BOOK REVIEWS

The Lysosome. By CHRISTIAN DE DUVE, of the Catholic University of Louvain, Belgium. Scientific American **208** (1963) No. 5 (May) pp. 65-72.

> "This small particle acts as the digestive tract of the living cell. Its enzymes dissolve the substances ingested by the cell, and under certain circumstances can dissolve the cell itself."

The foregoing statement is part of the heading of this article, which is an adequate and well-illustrated description of the new intracellular particle, or structure. Such particles were first characterized chemically because of a chance observation, made in 1949, in work on rat liver cells after homogenization and differential centrifuging to separate the various formed elements of the homogenate. At one time it was thought that they might be the mitochondria, but in 1955 they were identified by electron microscopy.

In the living cell these bag-like particles contain the intracellular enzymes. Normally their surface membrane is able to retain the enzymes, acting as a shield between the digestive juice within it and the rest of the cell, and it also resists the penetration of the small molecules of phosphate esters used in the assay for acid phosphatase. The number of acid hydrolases found in these particles was, at the time of writing, more than a dozen. The function of these bodies can only be digestive; hence the name lysosome (lytic body).

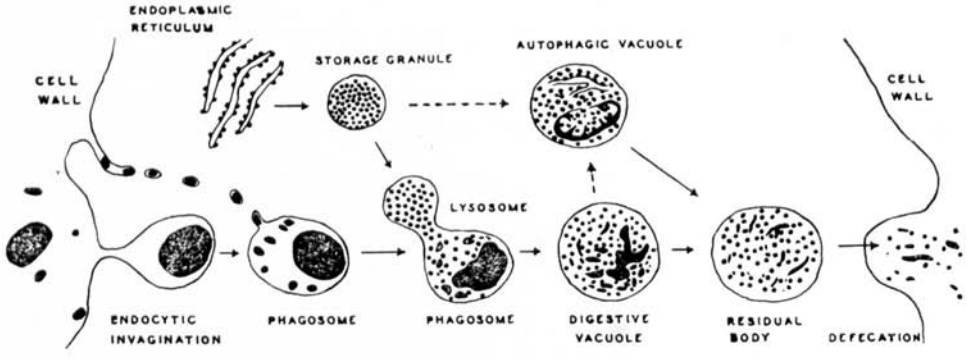
Lysosomes may be separated by essentially the following process, shown in a diagram. The tissue cells are ground up in a pestle-type tissue grinder; the Waring blendor (or disintegrator), is too harsh, disrupting virtually all of the particles. The hemogenate is first centrifuged lightly (600 g for 10 minutes), to throw down the nuclei. The supernatant is then centrifuged more vigorously (8,500 g for 10 minutes) to deposit the mitochondrial fraction—or it is centrifuged in a sucrose gradient to bring that fraction to the top. A final high-speed centrifuging (25,000 g for 10 minutes) in a sucrose gradient makes a final separation of the lysosomes from the remaining mitochondria, the former going to the lower part of the tube.

The electron microscope demonstration of lysosomes was accomplished (by the author with Alex B. Novikoff at the Albert Einstein College of Medicine in New York), in rat liver cells, in which these bodies are electron-opaque. Further studies, however, showed that they cannot be identified solely from their appearance, for they occur in a bewildering assortment of shapes, sizes, and densities. This is because their digestive activity causes them to be filled with a variety of objects in a state of disintegration, and these determine their appearance. However, one of their enzymes, the acid phosphatase, lends itself to visual identification after Gomori staining of the released phosphate, which precipitates with lead as the sulfide.

Four small electron micrographs (magnifications 41,000 to 76,000) of mouse kidney cells show single lysosomes of different forms, with the lead phosphate precipitate either confined to the outer membrane, or—in the presence of certain ingested materials— there and also in the interior. One is filled with a laminated collection of undigested material [of lipoid nature?]. Four other, larger, micrographs show other particular features.

The process of intracellular digestion by lysosomes is shown in a diagram which is reproduced here by permission of *Scientific American*. Outside the cell wall to the left are represented foreign particles about to be phagocytosed. A relatively large particle has entered one invagination, and when the narrowing neck of the invagination is pinched off the body becomes a phagosome (or food vacuole) enclosed by a membrane derived from the cell wall. The drawing also shows a second, small, invagination by means of which several small bodies have entered the cytoplasm, with appropriately small cell-wall encapsulations. One of those has reached and is entering a phagosome, contributing its modicum of cell-wall encapsulation to the membrane of the phagosome.

The next feature for attention is the "storage granule" form of the lysosome. The enzymes contained in it are supposed to have come from the endoplasmic reticulum (known to produce enzymes), but the origin of the membrane that contains them is unknown.



The storage granule (or other lysosome) and the phagosome are attracted to each other, and when they make contact there is fusion of the membranes. Then follows an outpouring of the enzymes into the phagosome, to digest the foreign substances. The combined body is then the "digestive vacuole," the second form of the lysosome. The products of digestion diffuse through the membrane into the cell.

The digestive vacuole can continue its activity until, having gradually accumulated indigestible material, it sooner or later becomes a residual body—the third form of the lysosome. (A fourth form is also recognized, the autophagic vacuole, distinguished by the material which it digested, i.e., parts of the cell itself and mitochondria and portions of the endoplasmic reticulum. How they become engulfed is not known.)

In some cells, especially protozoa, the last stage of the process is a sort of "defecation," or "endocytosis in reverse." In this phase the residual body discharges its content to the exterior, its membrane fusing with the cell membrane from which it originally derived.

The most dramatic form of the cellular eating and digesting process (brought out by James G. Hirsch and Zanvil A. Cohn of the Rockefeller Institute), is to be seen in the polymorphonuclear leucocytes of the blood, most conspicuously the eosinophils in which the granules are largest. When such a cell takes up a particle, e.g., a bacterium, the granules pour their enzymes into the vacuole containing the foreign body and then disappear.

The integrity of the lysosome membrane, which normally contains and localizes the digestive effects of the enzymes, may be affected in different ways. It appears that cortisone and hydrocortisone have a stabilizing influence, which may have a part in the anti-inflammatory effects of those drugs. On the other hand, under some circumstances, as sudden anoxia or exposure to cell poisons, the lysosomal membranes will break down and release their enzymes into the cytoplasm, which is then digested (autolysis). This effect led the author to speak of the lysosomes as "suicide bags."

Various effects in pathology, some of them speculative, are discussed. "It would seem that in the individual cell, as in the multicellular organism, the digestive system occupies a pivotal position both in physiology and in pathology."—H.W.W.

Lysosomes. Ciba Foundation Symposium. Edited by A. V. S. de Reuck, M.Sc., D.I.C., A.R.C.S., and Margaret P. Cameron, M.A. London: J. & A. Churchill, Ltd., 1963, pp. 446+xiii, 79 illustrations. £3.

Lysosomes are perhaps the latest favorites in the list of starters in the cellular handicap, and for very good reasons. Their discovery by Professor Christian de Duve and his colleagues at Louvain in 1955 was a daring and unexpected adventure whose

end is far from being in sight. How appropriate then for the Ciba Foundation to invite authorities in this field from various parts of the world to discuss with de Duve and his team the many exciting discoveries that have already been made about lysosomes, to compare their technical methods, and to attempt to reconcile the discrepancies of fact and interpretation that litter the pathway of all virile and imaginative investigations!

Quite properly the master himself opened the debate with his latest thoughts on the lysosome concept, wherein he compared these bodies, smaller on the whole than mitochondria, with bags of acid hydrolases exhibiting structure-linked latency quite likely due to the existence around [them] of a lipoprotein membrane that restricts their accessibility to external substrates. [These bodies] vary greatly in size, internal structure, and other properties, and are involved in the phenomenon of cellular injury, tissue regression, especially autolysis and necrosis, and may even be the starting point of death in their host cells. A convenient way of demonstrating them is to use their acid phosphatase as a marker, and in this fashion all sorts of cellular inclusions have been traced to them (Novikoff). They are widely distributed throughout the animal kingdom (Tappel *et al.;* Muller *et al.*), and they seem to enjoy the peroxidase of horseradish (Straus), though they dislike detergents (Wattiaux *et al.*) Apparently they dislike an excess of vitamin A (Dingle). Students of developmental processes are linking them with regression and resorption of embryonic cells and metamorphosis (Dulcq; Scheib; Weber). However, evidence for and against their participation in the production of cellular damage (Slater *et al.;* Diansani; Bitensky) is confusing and serves merely to bring out what many of us have realized for a long time, the highly complex nature of cell injuries and death.

