

## **Leprosy : summary of recent work no. 4.**

### **Contributors**

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# LEPROSY :

## SUMMARY OF RECENT WORK.

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## LEPROSY.

ROGERS (Leonard). **The Croonian Lectures on Leprosy Researches.**—*Ann. Trop. Med. & Parasit.* 1924. Oct. 31. Vol. 18. No. 3. pp. 267-322. With 2 figs.

The first of these lectures is devoted to a general survey of the distribution of leprosy and of the factors influencing its spread, based on a consideration of previous records and the history of the disease. An attempt is made to show the correlation of inverse ratio between the prevalence of leprosy and tuberculization as evidenced by the von Pirquet test. The fallacies attendant on the interpretation of figures of prevalence are next pointed out, the text of the discourse being the apparent decline of leprosy in British India during the last 50 years.

Lecture II deals with the mode of infection and prophylaxis. The various ways in which the bacillus may gain entrance according to the views which have been put forward from time to time are briefly referred to, together with the possible effect of humidity in relation to leprosy, details of which have been given in previous papers by the author and reviewed in this *Bulletin* (see Vol. 20, p. 821).

Methods of prophylaxis as carried out in different countries, cold, temperate, and tropical, are mentioned, with statistical figures for each, and reasons for the failure of these methods, which consist mainly of segregation, are stated; the chief appear to be vacillating policy and defective administration. Measures to be adequate must include compulsory notification, isolation or institutional segregation of patients, examination of contacts at regular intervals, removal of children from their parents as soon after birth as possible, separation of the sexes in institutions, prohibition of lepers from engaging in the preparation and sale of food, in nursing and domestic employment, and, most important of all, treatment, thorough and early if possible.

From the point of view of the tropical worker the third lecture, on Treatment, will probably be of paramount interest. Previous modes of treatment by serums, vaccines, mineral preparations, and so on, are briefly reviewed, the remainder of the lecture being concerned mainly with chaulmoogra oil and its derivatives. The difficulties of estimating the effects of treatment are duly stressed, namely, the intermittent improvements which may take place spontaneously, and the comparatively sudden exacerbations arising in a disease with, typically, a chronic course; also the improvement in ill-nourished patients when placed under a good régime and properly cared for, even when no drugs are given. An interesting historical account of the use of chaulmoogra precedes a discussion of its various preparations and modes of administration.

Sodium gynocardate intramuscularly was found to be better borne by Indian patients than the whole oil, but preparations containing both gynocardic and hydnocarpic acids, injected intravenously, gave much better results. The author shows how, without any reaction noticeable to the patient, the bacilli may be broken down and the nodules absorbed, till, finally, bacilli are no longer detected either in the tissues or in the nasal mucus, so that in a case of average severity the patient became free of symptoms and infectivity in 6-18 months. Exceptionally, prolonged improvement may follow injection of a



single small dose of the drug, e.g., 0.2 cc. of a 3 per cent. solution, but to ensure good results it is necessary in most cases to continue treatment regularly after clearing of symptoms and better for 12-18 months.

An account is given of the development of the idea that it is the unsaturated fatty acids which constitute the chief factor influencing the therapeutic value of oils in leprosy, so that many other oils besides that of chaulmoogra may prove beneficial in this disease. Although such good results were obtained by intravenous administration of the drug, the method has the disadvantage of leading to obliteration of the vein by its local irritant action. The results obtained by Professor DEAN, of Honolulu, and others with the ethyl esters from chaulmoogra also receive mention, but the author does not record any experiences of his own with these. They have the advantage of causing little or no pain when injected intramuscularly and are, therefore, more convenient for administration than irritating preparations intravenously.

The final pages of the lecture deal with results of treatment by ethyl chaulmoogrates and hydnocarpates statistically compiled, showing that the degree of improvement depends largely upon the duration of the disease and the length of treatment. Thus, in Honolulu, of cases of less than 6 months' standing, 44 per cent. are stated to have recovered, but only 3 per cent. of those who had suffered for 8-10 years, while, as showing the influence of prolonged treatment, the percentage of those improved after 3 months' treatment or less was 26, but of those who submitted to 12-15 months' treatment 93 per cent. showed improvement. Finally, the question is asked: "Can lasting cures be obtained?" The author concludes that the outlook is hopeful, provided treatment is undertaken sufficiently early and continued sufficiently long. Most early and some more advanced cases lose all symptoms, and one patient has "remained free for over eight years from all signs of the disease . . . although he has had no treatment during the last three years."

H. Harold Scott.

**IIIe Conférence Internationale de la lèpre, Strasbourg—28 au 31 juillet 1923. Communications et débats recueillis et colligés par le Dr. E. MARCHOUX.—528 pp. With 1 plate & 89 figs. 1924. Paris: Librairie J. B. Baillière et fils, 19, rue Hautefeuille.**

This handsome volume of 528 large pages appeared late in 1924; much of its information has already appeared elsewhere, and been referred to in this *Bulletin*, so that only a brief summary of its more important items need be given here.

After opening speeches a sitting was devoted to statistics on the incidence of leprosy in various parts of the world, which brought out little new. It indicates a further decline of the disease in the Maritime Alps, Norway, Sweden and the Baltic Provinces, States of Livonia and Esthonia, largely due to the death of a number of lepers during the war in the last mentioned area. In Russia the present numbers are quite unknown; in Japan leprosy is said to be decreasing yearly as the result of prophylactic measures, the number known being placed at 16,261 in 1919, which is far less than some earlier estimates; in Brazil 7,224 cases were registered in 1921, but there are many unknown



cases. A number of the French tropical colonies, particularly Cameroun, are severely infected, the sum total being estimated at 80,000. The Belgian Congo is infected throughout with unknown numbers.

Etiology was dealt with at the second sitting, which opened with a paper on the relation of leprosy to humidity by L. ROGERS (this *Bulletin*, Vol. 20, p. 821). Then followed an important paper by the Secretary of the Congress, M. E. MARCHOUX, on rat leprosy and its transmission to man, in which he showed that the bacillus is rapidly killed by drying or by a temperature of 60°C., cannot be cultivated, and is as essentially parasitic as the human form, while it can readily be inoculated through a slight abrasion of the skin, or even through epilation; these observations strongly suggesting a similar mode of infection in human leprosy, through close association with an infective leper. The bacilli in both forms may also remain long latent in lymphatic glands, the organism being anaerobic according to this worker. The vexed question of the cultivation of the lepra bacillus was inconclusively discussed by KEDROWSKY and others, and Professor STANZIALE spoke on his well-known work on inoculation of rabbits' eyes with leprosy material. A. PALDROCK of Dorpat described branching lepra bacilli containing acid granular bodies, which he considered to be reproductive elements, but MARCHOUX pointed to the low resisting power of the organism as opposed to this theory.

The third sitting, devoted to the comparative pathology of leprosy, began with an interesting paper by MARCHOUX on the progress of the infection in which he showed the close similarity with tuberculosis. Latent leprosy with spontaneous cures is believed not to be rare, and concomitant infections may favour the development of active leprosy, as has also been shown by MUIR, whose paper on the nomenclature of leprosy follows. The disease is divided into quiescent, inflammatory and resolving phases of activity applicable to all cases, and into dermal, including nodular and diffuse varieties, and nervous, either of ascending or metastatic distribution.

