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ABSTRACTS

Retention and Differentiation of Mycobacteria in Tissue Section. J. H. Hanks. Am. Rev. Tuberc., 1956, 74, 608.

Rapid deparaffinization and turbulent interactions between alcohol and solvents and alcohol and water cause the loss of mycobacteria from paraffin-embedded sections. This loss can be decreased by slowing the deparaffinization, by avoiding the use of alcohol, and by differentiating and decolourizing in aqueous reagents. Sulphuric acid differentiators and acidified sulphates as decolourizers are the best, because of their fixative action and their high selectivity in discharging carbolfuchsin from tissues, while leaving it in mycobacteria. A more sensitive and reliable method of obtaining essential information on mycobacterial lesions may be that of making impression films directly from the cut surfaces of organs.

Retention and Differentiation of Carbolfuchsin-stained Mycobacteria in Diagnostic Films. J. H. Hanks. Am. Rev. Tuberc., 1956, 74, 597.

The best demonstration of mycobacteria in diagnostic films depends more on other factors than the choice of the primary stain. These other factors comprise the use of protective protein films to cover or imbed the mycobacteria; the use of reagents which exert fixative rather than disruptive effects on cells and protein films, namely carbolfuchsin solutions, alcohol buffered at mild acidities, and acidified sulphates, whereas acid-alcohol is destructive; the use of judicious rather than excessive staining with carbolfuchsin; the use of decolourizing agents which keep the carbolfuchsin in mycobacteria while displacing it from cells, and in this matter acidified sulphates are better than acid-alcohol, alcohols buffered at mild acidities, and citric, hydrochloric and nitric acids; the use of sulphuric differentiators containing dilute methylene blue; the use of the differentiators in such concentrations as will permit of timing their action to end points. The paper gives details of materials and methods and discusses observations made and the factors concerned.

The Present State of the Leprosy Problem in Minas Gerais. J. Mariano, Arquivos Mineiros de Leprologia, Oct. 1956, No. 4, 416-426.

In the state of Minas Gerais, Brazil, there were 26,263 recorded cases at the end of 1955. Lepromatous cases comprise 66.89%;

tuberculoid 21.60%, and indeterminate 11.50%. The prevalence index varies in the 14 zones of the state from 4.2 to 40.1 per thousand, in a total population of 7,877,566. The 6 leprosaria in the state cost the Government about £337,000 in 1955, and for advances in the leprosy campaign it is estimated that an annual expenditure of about £50,000 will be needed, to cover staff including 14 leprologists, medication, equipment, food, etc. The leprosy service is to be interwoven with the general health service, and great benefits are expected to follow the introduction of domiciliary treatment, BCG vaccination of contacts, census of contacts and search for early cases, and health education of the people.

The Uptake of DDS by Leprosy Patients as Detected by Tracer Technique. **K. T. Chatterjee, R. K. Poddar, N. Mukerjee and R. Bose.** Bull. Cal. School of Trop. Med., 5: 4, 1957.

Studies on the DDS uptake by 22 leprosy patients using radioactive tracer technique showed that on oral administration there was initially a rapid increase to reach 8% of the dose in about 6 hours. The level then gradually decreased at an average of 62% a day to almost nothing in about 5 days. Excretion via the kidneys deals with about 78% of the drug within a week, at an average rate of excretion of 42% per day. The drug level in bone marrow and healthy tissues ran almost parallel to that in blood. The drug concentration was 10 times greater in affected than in healthy tissues. Findings after subcutaneous administration were similar to those after oral. The tracer technique was found to be 10 times more sensitive than the colorimetric.

Haematological Effect of Adding Yeast and Iron to DDS in the Treatment of Lepromatous Cases. **N. Mukerjee and N. R. Sen.** Leprosy in India, Vol. XXVII, No. 4, Oct. 1956, 121-127.

The authors refer to the results of Dharmendra and Chatterjee, S. N. (1953) which showed that the routine use of yeast and iron was not necessary during the sulphone treatment of leprosy. They have studied 36 lepromatous cases to which a DDS product was administered, and of these 12 were given the DDS product alone, 12 had yeast added 0.5 gm. to each 50 mgm. tablet of DDS, and 12 had in addition 1.5 grains of ferrous sulphate. They found that the blood picture before and after gave no indication that these additions counteracted the tendency to produce anaemia, nor do they help very much in improving the blood picture subsequently.