Of course, a short notice such as this can scarcely hope to give the reader any idea of the industry and thought that back up the trends so clearly displayed in the Symposium. The full discussions appended to each paper are lively, often amusing, and exhale the convivial spirit that makes for success and true enjoyment even when a group of highly strung, sometimes touchy scientists meet together. Clearly a great deal depends upon the chairman, in this instance Professor J. F. Danielli, but all who know the admirable work of the Ciba Foundation will recognize the skillful touch of the Deputy Director, Mr. A. V. S. de Reuck, and the other devoted members of the staff in providing perfect conditions for the meeting and a splendid record of what came out of them.—[By Roy Cameron, *British M. J.* **1** (1964) 1102-1103, used by permission.]

The Ultrastructure of Cells. By M. Bessis. A Sandoz Monograph. Basle, Switzerland, 1961, 112 pp., paper.

To appreciate the abnormalities shown in electron micrograms from ultra-thin sections of pathologic conditions requires some familiarity with the normal structures within the cell as seen by this method of examination. This monograph is evidently designed as a primer to elucidate, by means of a series of magnificent electron micrograms, and numerous diagramatic representations and a minimum of text, organelles that normally exist within what the early microscopists thought was an "optically empty gel."

After pointing out certain essentials of the special technics employed, it is said that a white blood cell about 20 μ in diameter can be cut into about 400 ultra thin sections. In one picture shown, a whole red blood cell, hemolyzed and shadowed and photographed at 20,000 diameters, measures 7½" across. With the highest magnifications obtainable, even some of the larger of the molecules can now be demonstrated. As the molecular level is reached, it is pointed out, "morphology, biochemistry, and physiology meet and fuse together."

The monograph is divided into 12 chapters: I. From Cell to Molecule, ending with special mention of work done on collagen molecules. II. The Endoplasmic Reticulum and Ergastoplasm, which are elongate double-celled structures (sacs), with granules

(of Palade) on the outer surfaces consisting of ribonucleic acid, concerned with protein synthesis. III. Mitochondria, which are complicated structures in which oxidation in the cell takes place (said by someone elsewhere to be the "cytoplasmic 'power plants' of aerobic cells"). IV. The Nucleus, with a double-layered but porous outer membrane; and the nucleolus, which has no membrane and is irregular in contour. V. Centrosome and Golgi Bodies, complicated structures (not readily made out in ordinary micrograms). VI. The Cell Surface, smooth in appearance in the light-microscope, but shown to be "covered with extension and dotted with cavities;" brush-borders on the cells of the intestine and of the kidney (may be cut longitudinally, obliquely, or transversely), and microvilli on some cells (as those lining the canaliculi of the liver). VII. Leucocytic Granulations, small and numerous in the polymorphonuclears, larger and more conspicuous and with internal crystals in the eosinophils (nothing said here of the macrophages). VIII. Muscle Tissue, very complex. IX. Cilia and Flagellae, including spermatozoa, of complex structure, as well as cilia of the bronchial epithelium. X. Digestion of Red Cells, different stages in the reticular cells, from phagocytosis to reduction to hemosiderin with its constituent molecules of ferretin. XI. The Erythroblastic Islet, a long section, with emphasis on rhopheocytosis (the incorporation of ferretin molecules by erytroblast, analogous to pinocytosis or incorporation of liquid droplets). XII. The Cancer Cell, showing "viruses" in certain types of animal cancer, and the disorderly structure of human cancer, with great numbers of granules, vacuoles, and small rods of unknown significance.

The bibliography at the end is grouped according to the chapters, with a total of some 160 references. The book having been prepared in 1959 (according to the author, personal communication), the most recent are to 1958 publications.

(Nothing is said about lysosomes, although bodies probably of that nature are to be seen in some of the pictures.)

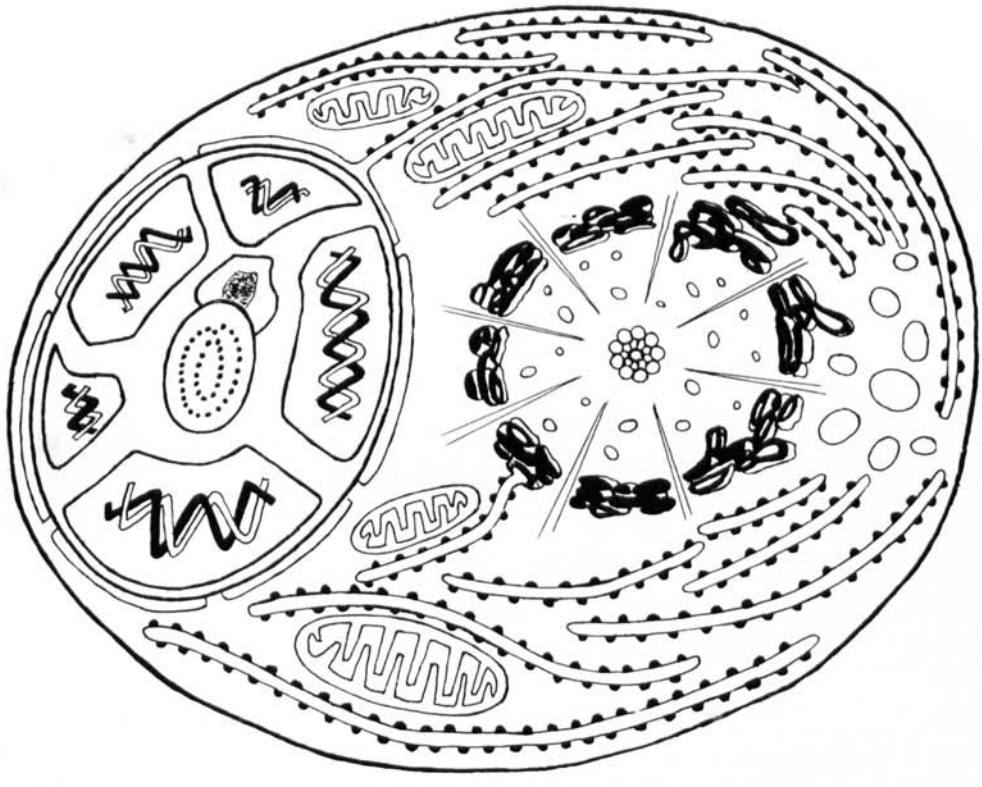
As for the illustrations, apart from diagrams (one introduces each chapter) the others are all electron micrographs, selected from thousands available in the Department of Cytology of the Centre National de Transfusion Sanguine, in Paris. Of these no less than 42 are full size of the page, without margins (page size ± 8″ × 10″), 14 are more or less half-page in size, and 16 are smaller. One of them (Fig. 52), which shows ferretin molecules in the cytoplasm, is rated at 850,000 magnification.

As for the book itself, the paper is heavy-weight coated stock, which provides for excellent detail; the cover is of heavier stock. The signatures are sewed, so that at any point the book opens flat. It is really a sumptuous publication. According to the publishers, it was not intended for sale, and will not be printed again. Anyone wishing to obtain a copy should communicate with the author.

ADDENDUM.— Attention is called to a longish report in the Medical News section of the *J. American Med. Assoc.* (May 4, 1964, adv. pp. 27-29), of a presentation by Dr. Bessis, entitled "Cell Pathology, 1964," at the 45th annual meeting of the American College of Physicians, in April 1964.

The electron microscope, he pointed out, has revealed a great deal about the subcellular units responsible for cell function. Nevertheless, present knowledge of the functions of the various kinds of organelles "may be no more accurate than that of medieval surgeons who thought that . . . the aorta was intended to transport air. . . ." However, Bessis suggested that "amino acids traverse the cell membrane and are transformed into 'activated amino acids,' the energy for which is provided by enzymes located in the mitochondria." The ribosomes act upon the prepared amino acids, under direction from messenger RNA, and the precursor fragments of gamma globulin are secreted into the sacs of the endoplasmic reticulum. The secretions are then found in the Golgi bodies, and are finally released from the cell. Interpolated here is a schematic representation, by Bessis, of the cell and its organelles.

At the left is the nucleus, in the surrounding membrane of which are shown its "pores." Inside that membrane are blocks representing the chromatin clumps, com-



posed of desoxyribonucleic acid (DNA), represented by intertwining helices. In the center is the nucleolus, which contains ribonucleic acid (RNA).

The round structure with radiating lanes in the right center represents a centrosome. This is built around a centriole, which consists of a central cylinder formed of nine (or multiples of nine) tubules with a double crown of satellites. Peripherally the centrosome is limited by the dark, convoluted Golgi bodies, and between them and the centriole there are vacuoles.

The long, worm-like sacs at the top and bottom represent the endoplasmic reticulum. The small black dots on the outer surfaces of those sacs are the ribosomes (the Palade bodies), which have an important role in the synthesis of protein; actually these ribosomes are arranged in rosettes of polyribosomes. (The sacs of the endoplastic reticulum are sometimes called "cisterna" because they accumulate proteinaceous substances, globulins. They are sometimes seen to be more or less distended by such substances.)