A number of clinical papers follow, the most interesting being J. DARIER'S on tuberculoid lesions closely resembling those of lupus, containing extremely few bacilli and occasional giant cells and showing alterations in sensibility. [Similar cases have been described by MUIR in India, where they are common.] Professor JEANSELME, the President, and others, discussed the pigmentary, and M. HIRSCHBERG the bony changes in leprosy, while Professor G. H. MONRAD-KROHN of Christiania dealt with the neurological aspect on the lines of his recent book. K. MITSUDA of Japan describes a reaction at the site of injection into the skin of an emulsion of a fresh leprosy tubercle broken up and boiled for two hours in water and diluted to contain 1 gramme in 10 cc. of 0.5 carbolic acid, the dose being 0.05 cc. In 403 lepers a hyperaemic reaction appeared at the end of 48 hours, which disappeared completely in a few days in nodular cases, but in 79 per cent. of macular and nerve cases it increased up to 15 days to form a papular infiltration lasting for over a week. In old persons not associated with lepers and in a healthy attendant (for twenty years) on lepers similar prolonged reactions were met with, and MITSUDA considers that healthy attendants should be thus inoculated to increase their resistance, as the slight short reactions in nodular lepers are thought to be a sign of absence of any resistance. The same worker discussed the question of the curability of leprosy, pointing out that though there is a tendency for the less resistant macular cases to become nodular and the more resistant



to develop into the nerve form, all forms may disappear sooner or later and some cases clear up completely. The Bordet-Wassermann reaction in leprosy was next discussed without much result, and Dr. M. GUILLEN described a particular albuminous reaction as diagnostic of leprosy. The same worker, after pointing out that successful treatment depends on early diagnosis, describes the first symptoms in order of frequency as (1) nervous symptoms of pain, atrophy or anaesthesia; (2) affections of the skin of the face and extremities and (3) obstruction and the formation of crusts in the nose.

An important section on Treatment brings out a very general consensus of opinion of the great value of the new methods of injecting the soluble products of chaulmoogra oil, especially in the form of the ethyl esters, while some remarkable results are also recorded by K. MITSUDA with the prolonged use of injections of chaulmoogra oil itself, a number of photos illustrating the results of such treatment continued in most advanced nodular cases for from two to five years being reproduced. R. F. PARRA and J. E. SANTOS, reporting on the extensive use of the esters in Colombia, tabulate 127 cases, the great majority of which, especially the nodular cases, showed improvement, though final conclusions regarding ultimate results must be awaited. E. RABELLO & I. VERNET of Brazil come to very similar conclusions, but add that ethyl chaulmoogrates may also be used in prophylaxis. Dr. GOUZIEN, the head of the French Colonial Medical department, reported favourably on the use of the new methods by various French Colonial medical officers, but points out that great care is required in the case of leprosy complicated by tuberculosis. Papers by M. ROBINEAU and by L. ROGERS deal with methods which have already been reviewed in this *Bulletin*, as do those of H. GUGEROT on injections of eparseno, which have not fulfilled the expectations aroused by the first reports, and of A. PALDROCK on the local application of carbonic acid snow. In the final resolutions the necessity of supplying the best treatment in all leper institutions was emphasized.

Prophylaxis provided some interesting papers. E. MARCHOUX, in discussing the mode of contagion, considered that latent unrecognized cases might be more dangerous than obvious ones, since they are not avoided. E. RABELLO & J. MOTTA report the great efforts now being made by the Brazil Government to deal with lepers in accordance with rules drawn up by Dr. C. CHAGAS in 1920, including compulsory notification and hospital or domiciliary isolation, the former preferably in agricultural colonies; marriage of lepers is permissible only under condition of the separation of any infants from birth, these measures being in accordance with the resolutions of the Rio de Janeiro leprosy commission of 1918; the Brazil Government has also made it obligatory on all medical students to be instructed regarding leprosy, an advance which should be introduced into all leprosy infected countries. The Government has voted 6,000,000 francs annually for the work, 1,823 of the 7,220 known lepers are already isolated, and six more colonies to accommodate 5,600 lepers are being arranged for; when these are completed Brazil will have set an example to other nations in her liberal provision for lepers. An American Leprosy Conference at Rio de Janeiro in October, 1922, recommended meetings every fourth year, and the formation of associations in each country to further prophylactic and research work on leprosy. An association for the help of lepers is being formed in Brazil.

Japan, in 1917, also made important advances in prophylaxis, as described by K. MITSUDA, arrangements being made to enlarge the



five leper hospitals to accommodate 4,500 patients, including the greater part of the contagious cases, as well as a hospital for the close study of 500 cases. The difficult question of the separation of the sexes has been carefully considered, the advisability of separation being weighed against the danger of formation of unnatural habits. During the last nine years 170 males have voluntarily submitted to vasectomy to prevent the procreation of children born to danger or misery, the fact that in progressive cases sterility ensues sooner or later as a result of the disease being cited in favour of this procedure. [The Americans have also adopted this wise measure in Panama.] Age figures show that 41 per cent. came to hospital by the age of 20 and 63 per cent. by 25, and 4 men were admitted to 1 woman, although the proportion in the whole country is  $2\frac{1}{2}$  to 1, while 58 per cent. were nodular, 31 per cent. anaesthetic, and 11 per cent. macular. The most frequent causes of death were pulmonary tuberculosis 28 per cent., nephritis 20 per cent., and pneumonia 5-6 per cent. In Cambodia C. MATHIS says that the lepers there were recently officially estimated at 1,200 in a population of 2,500,000, and that nothing appreciable has yet been done to deal with the problem; he advocates compulsory isolation of begging lepers. L. ROGERS deals with the present position of prophylaxis in British Colonies, and shows that while compulsory segregation has been followed by considerable diminution in the number of known lepers in those West Indian Islands that enforced it, an increase took place in those which neglected the measure, while little has yet been done in our badly infected tropical African possessions, where the problem is a most difficult one. The African problem is also dealt with by M. ROBINEAU in connexion with the badly infected Cameroons, where it is one of the chief medical problems, and there are now 578 lepers in three leprosaria, together with five villages containing 179 among 125,000 inhabitants in the Ebolowa division. The greatest difficulty is experienced in collecting the lepers, attempts to do so through the native chiefs or through guards failed completely; the only successful plan is to send selected lepers in pairs touring through the infected villages, who explain the care taken of them in the settlements, with the result that they generally return within a week bringing 10 to 15 new lepers with them. H. C. de S. ARAUJO gives a long account of prophylaxis in Guiana and Trinidad, including an interesting description of the new Trinidad settlement on the Island of Chacachacare, which will be a great improvement on the Corcorite asylum in the suburbs of the capital of the colony.

The last section dealing with legislation opens with a paper by E. MARCHOUX, in which he pleads eloquently for abandoning the harsh measures of the middle ages, and for treating leprosy on similar lines to the closely allied tuberculosis, the latter being the more infectious and dangerous of the two. Hospitals and dispensaries within reach of the patients' friends should be provided in place of distant segregation, special attention being paid to early diagnosis and efficient treatment; the marriage of lepers among themselves should not be forbidden as long as any offspring can be removed from their care, and the Norwegian mild isolation measures should be carried out, although under certain circumstances more severe measures may be necessary to deal with wandering lepers. For these purposes compulsory notification, with domiciliary isolation where practicable, and for others, especially indigents, comfortable leper homes, or, as



in Annam, a leper quarter in the villages. The isolated patients should be efficiently treated and provided with employment and amusements, and the people instructed in the precautions necessary to avoid infection from lepers. Other papers give the laws in Brazil and in Japan, and the report ends with the resolutions of the congress.

L. Rogers.

MARCHOUX (E.). **A Lepra em nossos dias. Etiologia-Prophylaxia.**—*Rev. Med.-Cirurg. do Brasil*. 1924. July. Vol. 32. No. 7. pp. 339-354. [3 refs.]

The first part of this paper might serve as an introduction to the bacteriology of leprosy. The second deals with rat-leprosy and points out analogies between it and the human disease. There are certain morphological differences in the organisms, notably the terminal swelling of the bacillus in the rat form; also it is readily inoculable and may be transmitted by flies direct, but not after an interval of more than 24 hours. There is no evidence of any insect vector in the true sense. Intraperitoneal inoculation produces extensive visceral lesions. In the rat, as in man, cases of latent leprosy occur, *i.e.*, infected individuals showing no clinical signs of the disease. Cases in which the leprosy lesion is small may undergo spontaneous cure. Emulsion of the spleen pulp of a leper was injected into a rabbit, a guineapig and six rats. Five of the last became infected, but not the others. The question of the susceptibility of man to the rat form is not decided.