Estados Reacionais na Lepra. (Reactional States in Leprosy.) N. Souza Campos and P. Rath de Souza. Rev. Brazil. de Leprologia, 25, Jan.-March, 1957, pp. 3-18. 20 illustrations.

This paper represents a valiant attempt to bring order into the confusion in the clinical phenomena massed under the name of lepra reaction, or leprotic reaction. The authors make a comparative study under four heads: (1) lepra reaction (erythema nodosum); (2) tuberculoid reactivation; (3) reactional tuberculoid; (4) borderline lesions.

(a) As regards *origin*, the first only intervenes in lepromatous cases, in about 60% of them; it can be the initial manifestation of the disease; it begins acutely. *The second* intervenes in the course of the chronic evolution of quiescent tuberculoid macules; it begins slowly. *The third* begins acutely in the tuberculoid form and in rare cases may follow a reactivation attack; it can appear as a primary manifestation in apparently healthy persons. *The fourth* begins acutely, secondary to the reactional tuberculoid form in relapses, or in apparently healthy individuals as a primary manifestation.

(b) As regards the *type of the eruption*, the first shows lesions of erythema nodosum type, which are polymorphic with many degrees of swelling, and often there are neuritic, ocular, and orchitic complications, and frequent relapses. In *the second*, the pre-existing lesions show infiltrated reactivated margins, increase in size, and take on a reddish colour. New lesions may appear, and they never appear abruptly as in reactional tuberculoid. In *the third*, the lesions are polymorphic, there being tubercles, nodules, plaques, and patches of erythema. The colour is purple and vinous, and the lesions are strongly infiltrated, swollen, and succulent. There is a site of election on the palms and soles, eyebrows, and the nasolabial furrow. *The fourth* has the same aspect as the reactional tuberculoid. The colour tends to be rusty, and the outer borders are indistinct, and infiltration is less marked. Flat pigmented lesions often occur in association.

(c) As regards *systemic phenomena*, the first is always accompanied in the acute forms by fever, sepsis, arthralgias, headache, neuritis, gland swellings, weakness. These are less marked in the more chronic forms. *The second* does not show systemic phenomena. *The third* rarely shows them in the acute manner, but there are moderate joint pains, a mild increase in temperature, and a cutaneous hyperaesthesia. Some cases do not show any general effects at all. *The fourth* has almost always some general signs.

such as pains and oedema of the large joints, fever, and headache. Often these patients have to remain in bed.

(d) As regards *evolution*, *the first* tends to be chronic, relapsing acutely and subacutely, with residual ecchymoses and local thickening. *The second* stops in the reactivation phase and the case returns to its chronic evolution, often with the lesions increasing in size and number. Relapses can evolve into reactional tuberculoid. *The third* stops in the acute phase and most cases tend to clinical cure. Relapse cases have a tendency towards borderline lesions. *The fourth* stops in the acute phase and often the lesions take on the lepromatous aspect; rarely do they resolve or take on the characters of the reactional tuberculoid form.

(e) As regards *bacilli in smears from the skin and nasal mucosa*, *the first* is positive as a rule, rarely negative. *The second* remains negative before, during, and after the attack. Almost always positivity coincides with a tendency to change into reactional tuberculoid. *The third* is often positive in the beginning and during the acute phase, the bacilli being abundant and globi absent. The skin is more often positive than the mucosa. There is a tendency to negative smears in a variable length of time. *The fourth* is positive as a rule before and during the attack, with globi. In negative cases there is a tendency to regression to reactional tuberculoid.

(f) As regards *the lepromin reaction*, *the first* is always negative. *The second* is almost always frankly positive before, during and after the attack. *The third* is either positive or negative in the beginning and during the attack, tending to be more positive as the attack recedes. *The fourth* is always negative and remains so; in exceptional cases there may be a positive, but it is weak.

(g) As regards *structure*, *the first* shows an acute inflammatory exudate on top of the pre-existing lepromatous infiltrate. Bacilli are present, with a granular aspect, or absent, and lipids are present. *The second* shows acute inflammatory features added to the classic tuberculoid granuloma; there is a variable amount of vascular dilation, endothelial swelling, and oedema with consequent loosening up of the foci. In general bacilli and lipids are absent. *The third* shows a tuberculoid structure which is less typical than in tuberculoid reactivation, combined with vascular dilation, endothelial swelling, and intra- and extracellular oedema with consequent vacuolization and separation and loosening up of the infiltrative foci. Bacilli are almost always present, and lipids are absent. *The fourth* shows a picture intermediate between reactional tuberculoid and lepromatous. There are always plenty of bacilli, with globi. Lipids have not yet been studied sufficiently.

