MEDICAL GRAND ROUNDS
PARKLAND MEMORIAL HOSPITAL
December 19, 1957

[Metabolic Diseases]

Eosinophilic Granuloma
Case #1

This 14 year old negro boy was first seen at [redacted] in 1945 because of a painful swelling of the thumb. At that time P.E was negative except for general lymphadenopathy of the anterior cervical chain. CA - 11.3, P - 5.4, Alk. Phos. - 6.9, Chol. - 125 & 131; bone survey normal except for a cystic lesion of the first metacarpal bone of the right thumb. Biopsy of this lesion revealed lipoid histiocytosis of bone, and a course of x-ray therapy was administered to the area.

In [redacted] 1956, he was readmitted for reevaluation. P.E. again was normal except for generalized lymphadenopathy. Bone survey again was negative except for the previously described lesion. Alb. - 4.61, glob. - 2.9, Ca - 10.7, 10.0, P.- 5.4, 6.2, Chol. - 162, Alk. phos. - 19.0, 13.5 (all thought to be normal values for the age).

Schüller-Christian's Disease
Case#2

This 8 year old negro boy was admitted to the [redacted] because of the development of a mass in the right parietal area, diplopia, anorexia, headaches, and lethargy. P.E. at the time of admission revealed a pulsating "defect" in the skull over the parietal area, 4 cm. in diameter, diplopia, and hyperactive DTR's. X-rays of the skull revealed a radiolucent area in the skull. Exploratory craniotomy revealed a necrotic mass in the area of the bony defect, slides of which revealed a lipid reticuloendotheliosis of bone. He did well following surgery and was discharged to be followed in the OPD.

In [redacted] of 1957 he was seen for following; headaches and diplopia were more severe, in spite of the fact that skull series showed no change.

Schüller-Christian's Disease
Case #3

This 6 year old negro boy had a left hemithyroidectomy in 1954 because of an irregular enlargement of the thyroid; pathologic diagnosis at that time was "chronic thyroiditis". In 1955 he was readmitted because of a mass in the right frontal area; exploratory craniotomy revealed "eosinophilic granuloma". X-ray therapy to the skull and the thyroid mass had no obvious salutary effect. Subsequently, he developed a draining otitis of the left ear, found on examination to be secondary to a granulomatous mass of the auditory canal, and in 1956 a large firm mass in the area of the right thyroid and a granulomatous lesion of the gums were noted on P.E. in the OPD.

At this time the slides from all the previous biopsies were reviewed both here and in another medical center; the concensus was that all the lesions were identical and were typical of eosinophilic granuloma. Subsequent biopsy of the gum lesion was again interpreted as showing eosinophilic granuloma. A course of x-ray therapy was given to the mass in the ear and to the gum with no obvious evidence of response. He has been followed periodically in OPD, never having developed any systemic manifestation other than retarded bone growth and poor weight gain.

Letterer-Siwe's Disease
Case #4

This boy was first seen at the age of 14 months, developed at the age of 6 months a papular skin rash in both inguinal areas, spreading slowly to involve the axillae, neck, mouth, scalp, nail beds and soles of the feet. These lesions progressed to ulcerations and became secondarily infected; subsequently, he developed a protuberant abdomen, wasting of the extremities, and lassitude. A biopsy of a lesion of the axilla in another hospital was interpreted as reticuloendotheliosis. P.E. revealed a protuberant abdomen, granulomatous lesions of the scalp, neck, axillae, and inguinal areas, splenomegaly, and generalized muscle wasting. Hgb - 8.2 gm., Chol. - 146. Bone survey revealed punched out areas of the skull and long bones. A course of steroid

therapy was given with some subsequent improvement in the skin lesions. He was discharged on steroids but died four months later.