Cell pathology deals with changes in organelles resulting from disease or induced experimentally. The first objective of the cell pathologist is to complete the catalog of alterations of the cell organelles. Like the tissue pathologist, he "must correlate postmortem findings with symptoms exhibited prior to death. Even more important, he must study the cell before and during death."

With this in mind, during the past five years, Bessis has been studying diseased cells and cells deprived of specific organelles. As an example of the former are cited the plasma cells from the bone marrow of a patient with a plasmocytoma, in which there was a blockage of the intracellular globulins, suggesting an analogy to intestinal occlusion. In other studies Bessis uses "micropunctures" made with microsurgical instruments (in very large cells, such as ova); also ultraviolet microbeams (0.2 μ), and most recently the laser, to "amputate" certain organelles electively. Use of the laser beam involves very complicated apparatus and technic, but with it many mitochondria can be killed with one emission.

An odd—not to say fantastic—finding is in connection with the reaction of five cells to the presence of a dead one, which indicates the existence of an "odor" of death. When a red blood cell is killed, the neighboring leucocytes engulf it and prepare to phagocytose it, but when a current of cold air is blown across the preparation the leucocytes do not move toward the dead cell. The opposite reaction is shown by a protozoan (Egnela). When one of their kind is killed, those that had previously swarmed in that region flee, and any that later stray into that area immediately turn tail.—H.W.W.

Regular Section

KHARABADJAKHOV, K. K. [Contribution to the history of leprosy in Don region.] Voprosy Leprol. i Dermatol. **18** (1964) 136-149 (in Russian, French abstract).

Working in the archives of Rostov-on-Don, the author discovered a manuscript of a military doctor of the Army Corps of the Don, entitled "On the particularities of the so-called Crimean disease in the region of the Don, the degree of its contagiosity, and the efficacy of the mineral water of the Caucasus in the treatment of patients struck by this disease." This manuscript is of great scientific value, and should be placed among the first works on leprosy published by Russian physicians in the middle of the 19th century.—N. TORSUEV.

BASSET, A. Caractères originaux de l'endémie au Sénégal. [Original characteristics of endemic leprosy in Senegal.] Ann. Soc. belge Med. trop. **44** (1964) 33-46.

In this report the characteristics peculiar to leprosy in Senegal are discussed. A census made in 1961 gave 40,533 cases in the population of about 2,800,000 (16 per 1,000). The prevalence varies from 10 p.m. in the semi-desert north to 30 p.m. in the forested south, conditioned by humidity and also by the ecology. The population of Senegal is far from homogeneous, each of the tribes having its own way of life. The people of the north are nomad shepherds, living in little groups of 3 or 4 huts; those of the south are sedentary agriculturists, living in villages without hygiene. As everywhere in Black Africa, the lepromatous rate is very low, between 5 and 10%. The source of the infection in individual cases is rarely found. Paradoxically, the children in the leprosy villages (of which there are 3 large ones and several smaller ones) are not contaminated; of 80 children in one of them, all born of leprous parents, none presented symptoms. In the cities, which are a recent phenomenon in Africa, the situation is peculiar. In Dakar, for example, there are many country people attacked by the "mirage" of the capital, and, being unemployed, they live in "medinas" without hygiene. Among these people there are many with leprosy, and in them the lepromatous rate is high (32%), as is the infection rate in children (24%). Antileprosy work under these conditions is most difficult. It is planned to increase the number of villages where, around an administrative center, the people can build houses for themselves and their families and can support themselves by agriculture and—in some places—by fishing.—H.W.W.

CAP, J. A. Quelques aspects particuliers de la lèpre dans différent groupes ethniques à Bangkok, Thailande. [Some peculiar aspects of leprosy in different ethnic groups in Bangkok, Thailand.] Ann. Soc. belge Med. trop. **44** (1964) 57-70.

Of the patients treated in the Special Clinics of Bangkok and Thonburi, 26% are Chinese, which is close to the proportions living in the towns. Among them, compared with the Thai people, the proportion of males is high (1.59 *vs.* 1.14); in general the age is lower; the lepromatous rate is higher (43.2% *vs.* 30.7%); mutilations are more frequent, especially among the tuberculoids, and seem to be more severe. This group of patients is not representative of the endemicity of the city, and no inferences can be drawn; this communication simply "adds one more drop" to the record of differences among ethnic groups.—H.W.W.

KALKOFF, K. W. and HOLTZ, K. H. Leprainfektionen in Deutschland. [Leprosy in Germany (report of two cases).] Deutsch. Med. Woch. **89** (1964) 1057-1063.

Report of 2 cases of leprosy in women living in Southern Bavaria. One of them, born in 1934, had never left Germany; the other, born in 1922, almost certainly contracted the disease in Germany. Contact with leprosy patients could not be proved in either case, but there was a probable connection between the two cases. It is likely that one of them contracted the disease through the use of utensils when she worked in the household of a French family from Hanoi who later lived in Germany, and the infection was probably passed to the other patient via this family. Special susceptibility to leprosy is presumed to have been present in these 2 patients because many other, tuberculin-negative, contacts failed to contract the disease.—[From authors' English summary, in *Trop. Dis. Bull.* **61** (1964) 1034.]

HAYASHI, Y. Provisional investigations in search for leprous disposition. La Lepro **33** (1964) 62-92 (in Japanese, English summary).

This report, one of the "special discourses" presented at the 37th general meeting of the Japanese Leprosy Association, is of an extensive effort to determine the existence of predisposition in various groups of Japanese patients (presumably at the Tama Zensho-en). With regard to sex, males are more frequently affected than females, have a higher lepromatous rate (12%), and tend to have a longer course of the disease. Of the patients in the leprosarium in 1954, 56 had been hospitalized for more than 30 years, and among them there were 3 times as many females as males, and 3 times as many of the former group as of the latter had the tuberculoid form. The similarity of the disease in monozygotic twins is illustrated by pictures of two such pairs. There are numerous observations of the disease among patients with other relationships, especially siblings, with many comparative pictures. Further, it is concluded that persons of the same family line as a patient have a somewhat higher susceptibility than the general public. This predisposition, however, is not specific to leprosy infection, "but it is the same disposition as in the case of tuberculosis" and other diseases.—H.W.W.

CASTRO, I. Ensaio sôbre previsão de novos cases de lepra num coletivo de comunicantes. [On calculating new cases of leprosy in a community of contacts.] Bol. Serv. Nat. Lepra **22** (1963) 11-14.

From a theoretic base the author suggests a statistical method for determining the maximum annual rate of leprosy contacts who are liable to become ill in a determined population. The following data are needed for the calculations: (1) Percentage of the contacts distributed according to age. (2) Percentage of Mitsuda-negatives according to the same age groups. (3) Percentage of lepromatous leprosy contacts.—[From author's summary.]

BERGEL, M. Elementos de leprología experimental. [Elements of experimental leprology.] Arch. argentinos Dermatol. **13** (1963) 12-160 and 351-400.

In this extensive article the author summarizes his experience with experimental transmission of *M. leprae* to rodents under special dietary conditions. In the first part are discussed theoretic considerations on the inoculation of *M. leprae* in animals, methods of staining and counting the germ, and the matter of special diets. The second one covers a series of 20 experiments dealing with a large variety of subjects. These include, to list only a part of them, anticeroid activity of antimycobacterial compounds; viability of *M. leprae* under refrigeration; viability of *M. leprae* from a patient under sulfone treatment; inoculation of *M. leprae* to rats fed fish-flesh and fresh beef; the action of prooxidant diets, alone or with the addition of iron gluconate or potassium iodide, on the growth of *M. leprae* inoculated into the foot pad (Shepard method); the effect of oxidized unsaturated fatty acid on the growth of *M. leprae;* the

effect of phenylhydrazine hemolysis on the growth of *M. leprae*, etc. The author then gives general rules to be followed in human leprosy. Although most of the experimental work related deals with prooxidant diets, the report can be useful to beginners in the field of experimental leprology.—E. D. L. JONQUIERES.

KANETSUNA, F., TODA, E., OGAWA, J. and NISHIURA, M. Inoculation of *M. leprae* into newborn golden hamster. La Lepro **33** (1964) 192-195 (in Japanese, English abstract).

Various quantities of human leprosy bacilli were inoculated subcutaneously or intraperitoneally into 175 newborn golden hamsters within 24 hours after birth. In 30 others, for controls, the bacilli were killed by heat before similar inoculation. None of the animals showed any mycobacterial lesions, either macroscopically or microscopically.—[From authors' abstract.]

TORSUEV, N. A. [Inoculation experiments with human leprosy in rats and mice.] Voprosy Leprol. i Dermatol. **18** (1964) 103-135 (in Russian, French abstract).