H. Harold Scott.

COOK (Cecil). **Leprosy in Australia.** [Correspondence.]—*Med. Jl. Australia*. 1924. Sept. 27. 11th Year. Vol. 2. No. 13. pp. 336-337.

The writer states that in spite of leprosy having been a notifiable and quarantinable disease for three decades it is still as prevalent as ever in some of the States. This he attributes to the early stages not being recognized or not reported by medical men, since in the case of a small outbreak among the natives at Roebourne, Western Australia, prompt isolation of the first four cases stamped out the disease, as should be possible in other places. In Queensland only cases found to be bacteriologically positive are isolated, but arrangements should be made to examine all cases at regular intervals to detect the early infective stage, while cases outside the lazarets should receive no regular treatment; as is not yet the case. Medical men should be taught to recognize early cases, and sanatoria-like conditions should be provided for lepers.

L. R.

PAGÉ (J. D.). **Leprosy in Canada.**—*Canadian Med. Assoc. Jl.* 1924. Sept. Vol. 14. No. 9. pp. 824-825.

Leprosy was first discovered in New Brunswick in 1815 and a lazaretto built at Tracadie in 1844, to which lepers were admitted later



from other parts of Canada, the Federal Government taking it over in 1869. A few years later the D'Arcy Island lazaretto was opened in British Columbia; it has recently been transferred to Bentinck Island, and now has nine patients, while Tracadie has ten, only four of whom now show active disease, the rest being mutilated quiescent cases. The average physician fails to recognize the early stages which may be a danger to others. The importance of early diagnosis cannot be too much emphasized, because if a leper is discovered within five years of his arrival in Canada he can be sent back to his native country, and because of "the marvellous results obtained of late years from the treatment with hypodermic injections of ethyl esters of chaulmoogra oil."

L. R.

HOFFMAN (Frederick L.). **The Leprosy Situation in the United States in 1923.**—*Jl. Amer. Med. Assoc.* 1924. Nov. 22. Vol. 83. No. 21. pp. 1707-1708.

The Federal leprosarium was opened at Carville in 1921, and by October 1st, 1924, 297 patients had been admitted. Letters addressed to every State Health Officer revealed most cases in the Southern States and California, nearly half those at Carville coming from Louisiana. Many of the States are now free, while only a few lepers are known in most of these remaining infected, the great practical value of the Federal leprosarium being already evident.

L. R.

MARTIN & DEKESTER. **Contribution à l'étude de la lèpre au Maroc et en particulier dans la région de Fès.**—*Arch. Inst. Pasteur d'Algérie.* 1924. June. Vol. 2. No. 2. pp. 204-218. With 1 fig. [12 refs.]

This further report on leprosy in Morocco shows that the disease is frequent in the country. A map shows that the cases mostly occur north of Fez, while the disease is believed to date back to the time of the Phoenicians. Notes of seven cases treated with eparseno are considered not to allow of any general conclusions regarding its value, but they show that the high doses advised by J. HASSON may be dangerous. The establishment of leprosaria on the lines of agricultural colonies with a hospital, and not as prisons, is advised.

L. R.

MORISSEAU. **Considérations sur l'étiologie de la lèpre au Soudan.**—*Rev. Méd. et Hyg. Trop.* 1924. May-July. Vol. 16. No. 5. pp. 129-133.

The writer confirms ROGERS' observations on the influence of climate on the incidence of leprosy, the regions of the Soudan with a short rainy season and a dry climate showing few lepers, while there are many lepers further South in the hot humid climate of the Boho-



Bouques area. Here, too, since the inhabitants wear few clothes and have no ideas of hygiene, and flies are very abundant, infections are more numerous. The people also eat earth, possibly contaminated by flies, which the author thinks more easily spread the lepra bacillus than mosquitoes. He considers that infection is more likely to take place through the alimentary canal than through the skin, but produces no evidence in favour of that theory and admits that it is not proved.

L. R.

MORGAN (F. G.). **Report on the Investigation of a Number of Cases of Leprosy at Nauru, Central Pacific.**—*Commonwealth of Australia Dept. of Health Service Publication.* No. 25. 24 pp. With 1 chart in text.

This is an interesting report on a careful investigation of a recent outbreak of leprosy in a small island under the complete control of a Company, where 39 cases have been discovered since 1920, all but two among the local inhabitants, probably originating from a Gilbert Island woman between 1911 and 1914, and spreading from three main centres of infection. Routine nasal swabbing proved of no value in detecting early cases, only two cases, both advanced, out of 29 being positive, but smears from excised suspicious lesions gave positive results, although not infallible. Early macules most frequently appeared on the upper arms, and in maculo-anaesthetic cases a piece of tissue excised without pain from the centre of a patch enabled bacilli to be found in 7 out of 17 such cases. The cases have been all isolated and are being treated efficiently, and new cases are being watched for, so the further progress of this outbreak will be of great interest.

L. R.

DE ALBUQUERQUE (Oswaldo Cavalcanti). **Formas clinicas e symptomatologia da Lepra.**—*Rev. Med.-Cirurg. de Brasil.* 1924, July. Vol. 32. No. 7. pp. 364-371.

The author presents in this paper a brief résumé of the symptomatology of leprosy. He mentions first the site of entrance of the bacillus and the variable incubation period, and then passes on to describe "cutaneous leprosy," dividing the disease into four periods: (1) That of the development of the maculae which may be hyperchromic, hyperaemic or achromic. During this there are various trophic and sensory symptoms; (2) the nodular period, which merges into (3) the period of evolution of the nodules; (4) progress and termination, death resulting in many cases from intercurrent disease.

The nervous form is divided into a period of invasion, followed by that of eruption which may resemble one or other of those of cutaneous leprosy, but is often pemphigoid. This is succeeded by a "neuritic" period which passes into the degenerative phase with consequent anaesthesia, amyotrophy and mutilation.

H. Harold Scott.



- i. HUDELO & PIERROT. **Gomme du dos du nez à bacilles de Hansen au cours d'une lèpre tuberculeuse.**—*Bull. Soc. Française Dermat. et de Syph.* 1924. July. No. 7. pp. 355-356.
- ii. DORE (S. E.). **Case of Leprosy.**—*Proc. Roy. Soc. Med.* (Section of Dermat.) 1924. Dec. Vol. 18. No. 2. pp. 16-17.
- iii. BRAYTON (Nelson D.). **Leprosy, with Report of a Case in Arizona.**—*Southwestern Med.* 1924. Oct. Vol. 8. No. 10. pp. 480-483. With 1 fig.
- iv. HOLDERMAN (H. H.). **Leprosy: Report of a Sporadic Case developing in Pennsylvania.**—*Jl. Amer. Med. Assoc.* 1924. June 14. Vol. 82. No. 24. pp. 1927-1928. With 2 figs. [8 refs.]
- v. BARRERA (F. de P.) & CHAVARRÍA (A. Peña). **[The Acute Phases in Chronic Leprosy.]**—*Rev. Méd. de Bogota.* 1924. Vol. 42. p. 69. [Summarized in *Jl. Amer. Med. Assoc.* 1924. Oct. 18. Vol. 83. No. 16. p. 1281.]

i. The writers record a case of leprosy with febrile attacks, accompanied by the formation of a sort of semi-fluctuating gumma-like swelling in the nose, which on puncture yielded a sero-purulent fluid containing Hansen's bacillus.

ii. A nodular case in a boy of 14, who developed leprosy this year. His father, with whom he lived for ten years, had suffered from anaesthetic leprosy since the child was eleven months old, having been born in this country and never left it, so the child must have been infected in England.

iii. A sporadic case of nodular leprosy of an advanced stage; the patient had come from Mexico, and had returned after being deported there.

iv. An early case of nodular leprosy in a woman aged 26. She had lived for many years in Brazil before coming to the United States in 1920, and presented no features of special interest. The author makes the curious statement that in Calcutta the nastin treatment is now used.

v. This paper deals with observations already noticed. (See this *Bulletin*, Vol. 21, p. 864.)