Histopathological Findings in a Case of Tuberculoid Leprosy. **D. G. Jamison and R. G. Cochrane.** Trans. Royal Soc. of Trop. Med. & Hygiene, **51**, July, 1957, p. 301.

This is a report of a demonstration specimen at a laboratory meeting of the Society. The lesion in a case of tuberculoid leprosy had been biopsied in the skin at the centre and at the margin; also the area adjacent to the lesion, and a segment of the nerve supplying the affected skin was removed. Silver-impregnated sections and haematoxylin and eosin stained sections were prepared. The former showed a relatively abrupt diminution of nerve fibres towards the zone of the lesion but there was a full complement of nerve fibres in the skin adjacent to the lesion. Silver-impregnated axis cylinders were much fewer at the margin of the lesion, and in its centre there were none at all. In both places empty and infiltrated Schwann cell pathways were still to be seen. Sections from the parent cutaneous nerve showed nerve destruction like that in the centre of the lesion.

Haematoxylin and eosin sections from the centre of the lesion showed a flattening of the epidermis, and in the subjacent dermis an extensive infiltration which included round cells, epithelial cells, and multinucleated giant cells, the picture typical of tuberculoid leprosy.

In the haematoxylin and eosin nerve section there was gross distortion of the pattern of bundles of nerve fibres. A central necrotic zone lay within the epineurium, surrounded by a cellular infiltration like that seen in the dermis of the centre of the lesion. Sensory tests (Lele, Sinclair and Weddell, 1954. J. Physiol., **123**, 187) showed that the skin adjacent to the lesion had normal sensation, but the centre of the lesion was anaesthetic to touch. The margin of the lesion had diminished sensation and impaired localization.

“ *Correlação Entre os Resultados da Leitura Clínica e do Exame Histopatológico da Reação de Mitsuda* ’ (*Correlation between the results of the clinical reading and the histological examination of the Mitsuda reaction*). **L. M. Bechelli, P. Rath de Souza and R. Quagliato.** Revista Brasileira de Leprologia, **25**, Jan.-Mar., 1957, 21-58.

The authors have made a careful correlative study of the Mitsuda reaction in its clinical and histological aspects. They sought information on the following questions:—(1) Is the $1+$ reaction always associated with a positive histology? (2) What is

the significance of a 1+ in prognosis? (3) Is there any difference in the histological picture of 1+ and 2+? (4) Does the reported unfavourable evolution in some 2+ cases contradict the prognostic value of the lepromin test? (5) What is the significance of a reaction with a slight thickening of the skin or a small papule under 3 mm. in diameter? (6) Can a new standard for reading the Mitsuda reaction emerge from the correlation with the histology?

In 118 cases of leprosy and 21 contacts the authors biopsied the site of the lepromin injection at about 30 days. Their histological interpretation was based on the following standards:—(a) *A positive histology* when there was a chronic inflammatory granulomatous infiltrate of a certain degree, with predominance of epithelioid cells, and tuberculoid structure, and the bacilli absent or very few; (b) *A negative histology* when there was a simple chronic inflammatory infiltrate with bacilli usually absent or few, or a granulomatous infiltrate without tuberculoid structure but made up of histiocytes and there being a great number of bacilli; (c) *A histology tending towards a positive* when the chronic inflammatory infiltrate is not totally granulomatous nor mostly made up of epithelioid cells, and these are grouped in places; giant cells may be present but are rare, and bacilli are absent or rare.

In their studies they found that the positivity in (c) above had a certain validity at the less definite end of the scale, especially if considered in relation to the clinical type. In their correlation of clinical with histological interpretations they found that the positive histology was not seen at all *in the clinically negative lepromin tests*, but a negative histology in 90%, and in the rest the histology tending towards a positive. *In doubtful lepromin tests*, about 64% had a negative histology and the rest had the histology tending towards a positive. *In the 1+ lepromin tests*, about 60% had a positive histology, about 27% had the histology tending towards a positive, and the rest a negative histology. *In the 2+ lepromin tests*, about 58% had a positive histology, about 23% tended to a positive, and the rest had a negative histology. *In the 3+ lepromin tests*, about 84% had a positive histology and the rest the histology tending towards positive, and there was no case with negative histology. *In ulcerated lepromin tests* without nodule there was a negative histology in the 2 cases found. Considering their results the authors remark on the clear histological picture of the negative and 3+ lepromin reactions. They think that the doubtful clinical reading may be associated with a certain degree of body resistance in about one-third of the cases. They draw attention to the considerable similarity in the histology of the 1+ and 2+, in the intensity and