A complete review of the special literature, Russian and foreign. Long bibliography, with 111 references—N. TORSUEV.

MOHAMED ALI, P. The age-at-onset of leprosy. Leprosy Review **35** (1964) 193-197.

The author's analysis of 3,527 patients detected during a recent survey in the Chingleput district of South India does not support the idea that the majority of persons acquire leprosy before the age of 20 and that many have been infected by the time they are 15. On the contrary, he found that: (1) signs of leprosy were first noticed before the age of 20 years in only about one-third of the patients; (2) 10% of the patients placed the age of onset above 50 years; (3) about one-half of the patients noted the first signs when over the age of 26 years, and one-half before that age; (4) there were 2 peaks for the first signs in males; age 22.7 and 8.74 years; female peaks were 8.4 and 22.7 years; (5) the highest peaks for males were 22.7 and for females 8.4, and the second peaks were just the reverse. It is suggested that a plausible explanation may be based on a genetic hypothesis of specific and individual susceptibility. The age of infection is probably determined by the period of contact between a suceptible person and an infectious one.—[From abstract by J. R. Innes in *Trop. Dis. Bull.* **61** (1964) 1145-1146.]

LONG, E. R. Tuberculosis and leprosy: some correlations in retrospect. Journal-Lancet (Minneapolis) **84** (1964) 395-400.

In this contribution to a "James J. Waring Series," the author points out advances in knowledge since the symposium of the American Association for the Advancement of Science on Tuberculosis and Leprosy in 1937, with respect to both diseases and also others due to mycobacteria. The study of these various infections is currently affording leads to the difficult problem of cultivating the leprosy bacillus. In the matter of transmitting the disease to experimental animals progress has been made, especially by Shepard in creating transmissible foci of infection in the foot pads of mice. By means of them the effects of antileprosy drugs can be evaluated. Both leprosy and tuberculosis are now controlled by public health practice and chemotherapy; rigid segregation of leprosy patients is no longer in favor.—H.W.W.

BROWNE, S. G. La lèpre; maladie à manifestations diverses et à problèmes multiples. [Leprosy: a disease of diverse manifestations and of multiple problems.] Ann. Soc. belge Med. trop. **44** (1964) 47-56.

The author reviews the principal differences in leprosy in the countries from Africa to the Far East, briefly discussing problems he met in them. He discusses the questions of the causative agent, the susceptibility and resistance of the human host, the immunology and histopathology, and the treatment and reactions to the drugs in use.

Regarding epidemiology, he considers the questions of the infectiousness of leprosy, the importance of sanitation, local beliefs, and recognition of the stigmata of the disease. He briefly summarizes the striking differences in the clinical manifestations of leprosy seen in the countries he visited, including the early symptoms, various skin manifestations, the clinical and bacteriologic aspects of the borderline and lepromatous forms in the East, and the importance of the reactional onset of the latter.—[From author's summary.]

Pierini, D. O. and San Martin, M. Lepra tuberculoide (variedad nodular de Souza Campos). [Tuberculoid leprosy, nodular variety of de Souza Campos.] Arch. argentinos Dermat. **14** (1964) 24-32.

Two cases are presented of de Souza Campos' nodular variety of tuberculoid leprosy in boys under 2 years of age. The first was diagnosed several months after the lupoid lesions had healed, when the mother herself sought advice for lepromatous leprosy. The second child presented papuloid elements so distinctive of tuberculoid leprosy that it led to the discovery that the father had lepromatous involvement. The spontaneous healing of the lesions in the children and their intense reaction to the lepromin tests are noteworthy.—[From author's summary, supplied by E. D. L. Jonquières.]

Sacheri, R. F. Lepra auricular y tratornos auditivos. [Auricular leprosy and disturbances of hearing.] Leprología (Argentina) **8** (1963) 240-242.

No mention having been found in the literature of leprous involvement of the medial or internal ear, the author discusses the pathology of the ear of leprosy patients due to the specific process of the rhinopharynx and nasal fossa. Tubular catarrh is frequent, and by its chronicity it leads to lessening of acuity of hearing, and thickening and slight sclerosis of the tympanic membrane. From his own records he finds that 160 of 565 cases (28.3%) presented auditory disturbances. [Nothing is said of specific involvement.] There were 25 cases with chronic suppurative otitis media, due to extension of the chronic affection of the nose and sinuses. It was never possible to demonstrate the leprosy bacillus in the purulent secretions, which parallels the experience of Chover Madramany in Spain.—H.W.W.

Rollier, R. and Rollier, M. L'érythème noueux lépreux. Etude analitique et essai pathogénique. [Erythema nodosum leprosum; analytic study and pathogenic inquiry. Ann. Soc. belge Med. trop. **44** (1964) 147-160.

Erythema nodosum leprosum is to be distinguished from the other types of reaction in leprosy. This name is not more satisfactory than "nodular hypodermatitis"; both refer to a syndrome peculiar to lepromatous leprosy, which appears as lesions of erythema multiforme type, or as a nodular hypodermatitis, or at times as both kinds in the same patient. The clinical and histopathologic features give evidence of its specificity and its allergic nature. In Morocco, where 69% of the patients are males and 31% are females, and 66.7% of the former and 51.7% of the latter are lepromatous, the frequency of ENL is 30.0% in the males and 36.5% in the females. Among the children with the condition, boys were affected more often than girls, whereas in women in the reproductive period it was more frequent than among men. With respect to sulfone treatment, the frequency of ENL is highest at the beginning and during the first year, decreasing thereafter and becoming rare after the third year. It may be a single event and of short duration, lasting for only some weeks (16%), or longer (6%). It is discontinuous and repeated in 66%, continuous in 12%. These and other data given, the authors discuss the etiology of the condition, the influence of treatment (DDS is not the most frequent cause; with the drug, overdosage is usually the actual cause), and the influence of various other factors. About treatment of the condition, the antihistamines and nivoquine are effective in only small proportions of cases; antimony and ACTH are similarly effective, but only in a minority of cases; corticotherapy "triumphs in 100 per cent of the cases."—H.W.W.

HARRIS, J. R. Criteria for assessing the results of treatment of acute ulnar neuritis in leprosy. Leprosy in India **36** (1964) 107-109.

The author mentions the conflicting results that have been obtained from drugs and surgical procedures in the treatment of acute ulnar neuritis in leprosy. For many cases the problem has been solved, but on the other hand grave clinical states and contractures persist widely. Success rates may have been based on the temporary relief of pain, without carrying out long-term follow-up studies. Another explanation of too optimistic reports may have been that they were based on spontaneous improvement, which takes place in one-quarter of untreated cases. Sufficient regard may not have been paid to the variation in the progress of paralysis which occurs in different kinds of leprosy. Finally, definitive criteria have not been set up by which the results of treatment could be assessed. For essential records, the author suggests an observation time of 5 years as the ideal, but not less than 1 or 2 years. Maps of the extent of anesthesia are essential, and these should be recorded repeatedly from time to time. In assessing tactile sensory loss the author uses a short length of nylon thread mounted on a holder. Maps of sweating-loss of pain to pinprick are valuable. The Ninhydrin test for sweating is recommended; this requires meticulous care in application, but it is extremely sensitive. The author also uses a "pinchometer"—a tray suspended by a metal disk that is held between index finger and thumb, weights being added to the tray—by which means the maximum pinch can be measured. A rubber bulb air dynamometer is used to measure the power of the grasp. A useful test for early ulnar palsy is the fatigue test for the finger muscles in adduction. At half a year, 1 year, 2 years, and 5 years, these and other tests should be made and recorded. Photographic record is very valuable, and if possible the handwriting of the patient should be recorded at intervals. By these means a clearer picture will emerge of the results of treatment in acute ulnar neuritis.—[From abstract by J. R. Innes in *Trop. Dis. Bull.* **61** (1964) 1039.]

BUKING, E. P. [Scheme of classification of the acute reactive phases of leprosy.] Voprosy Leprol. i. Dermatol. **18** (1964) 11-23 (in Russian, French abstract).

The author suggests a scheme for the classification of the acute and subacute phases of leprosy. Type 1, progressive dissemination phase, acute or subacute: (*a*) lepromatous (active lepromatization), (*b*) tuberculoid (tuberculoid reaction), (*c*) progressive leprous neuritis (for all types of leprosy). Type 2, acute transformation phase: (*a*) transformation from T to L (reactive tuberculoid leprosy), (*b*) dimorphous phase from T to L (borderline forms), (*c*) transformation from L to T (acute transformation of Tajiri). Type 3, acute paralepromatous phase (lepra reaction, leprous nodular erythema). The author proposes to use, instead of the term "erythema nodosum leprosum" the following terminology: acute or subacute paralepromatous dermo-hypodermitis, with a morphologic definition such as "nodular," etc.—N. A. TORSUEV.