L. R.

- LARA (C. B.), DE VERA (B.), SAMSON (J. G.) & EUBANAS (F. C.). **Chief Causes of Death among Lepers at the Culion Leper Colony.**—*Jl. Philippine Islands Med. Assoc.* 1924. Aug. Vol. 4. No. 8. pp. 289-306. [11 refs.]

This paper supplies much valuable information on a subject regarding which little has been recorded. Since its establishment almost eighteen years ago the colony has been a small town with the people living in their own houses under natural conditions, while during the last two years the new treatment has been carried out on a large scale with the aid of four additional physicians, and post mortems have been performed in one-third of the fatal cases; clinical records extend back to 1908. 360 recent autopsies showed the most frequent causes of death to have been Tuberculosis 24.0 per cent., Nephritis 16.3 per cent., Broncho-pneumonia 9.3 per cent., Dilatation of heart 7.6 per cent., Endocarditis 5.0 per cent., Amoebiasis 3.3 per cent., Lobar pneumonia 3.0 per cent., Gangrene 2.3 per cent., Leprosy 2.3 per cent. and other diseases in still smaller proportions. The earlier less accurate clinical records showed much higher figures for leprosy itself and for beriberi,



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TABLE 4.  
CHIEF CAUSES OF DEATH IN TREATED AND UNTREATED GROUPS OF PATIENTS, MAY, 1922, TO DECEMBER, 1923.

Group.	Total Deaths.	Tuber- culosis.		Nephritis.		Heart Disease.		Pneu- monia.		Gangrene Sept. Inf.		Dysent. or Enter.		Leprosy.		Cerebral Hemor.		Malaria.		Other Dis.	
		No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Treated ..	282	91		74		28		19		9		9		7		6		6		32	
			32.2		26.2		9.9		6.7		3.1		3.1		2.4		2.1		2.1		11.3
Untreated ..	415	309		41		26		9		4		2		11		7		1		5	
			74.4		9.8		6.2		2.1		0.9		0.4		2.6		1.6		0.2		1.2

NOTE.—Patients who received treatment for only a short time were not included in this table.



The high rate from tuberculosis in the untreated is due to that class containing a much greater proportion of tubercular patients, who do not stand the treatment well. Nephritis, on the other hand, gave almost three times as high a proportion in the treated class, in spite of more early cases being included among them; indicating that the prolonged use of the ethyl ester chaulmoogrates damages the kidneys in some cases. Deaths from organic heart disease, chiefly due to acute dilatation, were also slightly more common among the treated, as well as from acute concurrent affections, which is, however, attributed to the patients being stronger and engaging in activities exposing them to infections. Deaths from leprosy were about equal in the two groups, no decrease among the treated being evident, owing to the treatment occasionally exciting an acute exacerbation of the disease ending fatally or to repeated reactions leading to debility and emaciation; there is evidence to show that tuberculosis-complicated cases died sooner under the treatment, which is not now given in such cases, the tubercule death rate having since fallen slightly in 1923. The increase of nephritis deaths from 8.2 per cent. in 1922 to 18.4 per cent. in 1923 is undoubtedly due to the treatment, while in some it ended in acute dilatation of the heart. The nephritis occurred most in early cases, and tuberculosis in late nerve cases. Death from leprosy itself increases up to the 15th year of the disease, and then decreases owing to the tendency to arrest.

L. R.

KOBAYASHI (Wasaburo). [On a New Method of Detection of *Lepra Bacillus* in Testicular Tissues, and on Early Diagnosis of Leprosy.]—*Hifuka Kiyo*. (*Arch. of Dermat.*) 1924. Jan. Vol. 2. No. 3. [Summarized in *Japan Med. World*. 1924. Oct. 15. Vol. 4. No. 10. pp. 269-270.]

"The author examined the puncture fluid of the testes in numerous cases of leprosy and could demonstrate the bacillus from the fluid even from cases having no outward changes in the testes, even if the bacteriological examination of other materials should prove negative. He extols the necessity of the puncture examination of the testes for the early diagnosis of leprosy." The summary does not state if the method was popular with the patients.

L. R.

HASSELLTINE (H. E.) & GORMAN (P. J.). A Comparative Study of the **Schultze-Tigges** and the **Ziehl-Neelsen** Methods of Staining *B. leprae*.—*Public Health Rep.* 1924. Oct. 24. Vol. 39. No. 43. pp. 2683-2685. [1 ref.]

The writers have tested the new method described by SCHULTZE-TIGGES in duplicate slides to those stained by Ziehl-Neelsen from 100 lepers, snips of skin and nasal scrapings being taken for the purpose, and find the older method slightly more efficient; it is also easier for the microscopist's eye than the yellowish pink background of the new method.

L. R.



NICOLAU (S.) & BANCIU (A.). **Sur une particularité différentielle de la réaction de Bordet-Wassermann dans la syphilis et la lèpre.**—*C. R. Soc. Biol.* 1924. Dec. 19. Vol. 91. No. 36. pp. 1352-1354.

The writers' experience with the Wassermann test agrees with that of others. They obtained positive results in 22 out of 27 lepers, but on using the method of progressive dilutions with physiological salt solution in cases of leprosy and syphilis giving positive reactions they found that the titre of the reaction in lepers greatly surpassed those of syphilis. In syphilis the fixative power of the serum was lost at from the fortieth to the fiftieth dilution, while in 18 cases of leprosy it ranged from 1 in 70 to 1 in 280 dilutions, obtained by mixing 0.1 cc. of leprosy serum with 1-5, 1-10, 1-20, etc., of salt solution and using 0.1 cc. of the freshly made mixture for the test. In only four cases was fixation not obtained below 1-20 or 1-30 dilutions, all mixed cases, two of which were predominantly nerve cases. They have found this method of great value in the diagnosis of leprosy, including incipient cases.

L. R.

SCHÖBL (Otto) & BASACA (M.). **Contribution to the Serology of Leprosy.**—*Philippine Jl. Sci.* 1924. July. Vol. 25. No. 1. pp. 1-9. [2 refs.]

The authors have tested the globulin precipitin test by the following simple method. Blood is taken from a vein and the serum allowed to separate in a test tube wetted with normal saline; 0.2 cc. of serum is placed in each of a series of small tubes, to each of which 0.6 cc. of distilled water is added carefully to avoid its mixing with the serum with Wright's pipettes, one tube remaining undisturbed and the other mixed thoroughly by shaking, the tests being performed not more than five hours after taking the serum. A preliminary reading was made after standing at room temperature (average 27° to 28°C.) and again the next morning after placing in a refrigerator; a distinct contact ring, or a diffuse cloudiness in the mixed tube and a sediment in each at the final reading, most marked in the mixed tube, indicated a positive reading. Tables are given of the results in a selected series of cases, which indicate that all forms of leprosy, treated and untreated, early and advanced cutaneous cases, bacteriologically negative nerve and presumably cured cases, gave positive results, although less pronounced in the cured than in the active cases; while the control healthy sera were all negative. On the other hand, the Wassermann test was only positive in 35 per cent. of the cases. To establish a standard strength for the reaction the sera were diluted 1:1, 1:2, 1:3, 1:4 and 1:5 in both lepers and non-lepers, and no positive reactions were found in non-lepers with dilutions of 1:3 or less, but they might occur in dilutions of 1:4, the cured cases giving less marked reactions than active ones. The reaction is promoted by a low temperature and does not always occur at a high one. The reaction in leprosy is considered to be due to "an upset balance between the salts and globulin, possibly euglobulin."

L. R.



LEÃO (Antonio Eugenio de Arêa). [In Portuguese and English.] **As reacções de Wassermann e de Sachs-Georgi na lepra. The Wassermann and Sachs-Georgi Tests in Leprosy.**—*Mem. Inst. Oswaldo Cruz*. 1923. Vol. 16. No. 1. In Portuguese pp. 47-57. In English pp. 59-69.