Gaucher's Disease

Case #5

This 59 year old white female was in good health until 1944 when increasingly severe pain on movement developed in the right upper arm.. X-rays revealed calcification in the proximity of the shoulder joint; a Dx of bursitis was made, and she was treated with x-ray and novocaine infections. Physical examination at that time revealed a palpable spleen but was otherwise normal. Early in 1953 the patient began to complain of pain in the left thigh. This was intermittent but increased gradually until in [redacted] of 1954, when severe pain in left thigh appeared suddenly. X-rays then showed an impacted pathologic fracture of the neck of the left femur. The spleen had increased in size and a moderate anemia was noted. A sternal marrow smear at that time showed numerous Gaucher cells to be present. The patient was treated with P.A.S. 12gm. per day and in [redacted], 1954, a splenectomy was performed. The spleen on microscopic examination contained abundant Gaucher cells and chemical analysis showed elevated kerasin levels. The patient has not had further bone lesions and her hemoglobin has remained normal since the operation.

General Reviews of Lipoidosis

1. Thannhauser, S. J., The Lipoidosis, Oxford Press, 1950. The most complete monograph on the subject.
2. von Creveld, S., The Lipoidosis, Adv. in Ped., 6, 202, 1953. An excellent and readable review of the clinical-chemical aspects of all the Lipoidoses.
3. Thannhauser, S. J., Diseases of the Nervous System Associated with Disturbances of Lipid Metabolism, Metabolic and Toxic Dis. of the Nervous System, Assoc. for Res. in Nerv. and Ment. Dis., Vol. 32, 238, 1953. A short readable review of the lipoidosis.

Reviews of the Chemistry of the Lipids Involved in These Diseases

4. Rossiter, R. J., Chemical Constituents of Brain and Nerve, in Neurochemistry by Elliot, Page and Quastel. C. C. Thomas Pub. 1955.
5. LeBaron, F. N. and Folch, J., Structure of Brain Tissue Lipids, Physiol. Rev. 37, 539, Oct., 1957. The most recent but a rather incomplete review of the subject.
6. Bronte, G., Studies on Lipids in the Nervous System. Acta Physiol. Scand. 18, Supple. 63, 1949.
7. Sperry, W. M., The Biochemistry of the Lipoidoses, J. Mt. Sinai Hosp., 9, 799, 1943. An excellent discussion of the possible causes of abnormal lipid deposits.
8. Carter, H. E., Galanos, D.S., Fujino, Y., Chemistry of Sphingolipides. Can. J. Biochem. & Physiology. 34, 320, 1956. A brief review of modern concepts of Sphingolipid structure.

Eosinophilic Granuloma

9. Lichtenstein, L. and Jaffe, H.L., Eosinophelic Granuloma of bone. Am. J. Path. 16, 595, 1940. The first description of eosinophilic granuloma as a solitary lesion.
10. Green, W. & Farber, S., Eosinophylic or Solitary granuloma of Bone. J. Bone & Jt. Surg. 24, 499, 1942. Describes nine cases of eosinophilic granuloma all of whom healed spontaneously or with X-ray. Suggest that this disease is a variant of Schüller-Christian.
11. Jaffe, H.L. and Lichtenstein, Eosenophilic Granuloma of Bone, Am. J. Path. 37, 99, 1944. A further description of eosinophilic granuloma as multiple granulomata of bone. Now agree with Farber that this is the same disease process as in S-C.

Schüller-Christian Disease

12. Lichtenstein, L., Histiocytosis X: Integration of eosinophilic granuloma of bone; Letterer - Siwe disease and Schüller-Christian Disease as related manifestations of single nosologic entity. Arch. Path. 56, 84, 1953. Again it is emphasized that these are the same disease and an attempt is made to define the criterian of subclassification and give them a new name.
13. Avery, M.E., McAsee, J.G.,Guild, H. G. The Course and Prognosis of Reticulo-endothebosis (Eosinophilic Granuloma, Schüller-Christian Disease and Letterer-Siwe Disease). Am. J. Med. 22, 636, 1957. A review of 40 cases. Stresses the importance of chronic otitis as commonest presenting complaint in Schüller-Christian Disease. Only 3/29 cases had S.-C. triad but 27/29 showed skull defects.
14. Renzitti, A.D., Eastman, G., Auchincloss, J.H. Chronic Disseminated Histocytosis X (Schüller-Christian Disease) with Pulmonary Involvement and Impairment of Alveolor-Capillay Diffusion. Am. J. Med. 22, 834, 1957. Stresses the frequency of pulmonary involvement, which may cause death and potential reversability of this complication by X-ray therapy.