JONQUIERES, E. D. L. Sobre la controvertida identificación de lepra dimorfa con la lepra "borderline." [The controversial identification of dimorphous with borderline leprosy.] Dermat. Trop. (Philadelphia) **2** (1963) 14-19 (English summary).

The international classification of leprosy as accepted by the Madrid and Tokyo Congresses gives [parenthetically] dimorphous leprosy as identical with the borderline leprosy of Wade and Rodriguez. Khanolkar and Cochrane introduced an amplified concept, in which dimorphous leprosy includes macular forms. The author agrees with this, and thinks that there are 3 stages in the development of dimorphous leprosy, namely: an initial macular stage, a hyporeactive stage, and a reactive stage. The last of these he thinks is the borderline leprosy described by Wade and Rodriguez. so that the term "borderline" describes a more restricted picture than that seen in "dimorphous" leprosy. Unlike Wade, the author thinks that dimorphous leprosy is not a sequel of the polar types [sic], nor does he agree with Cochrane that dimorphous

leprosy is an "initial phase of all cases of leprosy." He regards it as a distinct form of leprosy in which the mechanisms of immunology are poorly adjusted, although not absent. An important clue to its diagnosis is the reactive picture, which is clinically similar to the "acute infiltration" of Tajiri and the tuberculoid "pseudo-exacerbation" under sulfone therapy of de Souza Lima. The dimorphous reaction differs from the lepromatous reaction in the absence of nodular erythema. The bacteriologic, immunologic, and histologic findings during the first stage of dimorphous leprosy are those of lepromatous leprosy, whereas during the reactive stages the clinical picture closely resembles that of reactive tuberculoid leprosy.—[From abstract by J. R. Innes, in *Trop. Dis. Bull.* **61** (1964) 1217-1218.].

Collomb, H., Basset, A., Faye, I. and Bourgeade, A., with R. Camain. Lèpre atypique avec paraplégie spasmodique. [Atypical leprosy with spasmodic paraplegia.] Bull. Soc. Méd. Afrique Noire Langue française (Dakar) **9** (1964) 16-18.

The authors comment that after 20 years of study of leprosy in different countries they are often surprised, in Senegal, by the extreme originality of certain clinical forms. They present notes on one such patient. A male aged 39 was admitted to the neurology department of the hospital in a marked febrile state with spasmodic paraplegia and disseminated nodules on all limbs. The nodules were deep subcutaneous or intramuscular, were painful, and varied in size from a nut to a small orange; some were fistulous. There was a beneficial reaction to corticosteroids but not to antibiotics. Leprosy was suspected because of the discovery of marked hypertrophy of the left superficial cervical plexus. Biopsy of a prominently enlarged nerve revealed the presence of numerous bacilli in globi among lepra cells; the nasal mucosa was negative. Under treatment the patient improved; above all, the paraplegia regressed completely, with disappearance of the pyramidal signs. The patient left the hospital, but returned repeatedly because of relapses, probably due to irregular treatment outside the hospital in bad conditions of hygiene and nutrition. The peculiar feature of this patient's case consisted in the spasmodic paraplegic phenomena. At the present time his reflexes are normal, and the Babinski reaction is negative. Regarding differential diagnosis, rheumatism, benign or malignant reticulosis, and collagenosis (particularly periarteritis nodosa) are mentioned.—[From abstract by J. R. Innes in *Trop, Dis. Bull.* **61** (1964) 1146-1147.]

REYNAUD

Raynald, R., Picca, M. and Basset, A., with R. Camain. Un nouveau cas de lèpre aigüe atypique. [A new case of atypical acute leprosy.] Bull. Soc. Méd. Afrique Noire Langue française (Dakar) **9** (1964) 13-15.

The authors have found difficulty in the differential diagnosis of leprosy, even in an endemic region like Senegal, from nodular allergies, periarteritis nodosa, malignant reticulosis, and especially collagenosis and dermatomyositis. They tell of a patient admitted to the hospital in Dakar in March 1963 for painful edema of all limbs, which appeared very rapidly and was accompanied by fever of 39°-40°C. Large hyperchromic plaques appeared on the back and on the limbs and joints, anesthetic to pain. Hypertrophied nerves, such as the radial, were palpable but the cubital and lateral popliteal nerves were not readily palpable because of the edema. Later, lenticular cutaneous nodular lesions appeared on the face, back and thorax, sometimes isolated, sometimes fused. Of the 2 diagnoses considered, acute dermatomyositic type of collagenosis and leprosy, laboratory findings showed the latter to be the correct one. The condition was reactional lepromatous leprosy.—[From abstract by J. R. Innes, in *Trop. Dis. Bull.* **61** (1964) 1146.]

Mercau, A. R., Depaoli, E. A., Culasso, L. R. and Martinez Prieta, P. R. Involución espontanea de lesiones cutáneas en dos enfermos lepromatosos. [Spontaneous involution of cutaneous lesions in two lepromatous cases.] Leprología (Argentina) **8** (1963) 243-245.

This brief report tells, with pictures, of 2 marked cases of lepromatous leprosy in whom, without treatment, the lesions improved clinically and showed corresponding histologic changes, but without bacteriologic modification.—H.W.W.

DE SOUZA LIMA, L. Influéncia da moderna terapeútica de lepro na profilaxia específica. [The influence of modern leprosy therapy in specific prophylaxis.] Rev. brasileira Leprol. **31** (1963) 66-83.

The terms "modern therapeutics" and "prophylaxis" refer to sulfone therapy and to the general prophylactic procedures of leprosy, "specific" referring to chemoprophylaxis of contacts. Sulfone medicaments, it is agreed, are supreme in treatment. The influence of sulfone therapy reached its culmination when the WHO seminar at Belo Horizonte recommended the abolition of compulsory segregation and its substitution by treatment of all patients and control of their contacts. Also considered are the results of sulfone therapy which permit changes in the orientation of prophylaxis: the influence of the phenomena of mutation of form which impedes the transformation from indeterminate to lepromatous on the one hand, and on the other its capacity to reduce the infectiousness of the infectious cases and in consequence gradually to reduce the diffusion potential of the disease. The limitations of sulfone therapy concern especially the long time needed for the sterilization of the infective cases, the probability of relapses, and the appearance of sulfone resistance. The possibility of adopting sulfone chemoprophylaxis of contacts is discussed, and finally the impracticability of the method as a routine one because of the inherent difficulties in technical and administrative matters.—[From author's summary.]

JONQUIERES, E. D. L. Tratamiento de la infección leprosa. [Treatment of leprosy.] Orientación Med. **13** (1964) 25-27.

A review of modern drugs. The need for the modification of the biologic ground in leprosy is stressed. Antioxidative drug complexes have been tried by Bergel and others in an attempt to reach this desideratum. The results of this procedure are doubtful. Sulfones are still the treatment of choice.—AUTHOR'S SUMMARY.

SALAZAR MALLEN, M. Tratamiento de los estados reaccionales en la lepra y en la oncocercosis. [Treatment of the reactional stages in leprosy and in oncocercosis.] Gac. Méd. México **94** (1964) 971-979.

After dealing with the reactions in oncocercosis ("therapeutic shock" reactions), the author says that the Scientific Council of the Health Department assigned to him the task of studying the reactions in leprosy and their treatment. In his study of 14 patients he rejected, for reasons stated, the idea of an immunologic substratum of the condition—i.e., that the symptoms may be due to the circulation of an antigen-antibody complex, or that it is a process of autosensitization. He also had to discard the idea that the reaction is a form of "therapeutic shock" for reasons that included the facts that 2 of the cases with severe reactions had never received treatment, and that none of those with a tendency to chronicity of the reaction showed improvement upon reducing the dose or suspending the treatment. In no case, therefore, did he suspend the treatment or diminish the dose. Certain drugs having had no effect, he tried Indomethacin, a synthetic nonsteroid, anti-inflammatory agent which he had used with success in the "therapeutic shock" reaction in oncocercosis. The results with this drug, in a dosage of 5 mgm. per kgm. of body weight, were uniformly good. In patients who had become dependent on corticosteroids, it was possible gradually to withdraw them—increasing the dose of Indomethacin—without rebound reactions.—H.W.W.

AKSANOVA, R. A. [Treatment of leprosy patients with ethoxide, alone or in combination with Solusulphone.] Voprosy Leprol. i Dermatol. **18** (1964) 76-82 (in Russian, French abstract).

Use of ethoxide in lepromatous cases for 2 years has convinced the author that

this preparation has a certain therapeutic activity, especially in cases which previously have not had any antileprosy medication. Regression of the specific lesions is most marked during the first series of injections, after which the efficacy of the treatment lessens and disappears completely after the third series. This preparation, which can be used in combination with the sulfone, causes hypochromic anemia and leucopenia.—N. TORSUEV.

