19
Dyananda	<i>ceylonica</i>	Man, Ceylon	120
Celledoni			
Celledoni	<i>celledoni</i>	Man, Australia, 1952	91; 29; 64
Whitcomb	<i>whitcombii</i>	Man, Malaya	6; 64
Canicola			
Hond Utrecht IV	<i>canicola</i>	Dog, Netherlands, 1931	57
Bafani	<i>bafani</i>	Man, Congo	77
Kamituga	<i>kamituga</i>	Man, Congo	77; 23
Jones	<i>jonsis</i>	Man, Malaya	6
Summer	<i>summeri</i>	Man, Malaya	6
Patane	<i>broomi</i>	Man, Australia, 1954	2
Bindjei	<i>bindjei</i>	Man, Indonesia, 1938	1; 2
Vleermuis 90 C	<i>schueffneri</i>	Bat, Indonesia, 1937	34; 36; 33
Benjamin	<i>benjamin</i>	Man, Indonesia, 1937	108
H 6	<i>malaya</i>	Man, Malaya	9
LT 1014	<i>azuli</i>	Bovine, Argentina	121
Ballum			
Mus 127	<i>ballum</i>	<i>Mus musculus</i> , Denmark, 1943	27; 14
Castellón 3	<i>castelloni</i>	Man, Spain	14
Arborea	<i>arborea</i>	<i>Apodemus sylvaticus</i> <i>dichrurus</i> , Italy	20; 97; 98

* This table, which includes strains not listed in Annex 1, reflects the situation as of April 1967. The names of well-known strains that are no longer recognized as reference strains are listed in brackets.

Group and reference strain	Serotype	Origin	References
Pyrogenes			
Salinem	<i>pyrogenes</i>	Man, Indonesia, 1924	104; 106; 22; 24
Zanoni	<i>zanoni</i>	Man, Australia, 1935	71; 107
LSU 1551	<i>myocastoris</i>	<i>Myocastor coypus</i> , USA	82
Abraham	<i>abramis</i>	Man, Malaya	6
Biggs	<i>biggis</i>	Man, Malaya	6
Hampton	<i>hamptoni</i>	Man, Malaya	6
HS 616	<i>alexii</i>	Man, Puerto Rico	3
Robinson	<i>robinsoni</i>	Man, Australia, 1951	91; 7
LT 398	<i>manilae</i>	<i>Rattus norvegicus</i> , <i>R. rattus</i> , Philippines, 1958	46
Cynopteri			
3522 C	<i>cynopteri</i>	Bat species, Indonesia, 1938	35; 33
CZ 188 K	<i>canalzonae</i>	<i>Proechimys</i> sp., <i>Liomys</i> sp. and <i>Philander</i> sp., Panama Canal Zone	45
Butembo	<i>butembo</i>	Man, Congo, 1938	5; 77; 115
Autumnalis			
Akiyami A	<i>autumnalis</i>	Man, Japan, 1925	67
Rachmat	<i>rachmati</i>	Man, Indonesia, 1923	21; 109; 33
Fort Bragg	<i>fort-bragg</i>	Man, USA, 1942	50; 4
Sapulette	<i>sumatrana</i>	Man, Indonesia, 1938	68; 118
Nikolaev	<i>bulgarica</i>	Man, Bulgaria, 1951	75; 16
Bangkinang 1	<i>bangkinang</i>	Man, Indonesia, 1929	90
<i>Erinaceus auritus</i> 670	<i>erinacei-auriti</i>	<i>Erinaceus auritus</i> , USSR, 1949	10; 16
Moores	<i>mooris</i>	Man, Malaya	6
Sentot	<i>sentot</i>	Man, Indonesia, 1937	108
LSU 1945	<i>louisiana</i>	<i>Dasypus novemcinctus</i> , USA	83
LSU 2580	<i>orleans</i>	<i>Myocastor coypus</i> , USA	83
Djasiman	<i>djasiman</i>	Man, Indonesia, 1937	68
Gurung	<i>gurungi</i>	Man, Malaya	6
Australis			
Ballico	<i>australis</i>	Man, Australia, 1937	71; 107; 62; 63
Lora	<i>lora</i>	Man, Italy, 1941	62; 63
Munchen C 90	<i>muenchen</i>	Man, Germany, 1942	111; 62; 63
Jalna	<i>jalna</i>	<i>Apodemus flavicollis</i> , Czechoslovakia, 1953	62; 63
Jez bratislava	<i>bratislava</i>	<i>Erinaceus</i> sp., Czechoslovakia, 1953	58; 62; 63
Fudge	<i>fugis</i>	Man, Malaya	6
Bangkok-D 92	<i>bangkok</i>	Dog, Thailand, 1964	119
LT 941	<i>peruviana</i>	Bovine, Peru, 1963	122
LT 932	<i>pina</i>	<i>Didelphis marsupialis</i> , Panama Canal Zone	123
LT 990	<i>nicaragua</i>	<i>Mustela nivalis</i> , Nicaragua	124
Pomona			
Pomona	<i>pomona</i>	Man, Australia, 1936	32; 37
Monjakov	<i>monjakov</i>	Man, Far Eastern USSR, 1937 and 1938	16; 30; 95; 96; 101; 31
5621	<i>mozdok</i>	<i>Microtus arvalis</i> , USSR, 1961	89; 31
CZ 299 U	<i>tropica</i>	<i>Proechimys</i> sp. <i>Liomys</i> sp. Panama Canal Zone	45
LT 1026	<i>kennewicki</i>	Bovine and water, 1964, Washington State, USA	125
LT 796	<i>proechimys</i>	<i>Proechimys semispinosus</i> , Panama Canal Zone	123