The author refers to previous literature, and then records his own experience, which cannot be better summarized than in his own conclusions :

" 1. In leprosy, the Wassermann test is frequently positive. In 50 per cent of cases with antigens of luetic liver (from foetus with hereditary syphilis), of cholesterinised human heart and of cholesterinised ox-heart ; in 32 per cent. of cases with the antigens of acetone-insoluble lipoids (NOGUCHI or BORDET processes) and in 14 per cent. of cases with LESSER's antigen (ethereal extract of organ).

" 2. The degree of fixation varies greatly according to the antigens employed. It is, however, the antigens prepared with liver of foetus with hereditary syphilis and those with cholesterinised ox-heart that give the greatest fixation.

" 3. The greatest number of positive Wassermann reactions is given by the macular (87.5 per cent.) and tubercular (65.2 per cent.) forms of leprosy. The nervous form of the disease furnished 17.7 per cent. of positive reactions.

" 4. The cause of complement fixation by leprosy serum when mixed with a syphilitic antigen is certainly to be explained by the poly-fixing properties of the serum.

" 5. The Sachs-Georgi test in leprosy gives a total percentage of 36 per cent. positive reactions.

" 6. The greatest percentage of Sachs-Georgi positive reactions is given by the macular form of the disease (62.5 per cent.), the next greatest by the tubercular form (39.2 per cent.). The nervous form gives a percentage of 17.7 per cent. positive Sachs-Georgi reactions."

L. R.

MUCHOW (Hermann) & LEVY (D. M.). **Een sero-diagnostische leprareactie.** [A Sero-Reaction of Diagnostic Value in Leprosy.]—*Nederl. Tijdschr. v. Geneesk.* 1924. Nov. 15. Vol. 68. 2nd Half. No. 20. pp. 2461-2464.

The following extract was prepared : A leprosy nodule was triturated with a mixture of equal parts of alcohol 96 per cent. and of physiological salt solution, the quantity used being equal to five times the triturated mass of tissue. The whole was left at room temperature for eight days. Then it was filtered and inactivated at 56°C. for half an hour. Of this extract 0.2 cc. was mixed with 0.5 cc. of a 10 per cent. solution of NaCl and 0.2 cc. of the serum of a leper (4 cases) or a man not suffering from this disease (4 cases). After shaking thoroughly, the mixture is centrifuged. The reaction is considered to be positive if the test-tube, when shaken, shows flakes floating in the fluid. It was strongly positive in all of the four cases of lepra, completely negative in the others. The serum of 33 patients suffering from other disease (among which there were 18 suffering from various dermal diseases) was tested in the same way, with a negative result. If the extraction of the leprosy tissue was performed with alcohol 96 per cent. alone, the reaction proved negative ; with equal parts of alcohol 96 per cent. and ether or with physiological salt solution alone the specificity was lost, the non-leprosy sera sometimes showing a slight positive reaction.

N. H. Swellengrebel.



MARIANI (Giuseppe). **Osservazioni sopra una forma speciale di allergia cutanea nella lebbra (lepra tubercoloide sperimentale nell'uomo).** [A Special Form of Cutaneous Anaphylaxis in Leprosy.]—*Pathologica*. 1924. Sept. 15. Vol. 16. No. 380. pp. 471-477.

The author excised a recently developing leprous nodule, rich in bacilli, but still covered with intact skin, and emulsified it. Part of the emulsion was injected subcutaneously and intraperitoneally into guineapigs and white mice. An inflammatory reaction ensued with disintegration of the bacilli, but no nodules developed. The remainder of the emulsion was used for the intradermal reaction in 10 lepers, 8 of the nodular or mixed form and 2 of the purely nervous. In the former there was erythema with itching and a sense of heat, followed in 3-6 days by a faintly visible infiltration. There was no febrile reaction nor any glandular enlargement. The whole disappeared in 8-12 days. Repeated examinations showed that the bacilli rapidly disappeared and in 3 days there were merely a few scattered granular organisms seen.

In patients suffering from the nervous form there was a very slight local reaction with itching in 4-8 days, no rise of temperature. After 10 days there was some infiltration, and local swelling developed slowly with the formation of a central vesicle by the 20th day which attained the size of an orange pip, and was surrounded by a reddish, dense border. The lesion reached its maximum development in 30 days and remained thus for the next 10 days, after which it gradually receded, finally clearing up, with some central loss of tissue, in about 60 days. There were no constitutional symptoms nor any enlargement of glands. The bacilli which were abundant in the inoculated emulsion showed similar disintegration as with the nodular type of cases. The reaction in the nervous form was more of a granuloma-like nature than in the nodular. The remainder of the paper is devoted to an account of the histological changes produced. The reverse of the above experiments, namely, inoculation of tissue from a nerve-leprosy patient into one with the nodular form has not yet been carried out.

H. Harold Scott.

READ (Bernard E.). **The Toxicity of Chaulmoogra Oil (Oleum Hydnocarpus).**—*Jl. Pharm. & Experim. Therap.* 1924. Oct. Vol. 24. No. 3. pp. 221-257. [39 refs.]

This is a valuable paper on the little investigated subject of the toxicity of chaulmoogra oil when administered in large doses to animals either orally or by injections of the oil itself or of the ethyl hydnocarpate made from it, rabbits being chiefly used in the experiments. The author concludes.

"1. The toxic affect of chaulmoogra oil is first manifest in producing anorexia, nausea and emesis.

"2. The character of the emetic effect is probably both that of a local irritant and that of a central excitant. The central action is most pronounced and is produced irrespective of the path of administration of the drug.

"3. There is evidence of a cumulative central effect, which after a succession of therapeutic doses may produce emesis and anorexia.



"4. The emetic and other toxic effects of chaulmoogra are apparent after the administration of ethyl hydnocarpate. On account of its solubility, hydnocarpic acid, as the glyceride or the ethyl ester or as a salt, is probably the most active constituent of chaulmoogra preparations.

"5. Toxic doses of the hydnocarpates show hemolysis of blood cells, renal irritation with hemoglobinuria, and fatty infiltration of the liver. When injected subcutaneously and intravenously there is local irritation, often leading to necrosis of tissue.

"6. Ethyl hydnocarpate injected intravenously into a dog produces a marked increase in the lymph flow.

"7. The M.L.D. of chaulmoogra oil to rabbits by mouth is 5 cc. per kilogram of body weight. Ethyl hydnocarpate by intravenous injection produces death after 0.5 cc. per kilogram of body weight.

"8. Fatal doses of chaulmoogra oil given to rabbits produces a hypersensitivity with lowered blood calcium and inco-ordinated movement, followed by a period of convulsive retching of a strychnine-like character. Death results from respiratory failure.

"The local pulmonary effect is considered to be less important than that active centrally, which produces excitement with subsequent paralysis associated with deafness and blindness, and loss of control of the motor nerves.

"9. There often occurs a rise in temperature following the intravenous injection of ethyl hydnocarpate. A fatal outcome is preceded by a fall in temperature.

"10. Administration of therapeutic doses of the hydnocarpates to dogs assists the well-being of the animal as demonstrated by the general appearance and by increase in weight; but when given to rabbits maintained on a plain oat diet it has an intense toxic effect. There is produced anorexia, albuminuria, loss of body weight, and eventually death."

L. R.

ROUILLARD (J.). *Chaulmoogrates et morrhuates de soude : leur emploi dans le traitement de la lèpre et de la tuberculose.*—*Presse Méd.* 1924. Nov. 22. Vol. 32. No. 94. pp. 929-931. [6 refs.]

A long abstract of the Croonian Lectures of 1924. [See above, p. 208.]

L. R.

MUIR (E.) assisted by DE (N. K.), LANDEMAN (E.), ROY (T. N.) & SANTRA (I.). *The Preparation of Hydnocarpus Esters and their Use in Leprosy.*—*Indian. Jl. Med. Res.* 1924. Oct. Vol. 12. No. 2. pp. 221-233. With 1 text fig. & 3 plates.