ETCHEVERRY, V. P. Uso terapéutico del alcohol cetylico en la lepra. [Therapeutic use of cetylic alcohol in leprosy.] Temas de Leprol. (Buenos Aires) **11** (1964) No. 36, pp. 2-4. Inducción de reacciones lepromínicas en enfermos lepromatosos. [Induction of lepromin reactions in lepromatous patients.] Ibid., pp. 5-7.

This issue of the *Temas* is largely devoted to these articles. The present editor explains in a foreword that they were being prepared by the author, shortly before his death, to explain certain unorthodox work upon which he had been engaged for some years but had not reported.

1. Cetyl alcohol, a waxy substance of low melting-point [49.3°C], obtained from whale oil, was used with good effect by intradermal injection into lepromatous lesions. The preparation used consisted of 2% of this substance in a vegetable oil excipient, to which was added for anesthesia procaine hydrochloride emulsified with the aid of 0.25% polyglycol stearate. This was used together with the routine sulfone treatment. The dosage was 5 to 10 ml. weekly; much larger doses were liable to cause general reactions. The lepromas, particularly the well-defined nodular ones, more or less promptly showed signs of reduction, and with repeated injections they flattened. With the combined treatment general beneficial results were obtained, and most of his patients were taking this medication. Commercial cetyl alcohol being an impure substance, containing 20% of other fatty derivatives, no report of its use has heretofore been made awaiting the testing of these other substances in the pure state.

2. This report is of an experiment in which heat-killed tubercle bacilli were used in a "cetylic emulsion" to potentiate the Mitsuda reaction in a group of lepromatous cases. The emulsion was made with 0.5 gm. of cetylic alcohol with 0.5 gm. of gelatin as a stabilizer. The mixture was heated to 70°-75°C. A 10% solution of sodium oleate was added to bring the mixture to pH 7.5, after which distilled water was added to make the volume 100 ml. To this emulsion were added heat-killed tubercle bacilli in the proportion of 1:100,000 wet weight (10 micrograms in 1 ml.). (Using integral lepromin instead of the tubercle bacilli gave no results.) After intradermal injections late nodules appeared, suppurated, and healed with scarring, but when the injections were made into the deep dermis there was no such trouble. The dosage settled on was 0.2 ml. (2 mgm. of bacilli), with a total of 0.8 ml. per week. Of the 11 cases so treated, 7 became positive to lepromin within a few months; the others became positive with larger doses (total of 10 ml., i.e., 100 mgm. of bacilli). In all cases, whether lepromin-reactive or not, there was improvement ascribable to the vaccination. Further experiments are needed to determine the real value of this procedure, but the author believes that these methods, which stimulate the biologic terrain, are of immunologic and therapeutic value.

(Two technical appendices follow, dealing with the preparation and uses of (1) the vaccine with heat-killed bacilli, and (2) the lipoids extracted from the heat-killed tubercle bacilli [the latter not mentioned in the foregoing report].)—H.W.W.

FERNANDEZ, J. M. M. Bases para una terapéutica reactional de la lepra. [Basis for a rational therapy of leprosy.] Ann. Soc. belge Med. trop. **44** (1964) 89-100.

The author pointed out that the majority of the therapeutic trials performed in leprosy lack a rational base grounded on the pathology of leprosy and on the biologic characteristics of the causative agent. On this premise, he discussed several characteristics of the disease in relation with its histopathology, bacteriology, immunology, evolution tendencies and other aspects, suggesting in their connection different thera-

peutic schemes, most of them based on his personal experience.—[From author's summary.]

Ioffé, Y. L. [Use of vitamin E in the treatment of trophic ulcers in leprosy.] Voprosy Leprol. i Dermatol. **18** (1964) 83-93 (in Russian, French abstract).

This preparation has been found efficacious in the treatment of the ulcers in leprosy patients, except those ulcers which result from the break-down of lepromatous infiltrations. To obtain durable results, repeated series of injections are necessary.—N. Torsuev.

Reyes-Javier, P. D. The role of Pyrason in reactions in tuberculoid leprosy. J. Philippine Med. Assoc. **40** (1964) 913-923.

The author recalls that in the treatment of reactions in leprosy cases, active [sulfone] treatment of the disease itself is often withdrawn or reduced to a minimum, thus delaying the cure. She reports, in some detail, with a 2-page table, the results in 18 tuberculoid reaction cases (6 of them labelled borderline) of a triple-drug treatment—Avlosulfone (DDS), Pyrifort (isonicotinic acid hydrazide with pyridoxine), and Pyrazon (phenylbutazone calcium). The first two drugs are said to act directly on the causative organism, while the third acts as a "host reaction modifier." The combination gave encouraging results, although the author refrains for the present from making a definitive statement about the effectiveness of phenylbutazone.—H.W.W.

Bile, T. Griseofulvina y lepra. (Griseofulvin and leprosy.) Dermat. Trop. (Philadelphia) **2** (1963) 204-206 (English summary).

A preliminary study was carried out with griseofulvin in 7 patients in Venezuela, with special attention to reactional episodes. Five of the patients had been in reaction more than 6 months and had received little benefit from the corticosteroids; 1 of the other patients presented intense cubital and medial neuritis, and the last one had lepromatous leprosy without reaction. The drug was given by mouth, in a dosage of 3 tablets daily. All patients showed prompt subjective and objective improvements. The author thinks that griseofulvin in leprosy has a direct and specific antibiotic activity, but that much more work is needed with balanced trials.—[From abstract by J. R. Innes, in *Trop. Dis. Bull.* **61** (1964) 1218-1219.]

Khazizov, E. I. [Bacteriologic relapse of leprosy patients treated in the dispensary.] Voprosy Leprol. i Dermatol. **18** (1964) 99-102 (in Russian, French abstract).

Among the patients of the central zone of North Caucasus treated in the dispensary between 1954 and 1963, bacteriologic relapse has been observed in 25% of the cases. This condition occurred especially in those in whom the disease evolved without any reactive phase.—N. Torsuev.

Hayashi, K. On the operations of leprosy eyes. (Chiefly secondary cataract.) La Lepro **35** (1964) 181-186. (In Japanese; English abstract.)

Between 1959 and 1962 the author operated on 204 eyes of leprosy patients in 3 leprosaria in Japan, chiefly for secondary cataracts. The eyes operated on were observed for 3½ years, with the following findings: (1) Visual acuity was improved in 82%. (2) In 35% of 130 eyes which were improved, aggravation occurred during the period. (3) The main causes of aggravation were opacity of the cornea due to lagophthalmos; occlusio pupillae caused by uveitis; glaucoma; hyphema; and chorioretinitis. (4) An intimate relationship was found between aggravation of the patient's leprosy and visual acuity. (5) The possible hindrances of improving visual acuity seemed to be an outflow of vitreous body, over-iridectomy, remains of nucleus, cortex, or capsule of the lens, incomplete suture of the wound, hyphema, abscess of the corpus vitrei, luxatio lentis, and explosive bleeding.—[From abstract.]

HAYASHI, K. Comparison of leprosy ophthalmic symptoms in three leprosaria in Japan (north, middle and south). La Lepro **33** (1964) 187-191. (In Japanese; English abstract.)

The ophthalmic symptoms of leprosy in the northern leprosarium were more severe than those in the southern leprosarium, and this applied to patients born in the same district but living in the two different institutions. Details of the comparisons were as follows: (1) Depilation of the eyebrows in lepromatous cases, 82% in the north, 65% in the middle, and 56% in the south. (2) Uveitis in the lepromatous cases, 74% in the north, 66% in the middle, 47% in the south. Secondary cataract, lepromatous cases, 23% in the north, 20% in the middle, 11% in the south. (4) Opacities of the cornea, 23% in the north, 19% in the middle, 13% in the south. (5) Lagophthalmos. 47% in the north, 38% in the middle, 25% in the south. (Lagophthalmos was more frequent in the lepromatous cases than in the tuberculoids.)—[From abstract.]

RAMOS, J. Algunos Estudios Endocrinológicos en Enfermos de Lepra. [Endocrinologic studies in leprosy patients.] Thesis. University of Mexico, 1964, 99 pp.

Leprosy in general is first discussed and then the alteration of endocrine functions especially related to the general adaptation syndrome. The study concerns the thyroids and suprarenals of 20 leprosy patients (13 lepromatous—4 in reaction—, 4 tuberculoid, and 3 indeterminate). The study included the determination of protein iodine, and the 17-ketosteroids and 17-hydroxycorticoids of the urine and the blood plasma. The results showed that there were no apparent changes in the thyroid function. The suprarenal function seemed to be altered in the tuberculoid cases, and hypofunction was clearly evident in the reactional lepromatous cases. In contrast, it was normal in the quiescent lepromatous cases. At the end it is stated that leprosy produces a suprarenal hypofunction which in lepromatous cases constitutes a "stress" producing an "alarm" reaction for which a period of adaptation is elicited. If other, nonspecific stresses are added to the "leprosy stress," the reactional periods of the disease may occur. These data, although few, are the only ones obtained in Mexico with Mexican patients, and they are in accordance with those published in other countries on this subject.—[From abstract by A. Saúl in *Dermatología* (México) **8** (1964) 191.]