Group and reference strain	Serotype	Origin	References
Grippotyphosa			
Moskva Valbuzzi	<i>grippotyphosa</i> <i>valbuzzi</i>	Man, USSR, 1928 Man, Australia	93 92
Hebdomadis			
Hebdomadis Nona Kambale Kremastos Worsfold Jules CZ 285 B	<i>hebdomadis</i> <i>nona</i> <i>kambale</i> <i>kremastos</i> <i>worsfoldi</i> <i>jules</i> <i>maru</i>	Man, Japan, 1918 Man, Congo Man, Congo, 1956 Man, Australia, 1952 Man, Malaya Man, Congo <i>Proechimys</i> sp. and water, Panama Canal Zone	53 79 79 91; 113 6 113 45
HS-622 Kabura Sari Szwajirak LT 117	<i>borincana</i> <i>kabura</i> <i>mini</i> <i>szawjizak</i> <i>georgia</i>	Man, Puerto Rico Man, Congo Man, Italy, 1941 Man, Australia, 1951 <i>Procyon lotor</i> , 1952, USA. Also from <i>Didelphis marsupialis</i> and <i>Mephitis mephitis</i>	3 78; 113 72; 74; 15; 113 91; 113 47
Bandicoot 343	<i>perameles</i>	<i>Perameles nasuta</i> , Australia, 1958	117
Hardjoprajitno Hond HC 3705 M 84 1627 Burgas 493 Poland	<i>hardjo</i> <i>medanensis</i> <i>wolffi</i> <i>sejroe</i> <i>balcanica</i> <i>polonica</i>	Man, Indonesia, 1938 Dog, Indonesia, 1929 Man, Indonesia, 1937 Man, Denmark, 1937 Man, Bulgaria, 1958 <i>Erinaceus roumanicus</i> , Poland, 1957	111 69; 70; 33 112; 88; 33 28; 25 19 117; 76
Mus 24	<i>saxkocbing</i>	<i>Apodemus ravicollis</i> , Denmark, 1942	26
Gamsulin Marsh Richardson LT 957	<i>nero</i> <i>haemolytica</i> <i>ricardi</i> <i>recreo</i>	Man, USSR, 1950 Man, Malaya Man, Malaya <i>Philander opossum</i> , Nicaragua	11; 16 6 6 124
LT 1098 LT 829	<i>jrinidad</i> <i>gorgas</i>	Man, Trinidad <i>Proechimys semispinosus</i> , Panama Canal Zone	126 123
LT 844	<i>beye</i>	<i>Proechimys semispinosus</i> , Panama Canal Zone	123
TVRL 34056	<i>tabaquite</i>	Man, Trinidad	126
Bataviae			
Van Tienen ¹ (Swart) ¹ Paidjan HS 26 CZ 320 K	<i>bataviae</i> <i>bataviae</i> <i>paidjan</i> <i>djatzi</i> <i>kobbe</i>	Man, Indonesia, 1932 Man, Indonesia, 1925 Man, Indonesia, 1939 Man, Puerto Rico <i>Proechimys semispinosus</i> , Panama Canal Zone	38; 112 105 111 3 45
LT 761	<i>balboa</i>	<i>Proechimys semispinosus</i> , Panama Canal Zone	123
LT 818	<i>claytoni</i>	<i>Proechimys semispinosus</i> , Panama Canal Zone	123
LT 966 LT 1019	<i>brasilensis</i> <i>argentiniensis</i>	<i>Proechimys semispinosus</i> , Panama Canal Zone <i>Didelphis marsupialis</i> , Brazil <i>Didelphis marsupialis</i> , Argentina	127 121
Tarassovi			
Perepelicin (Mitis Johnson) LT 79	<i>tarassovi</i> ² <i>(hyos)</i> <i>bakeri</i>	Man, Far Eastern USSR Man, Australia <i>Didelphis marsupialis</i> , USA, 1955	16; 56; 11; 60; 96; 102 54; 86; 87; 12 48; 114