Letterer-Siwe Disease

15. Siwe, S. The Reticulo-endothelioses in Children. Adv. in Ped. 4, 117, 1949. The relationship between eosinophilic granuloma, Schüller-Christian Disease and Letterer-Siwe Disease are discussed. This author is not convinced that they are the same disease.
16. Batson, R., Shapiro, J., Christie, A. and Riley, H. D., Acute Nonlipid Disseminated Reticulo-endotheliosis. Am. J. Dis. Child. 90, 323, 1955. The most complete (15 cases) presentation of Letterer-Siwe Disease to date. Authors agree that it is an acute and severe form of "reticuloendotheliosis=. Two patients receiving antibiotics recovered.
17. Wallgren, A., Systemic reticuloendothelial granuloma; non lipid reticuloendotheliosis and Schüller-Christian disease. Am. J. Dis. Child. 60, 471, 1940. Points out that there are sufficient features common to Letterer-Siwe and Schüller-Christian Diseases to suggest that they are variants of the same general disorder.

18. Schultz, D. M., Hamilton, G. B., and Leston, B. N. Non lipid Reticuloendotheliosis in an Adult. Arch. Path. 63, 49 (1957) A description of "chronic Letter-Siwe Disease in a 57-year-old man.

Treatment of L-S with Antibiotics (See also Batson et al)

19. Bierman, H. R. et al. The Ameliorative Effect of Antibiotics on Non lipoid Reticuloendotheliosis (Letterer-Siwe Disease) in Identical Twin. J. Ped. 40, 269, 1952. The only report of L-S in Twins. Both appeared to have recovered 2 1/2 years later on prolonged eg. 75 day courses of aureomycin and/or dihydrostreptomycin.
20. Aronson, R. P. Streptomycin Letterer-Siwe's Disease, Lancet 1951:2, 889. An 18-month with typical L-S was well 2 years after 5 weeks of Streptomycin therapy.

Gaucher's Disease

Infants and Children

21. Atkinson, F. R. B., Gaucher's Disease in Children, Brit. J. Children's Diseases 35, 1, 1938. A review of 108 report cases of Gaucher's in Infants and Children. Splenectomy would appear to be of value in younger age groups.

Childhood and Adult

22. Groen, J., Garrer, A.H., Adult Gaucher's Disease, with Special Reference to the variations in its Clinical Course and the value of Sternal Puncture as an Aid to its Diagnosis. Blood 3, 1221. Stresses that the only means of making a diagnosis may be by typical cells in marrow. Splenectomy was valueless in this sense.
23. Bromberg, Y. M., Toaff, R., Diengott, D., Pregnancy and Gaucher's Disease. Brit. Med. J. 1953: 2, 761. A review of 7 cases of Gaucher's diseases in young women. Pregnancy was not effected by disease. The children were normal.
24. Bloem, Th. F., Groen, J., Postma, C., Gaucher's Disease, Quart. J. Med. 5, 517, 1936 In 5 cases stresses especially the diagnostic significance of pigmentation of the lower legs.
25. Medoff, A.S., and Bayrd, E.D., Gaucher's Disease in 29 Cases: Hematologic Complications and Effect of Splenectomy. Ann. of Int. Med. Reviews the childhood or adult cases. 29 Cases of Gaucher's seen at Mayo Clinic from 1950-1954. Splenomegaly was a constant finding but blood abnormalities (anemia or leukopenia) were seen in 83%. Splenectomy connected anemia and leukopenia in 14 of the 15 cases.
26. Reich, C., Seife, M., Kessler, B. J., Gaucher's Disease: a review and discussion of 20 cases. Medicine 30, 1, 1951. Ages ranged from 12 to 71 years. Splenomegaly in all but one case. Hematologic abnormality noted in every patient.