NISHIURA, M. A study of the relationship between the ultrastructures of leprosy lesions and their responsiveness to the antileprosy treatment. La Lepro **32** (1963) 86-87 (English summary only).

On the basis of a comparative study of the histologic and electron microscopic findings in the lesions of leprosy, the author has resolved the ultrastructure of the host-parasite relationship into three patterns. (1) Vacuolar segregation of the bacilli within the cytoplasm, seen most often in reactional tuberculoid and borderline lesions. The bacilli are in a phagocytic vacuole, the limiting membrane of which separates it from the cytoplasm. The bacilli inside the vacuole are quickly disintegrated by an unknown factor. This vacuolar segregation is readily distinguished from the ordinary electron-transparent zone (ETZ) by the presence within the vacuole of a network structure suggestive of fibrin. It is a sign of cell resistance against the bacilli, and indicates that under treatment the lesion is likely to resolve quickly. (2) Intracytoplasmic growth of the bacilli, they lying naked in the cytoplasm, in direct contact with the microsomes, not wrapped in an opaque droplet or surrounded by an ETZ. Bacilli in this state can be seen in actively growing lepromas, suggesting that they must be in close contact with the cytoplasm in order effectively to absorb nutrients. Being naked they are affected by the drug used in treatment, and as they degenerate they produce the ETZ. (3) Disintgration of the bacilli into a lipid mass. The ETZ is composed of lipids derived directly from the bacillary lipids. As the bacilli degenerate the cytoplasm coagulates and the lipid element seems to increase. Finally, their cell walls are destroyed and the extruded lipid acts as a cementing substance which embeds groups of surviving bacilli in water-repellent balls. In this state the bacillary dis-

integration proceeds very slowly even under treatment, and it takes years for their complete absorption. [It remains to be seen whether these ideas will be completely confirmed. The first process described, however, is particularly interesting in that it suggests action of the enzymes of the lysosomes of de Duve, the search for which in the lesions of leprosy has only recently been begun]. [From summary.]—H.W.W.

SOKOLOV, V. V. [Morphology of the bacillus in a histologic study of the skin during treatment by Etisul.] Voprosy Leprol. i Dermatol. **18** (1964) 94-98 (in Russian, French abstract).

The author, studying the skin lesions in 15 lepromatous patients treated by Etisul, observed a progressive resolution of the lepromatous infiltrates, with distinct disintegration of the lepra cells. The solid forms of the bacilli become less numerous, with an increase of the granular and degenerating forms. However, after a second series of the treatment the disintegration of the bacilli became much slower.—N. TORSUEV.

WHITAKER, L. Demonstration of the anti-nuclear factor and L-E cell in leprosy. Bull. Tulane Univ. Med. Fac. **21** (1962) 173-179.

In this senior thesis of a Tulane medical student, the technics used in the study of the bloods of 51 leprosy patients at Carville are described [but not the types or degree of advancement of the disease]. L-E cells were found definitely in the blood smears of 3 patients; the findings in 2 other cases were considered "borderline," and 18 were declared "questionable." The appearances of the inclusion bodies seen in 24 specimens ranged from small, dark, hyperchromic to large, light and homogeneous—typical L-E bodies. The search for antinuclear antibodies was highly inclusive but the chronicity of leprosy and its characteristics as a "connective tissue and antoimmune-like disease" suggest that they may have been demonstrated in certain cases.—H.W.W.

GHOSH, S., MUKERJEE, N. and BOSE. R. Complement fixation test in leprosy with cardiolipin cholesterol cephalin antigen. Indian J. Med Res. **52** (1964) 458-461.

Despite the disappointing results of the serology of leprosy from the point of view of diagnosis, the authors suggest that the complement-fixation test may conceivably be of value for prognosis or assessment of treatment. They attempted, therefore, to repeat the work of Tanimura *et al.*, who, using a cardiolipin-cephalin-cholesterol antigen, had obtained 92% positive tests in lepromatous cases and 74% in tuberculoids. A similar antigen, obtained from Dr. Venkataraman, was used in tests of 200 leprosy patients and 105 controls (including patients with syphilis, kala azar, and tuberculosis). The results were: lepromatous cases, 78% positive; tuberculoid cases, 24% positive; borderline cases, 54% positive; nonleprosy patients, 6.6% positive. It was concluded that this antigen is of no diagnostic value in leprosy.—[From abstract by D. S. Ridley, in *Trop. Dis. Bull.* **61** (1964) 1217.]

OGATA, T. Relationship between the symptoms of leprosy and the positivity of tuberculin reaction before the occurrence of leprosy. La Lepro **33** (1964) 206-210 (in Japanese; English abstract).

Because of the recognition of relationship between leprosy and tuberculosis in some points, and the expectation that BCG vaccination should be effective in the prevention of leprosy, the author investigated the influence of tuberculin allergy before the occurrence of leprosy upon the clinical symptoms of the disease. The patients examined were 1,229 under 35 years of age, who would be influenced by BCG vaccination in Japan. These cases were divided into three groups, according to the positivity of tuberculin reaction and the results of BCG vaccination. These three groups were then compared with respect to the clinical type, stage and symptoms of leprosy at the time of admission to the leprosaria and at present. No influence of the positivity to the tuberculin reaction before the occurrence of leprosy upon the clinical symptoms of leprosy before or after the admission could be recognized.—[From abstract.]

TUMA, M. Modificação de técnica do preparo da lepromina. Novas considerações sôbre a sua padronização [Modification of the technic of preparing lepromin; new considerations of its standardization.] Bol. Serv. Nac. Lepra **22** (1963) 15-20.

The standardization of lepromin should not be limited to the bacillus count. Homogenization, stability and controlled dilution should be included in the process of standardization. A modified technic now in use in the Institute of Leprology in Rio de Janeiro is given in full detail. The lepromas are either boiled or autoclaved in saline, and the tissue is ground up in the fluid in which it was cooked. The suspension, after infiltration, and the remaining pulp, are refrigerated over night. The supernatant is then removed and the sediment is added to the pulp, and this mixture is then treated repeatedly with chloroform to extract the bacilli. The chloroform is reduced in bulk by evaporation and added to the supernatant suspension. This is then counted and diluted to make the final count about 20,000,000 per ml.—[In part from author's summary.]

JADIN, L., WERY, M. and MORIS, P. Multiplication de *"Mycobacterium leprae;"* possibilité de test de sensibilité. [Multiplication of *Mycobacterium leprae;* possibility of the sensitization test.] Bull. Acad. Nat. Med. **148** (1964) 333-342.

The authors have succeeded in obtaining multiplication of *M. leprae* by planting them in Hanks' medium with 10% bovine serum and penicillin added. They obtained the material by gland puncture, and for the mycobacterium to develop it is necessary that the cells which were dragged out together with the bacilli during the puncture should also grow. The multiplication of the leprosy bacillus is relatively rapid, because in the 7th-day subculture an abundant growth is to be seen. This speed of development varies from strain to strain, and parallels the speed of growth of the cells. The bacilli develop in the endoplasmic reticulum or ergastoplasm, in contact with the ribonucleic acids of the individual; these ribonucleic acids are derived from the desoxyribonucleic acids of the nucleus, bearers of genetic information. For this reason it is not suitable for its development that the cells come from all of the subjects, but only from some of them. This, it is said, is in accord with our epidemiologic knowledge. These cultures were used in tests of the inhibiting potency of the drugs used in the treatment of leprosy. They showed great differences in their sensitivity to them, in accordance with the strains studied.—[From abstract by X. Vilanova in *Actas Dermo-Sif.* **55** (1964) 468.]

DELVILLE, J. P. Multiplication et comportement du bacille de Hansen en cultures de tissus: note preliminaire. [Multiplication and behavior of leprosy bacillus in tissue cultures: preliminary note.] Ann. Soc. belge Med. trop. **44** (1964) 77-88.