¹ The question of the reference strain for serotype *bataviae* is being examined.

² Previously named *hyos*, strain Mitis Johnson.

Group and reference strain	Serotype	Origin	References
Tarassovi (continued)			
RP 29	<i>guidae</i>	Swine, Brazil, 1949	51; 52; 114
LT 81	<i>atlantae</i>	<i>Didelphis marsupialis</i> , USA, 1955	48; 114
Kisuba	<i>kisuba</i>	Man, Congo	81
Bravo	<i>bravo</i>	Man, <i>Proechimys semispinosus</i> , <i>Liomys adpersus</i> , Panama Canal Zone	45
LSU 1013	<i>atchafalaya</i>	<i>Didelphis marsupialis</i> , USA	84
LT 924	<i>chagres</i>	Man and <i>Proechimys semispinosus</i> , Panama Canal Zone	123
LT 955	<i>rama</i>	<i>Philander opossum</i> , Nicaragua	124
LT 839	<i>gatuni</i>	<i>Didelphis marsupialis</i> , Panama Canal Zone	123
Panama			
CZ 214 K	<i>panama</i>	<i>Didelphis marsupialis</i> , Panama	45
LT 940	<i>crisobali</i>	<i>Didelphis</i> , Panama Canal Zone	123
Shermani			
LT 821	<i>shermani</i>	<i>Proechimys semispinosus</i> , <i>Didelphis marsupialis</i> , <i>Sigmondon hispidus</i>	123
Semarang			
Veldrat Semarang 173	<i>semaranga</i>	<i>Rattus brevicaudatus</i> , Indonesia, 1937	17; 40; 42; 43; 85
Patoc I	<i>patoc</i>	Surface water, Italy	17; 40; 42; 43
Sao Paulo	<i>sao Paulo</i>	Surface water, Brazil	13; 17; 40; 42; 43
Andamana			
CH 11	<i>andamana</i>	Man, Andamans, 1930	17; 40; 42; 43; 94