Inheritance of Gaucher

27. The Hereditary Mechanism of Gaucher's Disease. Blood 3, 1238, 1948 Of 25 cases of Gaucher's 17 were familial. There is very suggestive evidence that the disease is transmitted as a dominant trait generally becoming increasingly severe with each generation.
28. Stransky, E. and Dauis-Lawas, D.F., Heredity in the Infantile Type of Gaucher's Disease. Am. J. of Dis. Child 78, 694, 1949. Gaucher's cells found in assymptomatic parent of two diseased Phillopino infants.

Experimental Gaucher's

29. Ottenstein, B., Schmidt and Thannhauser, S.J., Studies Concerning the Pathogenesis of Gaucher's Disease. Blood 3, 1250, 1948. Galactosidocerebroside (Kerasin) as well as glucosido cerebroside may be increased in Gaucher's Cells. The brain cerebrosides are qualitatively and quantitatively normal. Serum and RBC normal.
30. Uzman, L.L., The Lipoprotein of Gaucher's Disease. Arch. Path. 51, 329, 1951. Evidence is presented that Kerasin is bound firmly in Gaucher's cells as a lipoprotein and the protein moiety may be the abnormal factor in Gaucher's disease.
31. Uzman, L.L., Polycerebrosides in Gaucher's Disease. Arch. Path. 55, 1953. A polycerebroside representing a small fraction of the total lipids was isolated from both the brains and spleens in Gaucher's Disease but not from normal spleens and in very small amounts from normal brains.
32. Christianson, O.O., Experimental Lesions produced by Cerebrosides. Arch. Path. 32, 369, 1941. Injected cerbrosides into rabbits and caused production of cells similar to Gaucher cells.

33. Halliday, N., Devel, H.J., Tragerman, L.J. and Ward, W.E., On the Isolation of a Glucose-Containing Cerebroside from Spleen in a Case of Gaucher's Disease. J.B.C. 132, 171, 1940. First demonstration that gluco lipids are present in Gaucher.

Neimann-Pick Disease

34. Videbaek, A., Niemann-Pick Disease. Acta. Paed. 37, 95, 1949. A review of all reported 73 cases of Neimann-Pick's Disease.

Other Case Reports with Reviews.

35. Canmann, M.F., Niemann-Pick Disease. J. Ped. 24, 335, 1944.
36. Murray, H. A. and Bernstein, T. C., Neimann-Pick's Disease. Arch. Pediat. 63, 497, 1946.
37. Knutti, R. E., Neiman-Pick's Disease and its Relationship to the Lipoidoses. Calif. Med. 72, 60, 1950.

Experimental

See chemical reviews for analysis of organs.

38. Tompkins, E. H., Effects of Intravenous injections of the either-insoluble fraction of Beef Brain. Arch. Path. 35, 787, 1943. Cells similar to Neimann-Picks and Gaucher cells can be produced by this technique but this may have little to do with the etiology of the disease.
39. Terry, R. D., Sperry, W.M., Brodoff, B., Adult Lipidosis Resembling Neiman-Pick's Disease. Am. J. Path. 30, 263, 1954.

Tay-Sachs Disease

40. Rothstein, J.L. and Welt, S., Infantile Amaurotic Family Idiocy. Am. J. Dis. Child. 62, 801, 1941. A report of two cases with an extensive discussion of the relationship between Tay-Sachs and Neimann-Picks Disease.
41. deSilva, C.C. and Tennekoon, G. E., Tay-Sachs Disease in Two Sinhalese Children. Brit. Med. J. 1955, 2, 768. Purple fovea centralis and marked C.N.S. symptoms in two infants showing autopsy finding of Tay-Sachs.

LIPIDS OF THE LIPOIDOSES