After a brief review of recent attempts to cultivate the bacilli of leprosy, the author tells of his own work with tissue cultures, in which he used human amniotic cells, trypsinized leproma fragments, and cells from an angiosarcoma cultured by himself. (*a*) In the amniotic-cell cultures the bacilli were found in large numbers in only a few of the cells, and it was believed that the increase in them was at least in part due to phagocytosis of bacilli freed by degenerated cells. Attempts at subculturing were unsuccessful. These cells, it was concluded, are not useful for the purpose. (*b*) Of six tubes planted with cells from lepromas (small glass slides in Leiton tubes), only one showed growth of the cells, which was active and abundant. Subculture was not successful; those cells that fixed to the support and resumed their polygonal form degenerated after a few days. The stained preparation from the original tube showed about 50% of the cells with large numbers of bacilli and also globi (in one place a microcolony 130 × 165μ). In view of the negative controls (i.e., the other 5 slides without growth), this finding is regarded as having represented growth of the bacilli. (*c*) The strain of Kaposi cells was regarded as especially suitable for the purpose, particularly because they remained attached to the slide in the culture tube and were

long-lived. A culture examined 4 days after seeding showed 81% of the cells parasitized, with an average of 5 bacilli per cell. In one culture 4 months old, 17% of the cells examined showed more than 10 bacilli each, and some of them contained more than 100; in one place there was a large mass of globi that measured 39 × 118μ. Subcultures are under study. It is concluded definitely that there was multiplication of the Hansen bacilli in the cultures of the Kaposi cells. Some of the photographs of bacillus masses are impressive.—H.W.W.

UYEDA, S. [Studies on *M. leprae* and *M. lepraemurium*. I. The different forms of *M. leprae* and *M. lepraemurium* in the smears of tissue lesions and their characteristic arrangements.] La Lepro **33** (1964) 169-174 (in Japanese, French abstract).

In preparation, without agitation, of the juices pressed from the tissues of human and murine leprosy, it was noted that: (1) Both kinds of bacilli always present a certain characteristic arrangement composed of more or less long mycelial filaments, with numerous ramifications. (2) Morphologically, these germs appear not to belong to the genus *Mycobacterium*, but to resemble genus *Nocardia* of the family of *Actinomycetaciae*. (3) To describe the polymorphism of these germs, we must note first the fact that the characteristic arrangement which they form, according to their development, always consists of various forms, long, short, branched, etc. (4) The observations made suggest that it will probably be possible to consider the culture positive when it is composed of germs arranged in a certain order similar to that which has been observed in the preparations made from the tissues of leprosy lesions.—[From abstract.]

UYEDA, S. [Studies on *M. leprae* and *M. lepraemurium*. II. Microscopic development and characteristic of *M. lepraemurium* on slide culture.] La Lepro **33** (1964) 175-190 (in Japanese, French abstract).

A thin suspension of ground-up tissue from infected white rats was cultured in Kirchner medium on a slide placed in a hermetically sealed and humidified glass jar. (1) The important fact, common to all cases, was that on the slides heated to 30°C the germs of slightly longer form showed growth in the course of weeks, gradually forming numerous small groupings in which the shorter forms have a certain characteristic arrangement similar to that which was observed in the leprosy tissue smears described in our previous report. From this fact it is possible to conclude that the groupings formed on the slides, no matter how small they were, may be the product of *in vivo* development of this microbe. (2) From the point of view of morphology, and from the characteristic arrangement which this microbe shows in developing on the slides, there is no doubt that this microbe does not belong to the genus *Mycobacterium* but rather to another genus which should be established in the vicinity of the genus *Nocardia* in the family *Actinomycetaciae*. (3) The growth at 30°C was always slightly superior to that at 37°C. This may indicate that this microbe may develop under more or less great variations of temperature.—[From abstract.]

NISHIMURA, S., KOHSAKA, K., HIROSE, Y. and KAWAGUCHI, Y. Comparative observations on virulence of seven strains in the murine leprosy bacillus. La Lepro **33** (1964) 200-205 (in Japanese; English abstract).

From the fact that this bacillus is present in a state of compatibility with the histiocyte in the host, it appears that the organism does not have marked toxicity. To determine the virulence, therefore, the quantity of bacilli required to kill the host should not be taken as the index, but evaluation should be based on the development of the leproma at the inoculation site. A comparative study has been made of the virulence of 7 strains of the bacillus, using 2 strains of mice that differed in susceptibility—C3H (onset delayed but leproma large) and $C57BL_6$ (onset rapid but leproma small). The strains of bacilli had been maintained for more than 10 generations in mice under similar conditions. Doses of 0.25 ml. of 10^{-2} to 10^{-3} diluted supensions were inoculated

subcutaneously, and the sizes of the lepromas produced were measured up to 20 weeks, after which the animals were sacrificed and the lepromas weighed. The distribution of bacilli in the organs was also examined. No significant differences were noted among the 7 strains.—[From abstract.]

NAKAMURA, M. Biological properties of *M. lepraemurium*. VI. Effects of physical treatments on the infectively of *M. lepraemurium*. La Lepro **33** (1964) 196-197 (abstracts only, in Japanese and English).

The effects of heating, ultraviolet irradiation, and agitation on the infectious activity of *M. lepraemurium* were investigated. The results obtained showed that the infectivity of the bacillus was completely suppressed by heating at 55°C for 30 minutes, or by exposure at a distance of 15 cm. for 120 min. to a germicidal lamp (Shimazu GL-15). Furthermore, the infectivity of the bacillus was lost by agitation in a water-bath at 37°C for 5 days, whereas it was maintained for 10 days under ordinary conditions.—[From abstract.]

GUPTA, S. K. and MATHUR, I. S. The effect of vaccination by atypical Mycobacteria in experimental murine leprosy. Indian J. Med. Res. **52** (1964) 435-440.

In these experiments groups of rats were vaccinated by intramuscular injections of suspensions containing, respectively, 1.1×10^8 viable units of BCG, 2×10^6 viable units of *Mycobacterium kansasii*, and 2×10^6 viable units of a strain of the Battey bacillus. After 37 days each rat was injected with a suspension of *M. leprae* over the sternum. The rats were then weighed and the lepromas measured at intervals of 2 weeks. The experiment was terminated 30 weeks later when all of unvaccinated control rats showed lepromas, and the lepromas were weighed and examined histologically. Whereas all of the unvaccinated rats had developed lepromas, only 71.4%, 55.0% and 37.5%, respectively, of the rats vaccinated with Battey bacillus, BCG and *M. kansasii* had lesions. The median weight of the lepromas developing in the rats vaccinated with the Battey bacillus was 5.18 gm. Histologically vaccination caused a delay in the progress of the disease. Other workers have shown that BCG gives some protection against infection; in the present work *M. kansasii* gave better protection than did BCG, in spite of the fact that the number of bacilli in the *M. kansasii* vaccinate was less than that in the BCG vaccinate.—[From abstract by S. R. M. Bushby, in *Trop. Dis. Bull.* **62** (1965) 36-37.]

BOOK REVIEWS

Hints on Diagnosis and Treatment of Leprosy, by R. V. WARDEKAR, M.D. Director, Gandhi Memorial Leprosy Foundation, Wardha. Pp. ii + 34, + 10 pp. of plates. Price (with postage) Rs 1.50.

This booklet is avowedly aimed at the family doctor, who should understand the basic facts of leprosy and so be able to diagnose and treat patients, and be willing to do that in his own dispensary.

In the classification of cases, six forms are recognized: tuberculoid (resistant), lepromatous (nonresistant)—these being the polar types—and also indeterminate, maculoanesthetic, borderline and polyneuritic. These are described in some detail, after which deformities, reactions, and complications are dealt with.

Sections are devoted to the presenting symptoms (briefly); methods of examination (in which it is said that, as far as possible the bacteriologic examination by the "standard 'slit and scrape' method" should be made in every case); and diagnosis and differential diagnosis. The physician is warned that, because of the social stigma involved, a definitive diagnosis of leprosy should not be made on suspicion alone, and that until he develops the clinical acumen to diagnose early cases they should be referred, if possible, to a consultative service.

The sheet anchor of treatment is dapsone (DDS), which is cheap, usually nontoxic, and very easy to handle "if one knows how to start it and when to stop it"; and detailed instructions are given. Derivatives of DDS and other drugs used are considered.

In discussing the treatment of reactions it is said first, with emphasis, "Please do not use corticosteroids" unless a fair trial has been given all other drugs. As for those, first place is given to potassium antimony tartrate. Then are listed mercurochrome i.v., methylene blue i.v., chloroquin or camoquin, streptomycin, antihistamines, and, finally, prednisone, for which instructions are detailed.

Treatment of complications—iritis, neuritis, ulcers (especially plantar ulcers)—is followed by sections on the care of the hands and feet and on measures to prevent these conditions. The rest of the text is devoted to a pertinent discussion of health education and its import on the medical profession.

The plates I to X are mostly of selected photographs of typical lesions (not well reproduced, although coated paper is used here). There are also four diagrams showing the location of the subcutaneous nerves that may be enlarged in leprosy.

This booklet is a good, no-nonsense exposition of essentials that should be of much value for those to whom it is directed.—H.W.W.