REFERENCES

1. Addamiano, L. (1959) *R. C. Ist. sup. Sanità*, **22**, 5
2. Addamiano, L., Babudieri, B. & Smith, D. J. W. (1960) *Zbl. Bakt., I. Abt. Orig.*, **180**, 419
3. Alexander, A. D., Benenson, A. S., Byrne, R. J., Evans, L. B., Gochenour, W. S. & Yager, R. H. (1963) *Zoonoses Res.*, **2**, 210
4. Alexander, A. D., Evans, L. B., Jeffries, H. Gleiser, Ch. A. & Yager, R. H. (1954) *Proc. Soc. exp. Biol. (N. Y.)* **86**, 405
5. Alexander, A. D., Evans, L. B. & Keen, B. C. (1959) *J. Bact.*, **77**, 668
6. Alexander, A. D., Evans, L. B., Toussaint, A. J., Marchwick, R. H. & McCrumb, F. R. jr (1957) *Amer. J. trop. Med. Hyg.*, **6**, 871
7. Alexander, A. D. & Smith, D. J. W. (1962) *Aust. J. exp. Biol. med. Sci.*, **40**, 81
8. Alexander, A. D., Stoenner, H. J., Wood, G. E. & Byrne, R. J. (1962) *J. Bact.*, **83**, 754
9. Alexander, A. D., Wetmore, P. W., Evans, L. B., Jeffries, H. & Gleiser, C. A. (1955) *Amer. J. trop. Med. Hyg.*, **4**, 492
10. Ananyin, V. V. (1951) *Dokl. Akad. Nauk SSSR*, **30**, 375
11. Ananyin, V. V. & Kiktenko, V. S. (1955) *Z. Mikrobiol. (Mosk.)* **9**, 92
12. Babudieri, B. (1951) *Boll. Soc. ital. Biol. sper.*, **27**, 104
13. Babudieri, B. (1952) *Rev. Inst. A. Lutz (S. Paulo)*, **12**, 93
14. Babudieri, B. (1955) *R. C. Ist. sup. Sanità*, **18**, 57
15. Babudieri, B. (1956) *Z. Hyg. Infekt.-Kr.*, **143**, 121
16. Babudieri, B. (1959) *Serological study of some East European strains of leptospira*. In : *Proceedings of the Sixth International Congress on Tropical Medicine and Malaria, Lisbon, September 5-13, 1958*, Lisbon, Vol. 4, p. 437
17. Babudieri, B. (1961) *Studio si erologico del grupo "Semarang-Patoc" di Leptospira biflexa*. In : *Atti dell'XI Congresso Società Italiana di Microbiologia, Cagliari-Sassari, 9-12 October 1961*, Naples
18. Babudieri, B. (1966) *Zbl. Bakt., I. Abt. Orig.*, **199**, 67
19. Babudieri, B. & Mateew, D. (1961) *R. C. Ist. sup. Sanità*, **24**, 614
20. Babudieri, B. & Moscovici, C. (1955) *R. C. Ist. sup. Sanità*, **18**, 70
21. Baermann, G. (1923) *Geneesk. T. Ned.-Ind.*, **63**, 885
22. Baermann, G. & Smits, E. (1928) *Zbl. Bakt., I. Abt. Orig.*, **105**, 368
23. Berghe, L. van den & Riel, J. van (1939) *Bull. Soc. Path. exot.*, **32**, 944
24. Bonne, C. (1924) *Bull. Soc. Path. exot.*, **17**, 623
25. Borg-Petersen, C. (1938) *Leptospirenuntersuchungen in Dänemark*. In : *Acta Conventus Tertii de Tropicis atque Malariae Morbis*, Amsterdam, vol. 1, p. 396
26. Borg-Petersen, C. (1944) *Acta path. Microbiol. scand.*, **21**, 165
27. Borg-Petersen, C. (1944) *Acta path. Microbiol. scand.*, **21**, 504
28. Borg-Petersen, C. & Christensen, H. T. (1939) *Ugeskr. Læg.*, **101**, 697
29. Broom, J. C. & Smith, D. J. W. (1956) *Lancet*, **2**, 866
30. Černuha, J. G. (1965) *J. Hyg. Epidem. Microbiol. Immun.*, **9**, 227
31. Černuha, J. G. (1966) *Trop. geogr. Med.*, **18**, 242
32. Clayton, G. E. B., Derrick, E. H. & Cilento, R. (1937) *Med. J. Aust.*, **24**, 647