quality of the infiltrate, as well as the frequency of each type of infiltrate. There may sometimes be a negative histology in the 1+ and 2+ reactions. They think that the certificate of definite arrest of leprosy should include a consideration of the lepromin test, the aim being to reach 2+ for formerly indeterminate and lepromatous, though 1+ would do for patients where the histology was positive. They found that the pure histology did not enable them to distinguish the intensity of the reaction 1+ and 2+, but a 3+ can usually be distinguished. In lepromatous cases which were already bacteriologically negative a clinically positive lepromin was rare, and its histology was uncertain in significance; there was no frankly positive histology. In indeterminate and tuberculoid leprosy and in contacts there was a definite histological positivity in the 1+ and 2+ reactions. In quiescent tuberculoid leprosy negative histology was never seen, whether with the 1+, 2+, or 3+. Prognostic value of the reaction they think is indicated by the histology to be as follows:—for about a third of the doubtful reactions a certain degree of resistance; for 1+ and 2+ a definite degree of resistance, but not much difference between 1+ and 2+; for 3+ an efficient resistance.

They suggest that the lepromin test in future might be read in a new way, putting the 1+ and 2+ in the same group, so that there would be readings possible of negative, doubtful, 1+, and 2+, the last being the highest. The paper has 7 illustrations of histological findings, 3 tables of results and data of case histories of patients of the study grouped under their lepromin results.

Lepra Conjugal: Estudo Epidemiológico dos Casos Observados no Dispensário do D.P.L. em Campinas, S.P. (1934-1954)."

R. Quagliato. (*Conjugal leprosy: epidemiological study of the cases observed in the dispensary of the Sao Paulo Leprosy Department at Campinas, Sao Paulo, 1934-1954*). *Revista Brasileira de Leprologia*, 25, Jan.-Mar., 1957, pp. 59-68.

From the records of 7,062 contacts of leprosy patients of the twenty-year period, the following table emerged:—

Relation	Totals of contacts	Developed leprosy	%
Children of patients ...	2,064	206	9.9
Brothers or sisters of patients	1,365	121	8.8
Conjugal partners of patients	639	50	7.8
Parents of patients ...	400	36	9.0
Others ...	2,594	87	3.3
	<u>7,062</u>	<u>500</u>	

Of the 50 conjugal contacts who developed leprosy, 52% were males, and the lepromatous incidence was 37% in the males and 41% in the females. The duration of living contact was up to 10 years in 44%, and the apparent incubation period was up to 5 years in approximately 94%.

A *leading article* in the *Lancet* of Aug. 17, 1957, pp. 330-331, is worthy of study by leprosy workers, as it gives a valuable short account of *gamma-globulin deficiency*, with 42 references to the workers in this field. The interest of leprosy workers will be aroused by the possibility of using this congenital condition to enlarge our understanding of resistance to disease. Hypogammaglobulinaemia is however rare in occurrence, and if leprosy workers wish to be able to use this "experiment of nature" for studies to throw light on leprosy resistance, they should be prepared to be able to recognise it. Gamma-globulin ranges in normal children are 600 to 1300 mgm. per 100 ml. In hypogammaglobulinaemics values of 0 to 30 mgm. per 100 ml. will be found. As the serum antibodies occur in the gamma fraction, the importance of the grave deficiency in it will be seen. The defect seems to be one of production, and there is a remarkable associated deficiency of plasma cells in the tissues. It is accepted by most workers that antibodies are formed mainly in the plasma cells.

Maruskenie Temperatury i Electrosoprotioliajemosti Irmennenykh i Vneshne Zdorovykh Vchastkov Kozhy Rannikh Projavleniyakh Lepry. (*Disturbance of Temperature and of Electrical Resistance in the Clinically Healthy Parts of the Skin, and in the Affected Parts of the Skin, in the Initial Stages of Leprosy.*) A. Letichvskaia. Sbornik Nauchnykh Rabot po Leprologii i Dermatologii (Collected Scientific Papers in Leprosy and Dermatology), N. 8, 1956, pp. 105-109. Rostov-on-Don Experimental and Clinical Leprosarium of the Ministry of Health of the U.S.S.R.