The authors point out that *Taraktogenos kurzii*, from which true chaulmoogra oil is obtained, grows in rather inaccessible places in Burma and North East India, and its fruit ripens and falls during the rainy season, when the forests are practically inaccessible, so the fruit is not obtained fresh; but *Hydnocarpus wightiana*, with which they deal in this paper, grows freely in a wild or cultivated state in South and West India, and its oil, which is at least equally effective in leprosy, is easily and cheaply obtained in unadulterated form, while on cultivation it fruits abundantly and at all seasons of the year after 6 or 7 years' growth, and is readily grown from fresh seed. In Calcutta the esters are now prepared solely from this oil, and can be made cheaply and simply by either of the following processes:—



" 1. *Hot process*.—425 grammes of crude, cold drawn hydnocarpus oil, 552 cc. of 96 per cent. ethyl alcohol, and 31.87 cc. of sulphuric acid (sp. gr. 1.845) are placed in a 2½ litre flask fitted with a reflux condenser, the alcohol and oil being mixed before adding the acid. The contents of the flask are allowed to boil vigorously on a water bath for four hours without intermission. Under the influence of the mineral acid catalyst, the glycerol radicle in the glyceride of the oil changes place with the ethyl group in the alcohol, forming the ethyl ester and glycerol. The reaction product is then transferred to a separating funnel and washed with an equal volume of water twice over, and then with a 0.2 per cent. solution of sodium carbonate in water which forms a thick emulsion; after half an hour crystals of common salt are gradually added in small quantities and brought in contact with the emulsion by slowly rotating the vessels so as to break the emulsion. As this takes place the water forming in the lower layer is gradually removed and the upper layer consisting of esters is filtered through thick filter paper. The esters, though now clear, still contain a certain amount of fine emulsion which makes them dark in colour. This may be removed rapidly by drying in a steam oven for two hours or by leaving at room temperature for 5 or 6 days, when the fine emulsion will sink to the bottom, whence it may be removed. The esters are then filtered again and the process is complete.

" 2. *Cold process*.—This takes a considerably longer time than the hot but it has the advantages that no special apparatus is required, labour is less, and any therapeutic value which would be destroyed by boiling is preserved. The oil, alcohol and acid are mixed in the same proportions as in the hot process in a 4 lb. bottle with a tightly fitting glass stopper and left until the process of esterification is complete. The bottle should be shaken once or twice a day to mix up the upper and lower layers. This hastens the process, as does also the placing of the bottle in the sun or in some warm place. Neither the shaking nor the heat is, however, essential if time is not a consideration. To begin with, the oil forms a lower and the alcohol and acid an upper layer. As esterification proceeds a point is reached at which the lower layer, now chiefly composed of esters, gains a less specific gravity than the upper layer, which now contains a large proportion of glycerol, and therefore rises to the top. To ensure the completion of the esterification it is well to allow the process to continue further for half the time which elapsed between the mixing of the ingredients and the rising of the lower layer. Thus, if the lower layer takes 14 days to rise, the ingredients should be left in the bottle for 7 days longer. The lower layer is then drawn off and the upper layer, consisting of esters, washed according to the method mentioned under the 'Hot Process.' The esters may be washed in the same bottle in which they have been prepared by substituting for the glass stopper a cork stopper perforated with two glass tubes, the one two inches in length inserted flush with the inner end of the cork and fitted with a piece of rubber tubing compressed with a spring clamp, and the other reaching from the cork to the bottom of the bottle. By inverting the bottle the esters rise to the top and the lower layer may be drained off by opening the spring clamp. Or the lower layer may be syphoned off through the long glass tube without inverting the bottle.

" The weight of the esters recovered is almost equal to the weight of oil used."

If *Hydnocarpus wightiana* is grown in all leprosy countries, as it should be, every leper institute could easily make its own esters by one of the above methods at very little cost. They may be bottled or put up in ampoules and sterilized at 120°C. for half an hour, while the pain and local reaction on injection can be very much reduced by adding an equal quantity of olive oil before sterilization; 3 per cent. iodine added to the esters will kill even anthrax spores in three days, and 1 per cent. iodine will safely sterilize the esters without the aid of heat,



and they may then be kept in glass-stoppered bottles for use on a large scale. Only three unimportant abscesses have occurred in many thousands of injections. The dose of equal parts of the ester and olive oil ranges from 0.5 to 10 cc. intramuscularly or subcutaneously, best into the soft parts of the gluteal muscle with the patient sitting down, or subcutaneous injections may be given beneath the lesions on the extensor surfaces of the limbs, the needle being inserted in several directions through two punctures at opposite edges of the lesions to distribute the dose and hasten its absorption; up to 4 cc. may be given in this manner and any excess into the gluteal region. Intravenous injections have practically been given up on account of coughing and pain in the chest sometimes following them. The initial dose of 0.5 cc. may be increased by 0.5 cc. at each bi-weekly dose up to the highest tolerated dose without raising the temperature to 100°F. for 24 hours or producing a local inflammatory reaction in the lesions. The addition of either creosote, or probably better thymol in the proportion of 8 grammes to 50 cc. each of undistilled hydnocarpus esters and olive oil, enhances the action, although thymol alone is inferior.

The treatment should be continued until all lesions have disappeared, except permanent nerve ones, and repeated negative bacteriological examinations have been made. Where failures have been reported either the treatment has not been carried out thoroughly and persistently with attention to diet, hygiene, etc., or unsuitable cases, with permanent lesions (due to nerve or tissue destruction) have been chosen. Early cases naturally give the best results, so early diagnosis is essential.

To clear up the question of the value of different oils, esters of hydnocarpus with a closed carbon ring, and the highest specific rotation, and linseed oil with highest iodine value and amount of unsaturated fatty acids, were tried, and the former gave 6 per cent. cleared up completely and 54 per cent. much improved, against 1 per cent. and 49 per cent. with linseed esters; while coconut esters, with the lowest proportion of unsaturated fatty acids, were less effective than linseed ones, so that both the closed carbon ring and the amount of unsaturated fatty acids appear to be factors of value. Illustrations of chaulmoogra and hydnocarpus seeds, as well as of the *Hydnocarpus wightiana* tree, are given, one of two years old being six feet in height. This paper contains many other points of minor practical interest and should be read in full by all who have to treat leprosy.

L. R.

WILSON (R. M.). **Chaulmoogra Oil and Ethyl Esters in Treatment of Leprosy.**—*China Med. Jl.* 1924. Sept. Vol. 38. No. 9. pp. 743-745. With 1 fig.

This paper opens with the cheering sight of a photograph of 59 lepers, who have been discharged as apparently cured after treatment with chaulmoogra oil, while on May 1st, 1924, 75 patients were discharged apparently cured and 40 more are expected to be ready for discharge in a few months. All these have been treated in Korea by injections of the oil, given by themselves, which in Dr. Wilson's experienced hands has yielded better results than the ethyl esters obtained from the Peking Union Medical College and from Dr. SHIGA of Seoul Hospital; after two years' use, with an average treatment of



six months, the lepers refused to continue the esters, as they complained of dryness of the skin, eye troubles, including disturbance of vision, general weakness and loss of strength, headache, muscular pain, or failure to improve.

The treatment now used successfully consists of weekly subcutaneous injections of 3-8 cc. of sterile chaulmoogra oil [species not mentioned, but *Hydnocarpus anthelmintica* is the common Chinese variety] to which 1 per cent. of camphor has been added, only slight pain resulting from the shallow injections into the muscles now given. During the past year 575 cases on the average were under treatment, half on injections and half on oil orally. After two or three years' injections the patients are so far restored to health that they continue on oil orally. Baths twice a week, regular work and good hygiene are equally important, and marked improvement is observable in three to six months' treatment. Complications are treated and infectious cases isolated, but those with tuberculosis improve but little.

L. R.

HEINEMANN (H.). **Ueber Behandlung der Lepra mit Thymol.** [Treatment of Leprosy with Thymol.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1924. Dec. Vol. 28. No. 12. pp. 523-525. [3 refs.]