33. Collier, W. A. (1948) *Acta trop. (Basel)*, **5**, 135
34. Collier, W. A. & Esseveld, H. (1938) *Meded. Dienst Volksgezondh. Ned.-Indië*, **27**, 262
35. Collier, W. A. & Mochtar, A. (1939) *Geneesk. T. Ned.-Ind.*, **79**, 226
36. Collier, W. A. & Mochtar, A. (1939) *Meded. Dienst Volksgezondh. Ned.-Indië*, **28**, 356
37. Derrick, E. H. (1942) *Med. J. Aust.*, **1**, 431
38. Dinger, J. E. (1943) *Geneesk. T. Ned.-Ind.*, **73**, 402
39. Esseveld, H. & Mochtar, A. (1938) *Geneesk. T. Ned.-Ind.*, **78**, 1513
40. Füzi, M. & Csóka, R. (1960) *Zbl. Bakt., I. Abt. Orig.*, **179**, 231
41. Füzi, M. & Csóka, R. (1961) *Nature (Lond.)*, **191**, 1123
42. Füzi, M. & Csóka, R. (1961) *J. Bact.*, **81**, 1008
43. Füzi, M. & Csóka, R. (1961) *Zbl. Bakt., I. Abt. Orig.*, **182**, 494
44. Füzi, M. & Csóka, R. (1962-63) *Acta microbiol. hung.*, **9**, 355
45. Gale, N. B., Alexander, A. D., Evans, L. B. & Yager, R. H. (1966) *Amer. J. trop. Med. Hyg.*, **15**, 64
46. Galton, M. M., Aragon, P. R., Jacalne, A. V., Shotts, E. B. jr & Sulzer, C. R. (1963) *J. infect. Dis.*, **112**, 164
47. Galton, M. M., Norman, G. W. & Shotts, E. B. jr (1960) *Publ. Hlth Rep.*, **75**, 917
48. Galton, M. M., Powers, D. K. McKeever, S. & Gorman, G. W. (1957) *Publ. Hlth Rep.*, **72**, 431
49. Gispén, R. & Schüffner, W. (1939) *Zbl. Bakt., I. Abt. Orig.*, **144**, 427
50. Gochenour, J. E. jr, Smadel, J. E., Jackson, E. B., Evans, L. B. & Yager, R. H. (1952) *Fedn Proc. Fedn Am. Socs exp. Biol.*, **11**, 1; *Publ. Hlth Rep.*, **57**, 811
51. Guida, V. O. (1948) *Arch. Inst. biol. (S. Paulo)*, **18**, 285
52. Guida, V. O. (1953) *Arch. Biol. Tecnol. (Curitiba)*, **7**, 21
53. Ido, J., Ito, H. & Wani, H. (1918) *J. exp. Med.*, **28**, 435
54. Johnson, D. W. (1942) *Med. J. Aust.*, **29**, 431
55. Karmanska, K. (1963) *Acta microbiol. pol.*, **12**, 55
56. Kiktenko, V. S. & Ananyin, V. V. (1914) *Ž. Mikrobiol. (Mosk.)*, **12**, 72
57. Klarenbeek, A. & Schuffner, W. A. (1933) *Ned. Tijdschr. Geneesk.*, **77**, 4271
58. Kmety, E. (1954) *Čsilká Hyg. Epidem. Mikrobiol.*, **3**, 41
59. Kmety, E. (1955) *Bratisl. lék. Listy*, **35**, 261
60. Kmety, E. (1955) *Zbl. Bakt., I. Abt. Orig.*, **163**, 464
61. Kmety, E. (1957) *Zbl. Bakt., I. Abt. Orig.*, **168**, 277
62. Kmety, E. (1959) *Q. Rev. scient. Publs Pol. Acad. Sci.*, **9**, 27
63. Kmety, E. (1960) *J. Hyg. Epidem. Microbiol. Immun.*, **4**, 171
64. Kmety, E. (1963) *J. Hyg. Epidem. Microbiol. Immun.*, **7**, 225
65. Kmety, E. (1964) *A factor analysis of strains belonging to the group javanicacelledoni and icterohaemorrhagiae*. In : *Proceedings of the Second International Symposium on Leptospirae and Leptospirosis in Man and Animals, Lublin, 1962*, Vol. 1, p. 105
66. Kmety, E., Plesko, J. & Chylo, E. (1956) *Zbl. Bakt., I. Abt. Orig.*, **167**, 243
67. Koshina, M., Shiozawa, S. & Kitayama, K. (1925) *J. exp. Med.*, **42**, 873