In the early stages of leprosy the study of autonomic disturbances in the skin by instrumental methods gives helpful information. The author measured the temperature of lesions and of outwardly healthy patches of skin, using an electric thermometer, and the electro-resistance by an ohmmeter. The electro-resistance of the skin indicated the degree of humidity of the skin. There were 73 patients in the investigation, of whom 14 were lepromatous, 13 tuberculoid, and 46 indeterminate. In erythematous and in

erythemato-hypopigmented lesions with definite outlines, it was found that the skin temperature was raised and the electro-resistance was lowered (corresponding to a raised skin humidity). In erythemato-hypopigmented lesions with a 'cyanotic edge' but without clear outlines, and also in hypochromic, achromic, and dystrophic patches of skin, the skin temperature was relatively lowered, but the electro-resistance raised (meaning that the skin humidity was lowered). On skin patches showing some changes brought out by a nicotinic acid test, in some cases there was a rise in temperature and a lowering of electro-resistance (a rise in humidity). There was relatively less disturbance of temperature and electro-resistance than in the frank lesions. Thus the author thinks that instrumental methods of investigation make it possible to reveal the presence of autonomic changes in the early stages of leprosy, and to determine the degree of these disturbances, and so provide a valuable practical diagnostic method.

Perforation of Gall-bladder during Prednisone Treatment. **G. L. Mouzas and J. H. Briggs.** Brit. Med. J., Aug. 24, 1957, 450-451.

They report the first case of this under corticosteroid therapy. The subject was a man of 45 years with psoriasis and rheumatoid arthritis. He had received previous treatment with cortisone in 1953, and prednisone acetate in 1955, and again in 1956. During the last he developed an acute abdominal condition which came to operation, where a posterolateral perforation of the wall of the gall-bladder was found. Cholecystectomy was carried out and hydrocortisone was given during the operation and corticotrophin post-operatively. Proteinuria was present up to the 10th day and was traced to amyloid involvement of the kidney. The histological study of the gall-bladder revealed amyloidosis. The patient made a good recovery.

Ensaios de Imunização contra a Lepra pela BCG. (Trials of BCG in immunization against leprosy.) **A. C. Pereira Filho.** Thesis published at Juiz de Fora, Brazil, 1955, pp. 151. 22 illustrations. Faculty of Medicine of Juiz de Fora.

Prof. Pereira Filho in his thesis studies the subject fully and reports much original work, and gives full attention to the work of others. He thinks the dispensary and the preventorium were of great value in the leprosy campaign, but with the advent of the sulphones and more particularly of BCG, the dispensary draws

ahead in importance. The favourable protective results of BCG even make it possible to dispense with the preventorium, and after protection by BCG the children can be cared for in a creche. In his studies of the Mitsuda reaction in leprosy he finds that it is universally valuable in prognosis, and it indicates the degree of resistance to leprosy for subjects of it as well as those who are free of it. The early Fernandez reading indicates only the degree of allergy, whereas the Mitsuda indicates the immunity. Children from a leprosy focus, or children not from such a focus, usually become reactive to the Mitsuda from 2 years of age. The reaction falls off rapidly in intensity after 60 years of age. Even 2 years after its application the Mitsuda may exert a mild influence towards awakening or reinforcing the immunity. The Mitsuda is especially valuable for separating contacts into immune and non-immune, and in discovering the grave cases. The author found that tuberculosis is a definite factor which directly or indirectly changes the Mitsuda reaction from positive to negative, and confirms the immunological connection between tuberculosis and leprosy, and that BCG can bring allergy and immunity towards *M. leprae*, as shown in data from preventoria and dispensaries. There is, however, a dissociation between tuberculin allergy and the Mitsuda reaction, and leprosy does not give immunity against tuberculosis. The origin of the immunity indicated by the Mitsuda is still not entirely understood: children living in an environment free of tuberculosis and leprosy can give a positive response. The practice of giving BCG by mouth in 3 doses of 0.2 gm. monthly was found to be effective 100% in conversion to a positive Mitsuda. BCG was also found to help the therapeutic action of the sulphones. Mitsuda conversions obtained by BCG were maintained over 4 years of observation.