The writer claims to have improved on HAMZAH's method of treating leprosy by intramuscular injections of 10 per cent. thymol in codliver oil [this *Bulletin*, Vol. 21, p. 182], by using intravenous injections of 651a, a thymol emulsion prepared by VON HEYDEN, and used by KRUTZSCH in tuberculosis. The first dose for adults is 0.2 cc., increased by 0.2 cc. at each injection up to a maximum of 0.8 cc., which can be continued every fourth day for months without harm, only slight cough being produced. He has treated 70 cases of leprosy, and given over 1,000 injections, and reports striking improvement in a relatively short time, although it is too early to say if cures can be obtained. As is so usual with German work, the exact composition of the new preparation is not published in this paper.

L. R.

TOURNIER (E.). **De l'emploi du kermès dans le traitement de la lèpre.**—*Bull. Soc. Path. Exot.* 1924. Nov. 12. Vol. 17. No. 9. pp. 761-765. [5 refs.]

Favourable reports of the use of antimony salts in tropical diseases, including leprosy, led him to look for a less toxic preparation than tartar emetic, and to treat two cases of leprosy with kermes (*Stibium sulfuratum rubrum*) alone, and two in conjunction with atoxyl and novarsenobenzol with favourable results, especially in the nodular and mixed cases. In adults daily oral doses of 0.50 to 0.60 cgm. in water are given without nausea or albuminuria and can be continued for nearly two months, while it is not depressing, and its use can be combined with ethyl chaulmoogrates or other treatment. In the nodular cases marked improvement, accompanied by breaking up of the bacilli into granules, was noted within a month or two, while the pains of the nerve form are also alleviated greatly. The method is so simple and easily carried out that it is worthy of a more extended trial, no cure having yet been obtained with it.

L. R.



WALKER (Norman). **A Case of Leprosy. Treated by a Vaccine prepared from a Nodule from the Patient's Arm. With a Note on the Preparation of the Leprosy Vaccine by LISTON (Glen), and a Note on the Histology of the Case by DAWSON (J. W.).**—*Lancet*. 1924. Sept. 13. pp. 542-543. With 1 coloured plate & 1 text fig.

An advanced nodular case of leprosy, in which after a few injections of chaulmoograte of sodium this treatment was abandoned on account of the pain produced. As the author had found a vaccine prepared from tuberculous glands of value in lupus, he got Lt.-Colonel Glen LISTON, I.M.S., to make a sterile emulsion in normal saline of a removed nodule after grinding it in a mortar with sand; the emulsion was heated to 60°C. for half an hour, diluted with carbol saline to contain roughly 200 million lepra bacilli per cc., and put up in ampoules. The first dose of 0.1 cc. was gradually increased to 1 cc. without any severe reactions. Improvement began within three weeks, and after two months was very marked, the large nodules on the arms having nearly disappeared in that time, as shown in a coloured plate, while the general condition had also improved, the result so far being apparently greater than in previously recorded cases of this method of treatment. Sections of nodules before and after treatment showed a great diminution of the rod-shaped bacilli with disintegration of many of them into acid-fast dots, together with some fibrosis of the tissues.

L. R.

GOODHUE (William J.) & HASSELTINE (H. E.). **Report of Reexamination of a Child in whom Leprosy developed at Nineteen Months of Age.**—*Public Health Rep.* 1924. Oct. 24. Vol. 39. No. 43. pp. 2680-2683.

This child of leper parents, at the Molokai settlement of Hawaii, developed leucodermic patches on the right cheek and on the back of the thighs (without anaesthesia) of doubtful nature, and a reddish-brown slightly-raised nodule, in sections of which acid-fast bacilli were found, the leucodermic patches and nasal smears being negative. The child had been removed from leprous surroundings within six hours of birth, as is now the custom of the colony, and had not since been in contact with lepers, and appears to have been the first child so removed to have developed leprosy among about 100 born in the settlement since their early isolation has been carried out. Four months after the excision of the nodules there was no evidence of the progress of the disease and the scar was free from acid-fast bacilli, this being in October, 1915; the child was kept separate from the other healthy children. In May, 1916, a few atypical acid-fast bacilli were found in the scar of the excised nodule, and the child was declared a leper and returned to her parents in the colony, although the writers now think that further observation would have resulted in negative findings.

On January 8th, 1923, the child, now 10 years of age, was re-examined, and only showed some old standing leucodermic patches with normal sensation, and the scar at the site of the former nodule was negative bacteriologically, as were nasal smears. On June 21st, 1924, negative findings were again obtained, and there is now no evidence of her being a leper, although she had received no anti-leprous treatment other than the excision of the nodule, and she is considered to be free from the



disease. The writers add: "This belief is strengthened by the results more recently obtained by us by the surgical removal of nodules in other patients who have a few nodules which are small and well defined." [This is a most important observation, especially in view of the numerous cases now coming forward in the earliest stages of leprosy, and it supports MUIR's contention that many of the first noticed lesions are the site of primary infection through the skin, for which early excision is now clearly indicated. If the value of this measure is confirmed by further experience it will be still easier to attract the early cases for treatment, with ultimately more rapid diminution of the incidence of the disease.]

L. R.

RHO (Filippo). **Cupric and Cyanocupric Preparations in the Therapy of Tuberculosis and Leprosy.**—*Jl. Trop. Med. & Hyg.* 1924. Dec. 1. Vol. 27. No. 23. pp. 315-320. [32 refs.]

Professor Rho of Italy, after giving the history of the ancient use of copper compounds in tuberculosis, and the recent use of cyanocupric compounds by KOGA and his followers in Japan in both tuberculosis and leprosy, narrates his own work on the subject in Italy, where Professor SERONO made a series of such salts, since the Japanese workers, in accordance with the practice of their German teachers, have not revealed the precise nature or mode of preparation of the compounds they used. A stable soluble compound named Cuprocyan, consisting of a double cyanide of copper and potassium, containing 22.26 per cent. of copper, and having the form of white clinorhomboidal crystals, very soluble in both water and alcohol, was made; a 2 per cent. solution is sold in 2 cc. ampoules, containing 4 mgm. of cuprocyan, one of which may be injected every other day hypodermically or intramuscularly with little pain. For slow intravenous injection every five to seven days 10 cc. phials are also supplied, the first dose being 5 cc., followed by 7½ and then 10 cc. doses, and either form of treatment may be continued for many months with occasional intervals. Another preparation, called cupriodase, is a lipoid compound of copper, iodine and cholesterin, used for local applications in surgical tuberculosis and to destroy the lesions of leprosy.

In pulmonary tuberculosis good results are claimed in first and second stage cases, but not in the third stage, while the cuprocyan is reported to lead to the formation of fibrous tissue around the lesions. In leprosy 20 cases treated in Sicily and Sardinia by cuprocyan intravenously gave improvement after 10 injections in almost all the patients, while cupriodase locally produced healing of local ulcers except perforating ones. Microscopically nodules were found to become fibrosed and the bacilli became fewer and broke up into granules with marked benefit, although the author cautiously adds that in such a chronic disease "it is quite impossible to think of putting a definite stop to the relapsing manifestations of the malady, unless with a very long treatment, even of many years." It is suggested that this method of treatment might be used with advantage in addition to the chaulmoogra oil preparations.