68. Kotter, G. F. (1939) *Ned. T. Geneesk.*, **83**, 3590
69. Kouwenaar, W. & Wolff, J. W. (1929) *Ned.-indische Bl. Diergeneesk.*, **41**, 457
70. Kouwenaar, W. & Wolff, J. W. (1930) *Ned. T. Geneesk.*, **74**, 377
71. Lumley, G. E. (1937) *Med. J. Aust.*, **24**, 654
72. Mino, P. (1941) *Münch. med. Wschr.*, **88**, 96
73. Mino, P. (1942) *G. Accad. Med. Torino*, **20**, 1
74. Mino, P. (1942) *Klin. Wschr.*, **21**, 337
75. Mitov, A. & Jankov, W. (1959) *Zbl. Bakt., I. Abt. Orig.*, **175**, 437
76. Parnas, J. & Cybulska, M. (1965) *Bull. Acad. pol. Sci. Cl. II Sér. Sci. biol.*, **13**, 505; (1966) *Int. J. system. Bact.*, **16**, 305
77. Riel, J. van (1946) *Ann. Soc. belge Méd. trop.*, **26**, 197
78. Riel, J. van (1952) *Ann. Soc. belge Méd. trop.*, **32**, 683
79. Riel, J. van & Riel, M. van (1960) *Ann. Soc. belge Méd. trop.*, **40**, 549
80. Riel, J. van & Szpaishaendler, L. (1955) *Ann. Soc. belge Méd. trop.*, **35**, 93
81. Riel, J. van, Szpaishaendler, L. & Riel, M. van (1956) *Bull. Soc. Path. exot.*, **49**, 118
82. Roth, E. E., Adams, W. V., Greer, B., Sanford, G. E., Moore, M. & Newman, R. (1963) *Publ. Hlth Rep.*, **78**, 727
83. Roth, E. E., Greer, B., Moore, M., Newman, K., Sanford, G. E. & Adams, W. V. (1964) *Zoonoses Res.*, **3**, 31
84. Roth, E. E., Moore, M., Greer, B., Newman, K., Adams, W. V. & Sanford, G. E. (1963) *Zoonoses Res.*, **2**, 91
85. Sardjito, M. & Mochtar, A. (1939) *Geneesk. T. Ned.-Ind.*, **79**, 2520
86. Savino, E. & Rennella, E. (1944) *Leptospira y leptospirosis en la Republica Argentina*, Buenos Aires, Tomas Palumbo
87. Savino, E. & Rennella, E. (1950-53) *Rev. Inst. bact. Malbrán*, **15**, 305
88. Schüffner, W., Gispén, H. & Bohlander, H. (1939) *Geneesk. Ned.-Ind.* **79**, 2470
89. Semanova, L. P. (1965) *J. Hyg. Epidem. Microbiol. Immun.*, **9**, 233
90. Slot, G. A. & Walle, N. van der (1932) *Geneesk. T. Ned.-Ind.* **72**, 1579
91. Smith, D. J. W., Brown, H. E., Tonge, J. I., Sinnamon, C. N., Macdonald, V. M., Ross, C. J., & Doherty, R. L. (1954) *Aust. Ann. Med.*, **3**, 98
92. Smith, D. J. W. & Brown, H. E. (1955) *Aust. Ann. Med.*, **4**, 287
93. Tarassoff, S. (1931) *Ann. Inst. Pasteur*, **46**, 222
94. Taylor, J. & Goyle, A. N. (1931) *Indian med. Res. Mem.*, No. 20
95. Terskikh, V. (1941) *Z. Mikrobiol. (Mosk.)*, **8**, 66
96. Terskikh, V. I. (1945) *Leptospirozy ludey i shivotnykh*, Moscow, Medgiz
97. Thomakos, A. & Babudieri, B. (1964) *A new serotype belonging to the leptospira serotype ballum*. In: *Proceedings of the Second International Symposium on Leptospirae and Leptospirosis in Man and Animals*, Lublin, 1962, Vol. 1, p. 101
98. Thomakos, A. & Babudieri, B. (1965) *Ann. Ist. sup. Sanità*, **1**, 407
99. Uhlenhuth, P. & Fromme, W. (1915) *Medische Klin.*, **44**, 1202
100. Varfolomeeva, A. A. (1948) *Leptospiral diseases in man*, Moscow, Medgiz
101. Varfolomeeva, A. A. (1957) *Zbl. Bakt., I. Abt. Orig.*, **171**, 71
102. Varfolomeeva, A. A. (1958) *J. Hyg. Epidem. Microbiol. Immun.*, **11**, 50