L. R.



- i. SCHÖBL (Otto) & KUSAMA (Hiroshi). **Chemotherapeutic Experiments with Chaulmoogra and Allied Preparations. III. The Disinfecting Power of the Vapors of Vegetable Oils toward Acid-Fast Bacteria.**—*Philippine Jl. Sci.* 1924. Apr. Vol. 24. No. 4. pp. 443-445.
- ii. —. **IV. A Survey of Certain Organic Compounds as to their Growth-Inhibiting Activity toward Acid-Fast Bacilli in Vitro.**—*Ibid.* Aug. Vol. 25. No. 2. pp. 123-134. [2 refs.]
- iii. —. **V. An Inquiry into the Mechanism and Nature of the Growth-Inhibiting Effect of Chaulmoogra and other Vegetable Oils.**—*Ibid.* pp. 135-150. [13 refs.]

i. These experiments were carried out by exposing the surface of glycerine-meat-infusion-agar slants, recently inoculated with a vigorous strain of human tubercle bacilli, to any vapours given off by about 0.1 cc. of the substances tested placed on the inner end of the cotton plug, which was quickly reinserted into the tube and sealed with liquid paraffin; freshly inoculated cultures of staphylococcus, cholera vibrio and dysentery and coli bacilli also being tested. The vapours of chaulmoogra and hydnocarpus oils showed no disinfecting action on the acid-fast bacilli, but many essential oils, including bergamot, cinnamon, caryophyllum, eucalyptol, Pinus sylvestris and turpentine, completely inhibited the growth of one loopfull of viable tubercle bacilli incubated at 37°C. under these conditions.

ii. This is a highly technical paper on further tests of the growth-inhibiting activity on cultures of tubercle bacilli of various organic compounds, by adding them in solution or mixture to culture media, as in former series, with the following results :—

"1. Water-soluble compounds showed an antiseptic effect, whereas the fat solvents such as benzol, toluol, xylol, carbon trichloride, and carbon tetrachloride which have a strong hypnotic effect were found to be only slightly antiseptic or not at all.

"2. Sodium, copper, and nickel salts of fatty acids were found about equally effective, whereas zinc, strontium, lead and uranium salts showed no effect.

"3. The double-bond-containing compounds all showed antiseptic effect, the double bond being more effective on the side chain than on the ring in aromatic compounds.

"4. Unsaturated alcohols showed an antiseptic effect, particularly when containing the phenyl group which proved to be the most powerful toxic group.

"5. High alcohols approaching waxes showed no effect. Secondary alcohols were equally or less effective than primary alcohols.

"6. Hydroxy compounds are highly antiseptic toward acid-fast organisms, as they are toward other bacteria.

"7. The antiseptic effect of phenols increases with the number of hydroxyl groups, the position of these groups being of importance, as the ortho-compounds are more antiseptic than the para or meta compounds.

"8. Alkylation on the ring increases the antiseptic effect of phenols, whereas alkylation on the OH group of polyhydroxy-phenols has no noteworthy effect, provided at least one hydroxyl is preserved free.

"9. The amino group ( $\text{NH}_2$ ) has a reverse effect on the antiseptic power of the aromatic compounds, inasmuch as it has no effect when located on the ring but is strongly antiseptic when linked to the ring directly on the side chain. It acts as a haptophore group, and the strong effect of benzylamine is no doubt due to the function of the phenyl group.

"10. Open-chain terpenes are more effective than their cyclic isomers.



" 11. In the cyclic hydrocarbons the double bond in the ring seems to be of importance in the presence of other groups on the ring, but not in itself."

iii. This paper discusses the way in which chaulmoogra and other oils act against acid-fast bacilli in the light of the extensive experiments of the author, from which he comes to the following interesting conclusions:—

" 1. The degree of unsaturation of vegetable oils which stimulate the growth of acid-fast bacteria and of those which inhibit the growth of acid-fast bacteria has no relation to their growth-stimulating or growth-inhibiting activity.

" 2. The growth-stimulating effect of certain vegetable oils is due to the glyceryl and not to the acid part of the oil.

" 3. The condition of unsaturation of the oils containing the acids from the chaulmoogra series and of the oils which stimulate the growth of acid-fast bacteria is paramount.

" 4. Saturated chaulmoogra oil lacks the growth-inhibiting activity toward acid-fast bacteria which is possessed by the unsaturated oil.

" 5. The growth-inhibiting activity of chaulmoogra oil depends on the structure of the ring of the fatty acids. When the structure of the ring is changed by saturation with hydrogen the oil loses this biologic property.

" 6. There are indications that, due to physical properties, acids from the chaulmoogric series containing a short side chain are more effective in vitro than are those having a long side chain.

" 7. Acid-fast bacteria adapt themselves to the acids from the chaulmoogric series in due time and then withstand larger doses than they did originally."

The adaptation of the acid-fast bacilli to the action of the chaulmoogra fatty acids explains the frequency with which patients cease to improve after a long course of the treatment with ethyl chaulmoogrates, and indicates a change in such cases to preparations from other oils or other drugs of benefit in leprosy.

L. R.

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[See this *Bulletin*, Vol. 21, pp. 861, 864.]

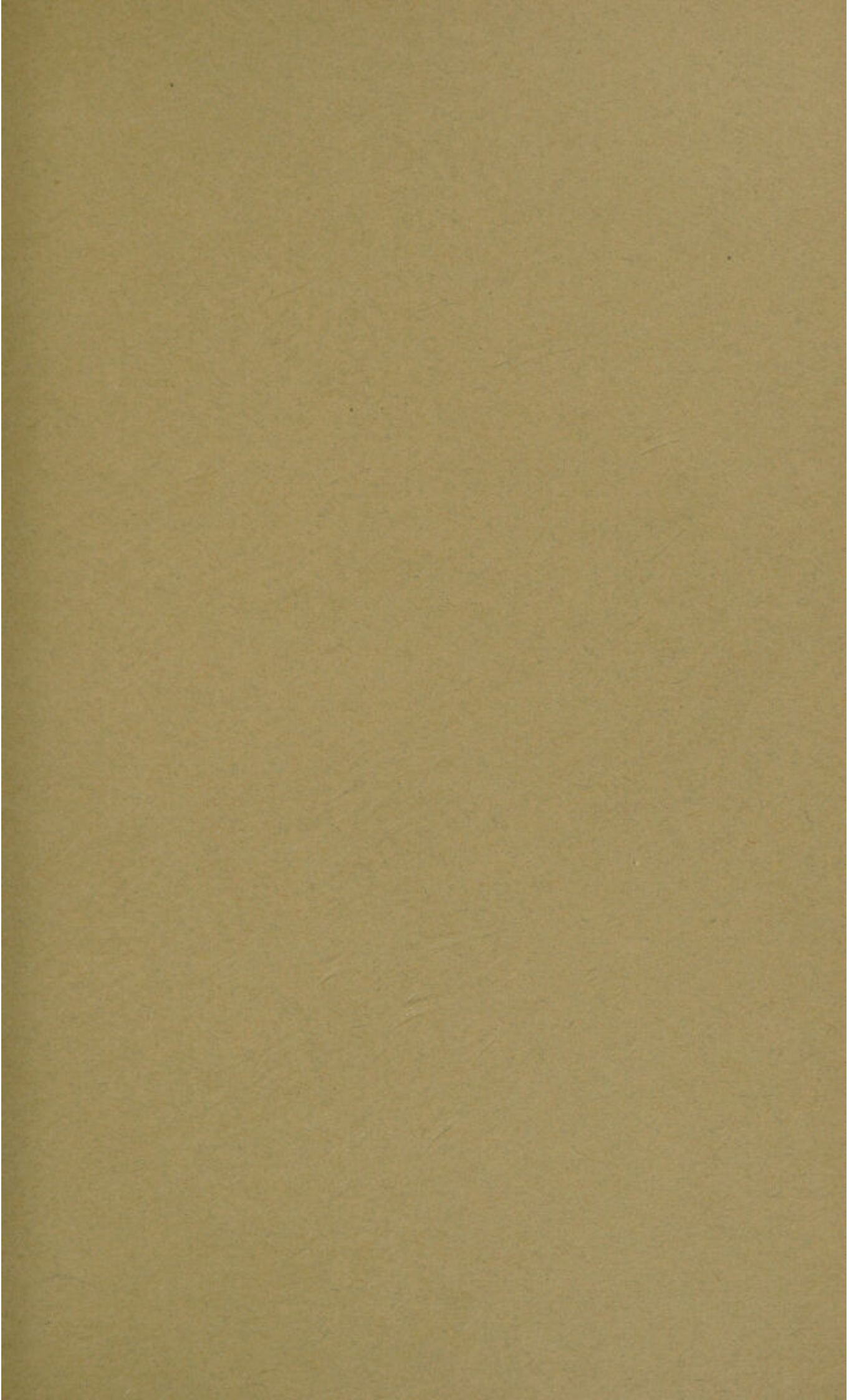
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