103. Varfolomeeva, A. A. (1964) *A system of pathogenic leptospirae isolated in the USSR*. In : *Proceedings of the Second International Symposium on Leptospires and Leptospirosis in Man and Animals, Lublin, 1962*, Vol. 2, p. 321
104. Vervoort, H. (1923) *Geneesk. T. Ned.-Ind.*, **63**, 800
105. Walch, E. (1926) *Geneesk. T. Ned.-Ind.*, **66**, 115
106. Walch, E. & Soesilo, H. (1927) *Geneesk. T. Ned.-Ind.*, **67**, 84
107. Walch-Sorgdrager, B., Bohlander, H. & Schüffner, W. (1938) *Geneesk. T. Ned.-Ind.*, **78**, 2299
108. Walch-Sorgdrager, B., Bohlander, H., Schüffner, W. & Wolff, J. W. (1950) *Geneesk. T. Ned.-Ind.*, **80**, 578
109. Wolff, J. W. (1925) *Arch. Schiffs- u. Tropenhyg.*, **29**, 111
110. Wolff, J. W. (1953) *Serological classification of type strains of Leptospira*. In : *Advances in the control of zoonoses, Geneva (World Health Organization : Monograph Series, No. 19)* p. 139
111. Wolff, J. W. (1953) *The classification of pathogenic leptospirae*. In : *Symposium on the Leptospiroses, Washington, D.C. (Army Medical Service Graduate School, Medical Sciences Publication No. 1)* p. 174
112. Wolff, J. W. (1954) *The laboratory diagnosis of leptospirosis*, Springfield, Ill., Thomas, p. 84
113. Wolff, J. W. & Bohlander, H. J. (1958) *Trop. geogr. Med.*, **10**, 37
114. Wolff, J. W. & Bohlander, H. J. (1960) *Trop. geogr. Med.*, **12**, 173
115. Wolff, J. W. & Bohlander, H. J. (1961) *Trop. geogr. Med.*, **13**, 173
116. Wolff, J. W. & Bohlander, H. J. (1961) *Trop. geogr. Med.*, **13**, 175
117. Wolff, J. W. & Bohlander, H. J. (1964) *Trop. geogr. Med.*, **16**, 88
118. Wolff, J. W. & Bohlander, H. J. (1966) *Trop. geogr. Med.*, **18**, 247
119. Wolff, J. W., Bohlander, H. J. & Sundharagiati, B. (1965) *Trop. geogr. Med.*, **17**, 20

UNPUBLISHED REFERENCES

120. Strain isolated by K. Nityananda, Medical Research Institute, Colombo, Ceylon; typed at the Communicable Disease Center, Atlanta, Ga., USA
121. Strains isolated at the Pan American Zoonoses Center, Buenos Aires, Argentina; typed at the Communicable Disease Center, Atlanta, Ga., USA
122. Strain isolated by J. de Hidalgo and A. Herrero, Lima, Peru; typed by M. M. Galton, Communicable Disease Center, Atlanta, Ga., USA
123. Strain isolated by N. B. Gale, Panama Canal Zone; typed by M. M. Galton, Communicable Disease Center, Atlanta, Ga., USA
124. Strains isolated by L. G. Clark, School of Veterinary Medicine, University of Pennsylvania, USA; typed by M. M. Galton, Communicable Disease Center, Atlanta, Ga., USA
125. Strain typed by M. M. Galton, Communicable Disease Center, Atlanta, Ga., USA
126. Strain isolated by L. Spence, Regional Virus Laboratory, Port-of-Spain, Trinidad; typed at the Communicable Disease Center, Atlanta, Ga., USA
127. Strain isolated by C. Santa Rosa, São Paulo, Brazil; typed by M. M. Galton, Communicable Disease Center, Atlanta, Ga., USA

Annex 3**WHO LEPTOSPIROSIS REFERENCE LABORATORIES**

Laboratory of Microbiology and Pathology, Department of Health and Home Affairs, Brisbane, Australia

London School of Hygiene and Tropical Medicine, London, England

Israeli Institute for Biological Research, Ness-Ziona, Israel

Istituto Superiore di Sanità, Rome, Italy

National Institute of Health, Tokyo, Japan

Institute for Tropical Hygiene (Royal Tropical Institute), Amsterdam, Netherlands

Division of Veterinary Medicine, Walter Reed Army Medical Center, Washington, D.C., USA

Gamaleja Institute of Epidemiology and Microbiology, Moscow, USSR
(Pan American Zoonoses Centre, Ramos-Mejia and Azul, Argentina)

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CURRENT PROBLEMS IN LEPTOSPIROSIS RESEARCH

Report of a WHO Expert Group

CORRIGENDA

- Annex 1, page 21 Serogroup Icterohaemorrhagiae, serotype *weaveri*: under "Reference strain", delete CZ 380 U, insert CZ 390 U.
- page 22 Serogroup Hebdomadis, serotype *maru*: under "Reference strain", delete CZ 285 D, insert CZ 285.
- Annex 2, page 24 Group Icterohaemorrhagiae, strain Grand River: under "Serotype", delete *naam*, insert *dakota*.
- Group Canicola: under "Group and reference strain", delete Summer, insert Sumner; under "Serotype" delete *summeri*, insert *sumneri*.
- Group Ballum, strain Castellón 3: under "Serotype", delete *castelloni*, insert *castellonis*.
- page 26 Group Hebdomadis: under "Group and reference strain", delete CZ 285 B, insert CZ 285.
- Group Hebdomadis: under "Group and reference strain", delete Szwajirak, insert Szwajizak, under "Serotype", delete *szawjizak*, insert *szwajizak*.
- Group Hebdomadis, reference strain Mus 24: under "Origin", delete *Apodemus ravicollis*, insert *Apodemus flavicollis*.
- Group Hebdomadis, reference strain LT 1098: under "Serotype", delete *jrinidad*, insert *trinidad*.
- page 27 Group Semarang: under "Group and reference strain", delete Sao Paulo, insert São Paulo; under "Serotype", delete *sao paulo*, insert *sao-paulo*.

