

Anachlorhydria in Puerto Rico¹

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AMONG 684 gastric analyses performed on indigent Puerto Ricans attending the University Hospital, 80, or 11.7 per cent of the cases, showed anachlorhydria. The fractional method of gastric analysis was used with the subcutaneous administration of .01 mg. of histamine per kilo of body weight, following the withdrawal of the gastric residue. Samples of the gastric contents were removed every fifteen minutes for a period of an hour and a half. All the cases which required a gastric analysis had complaints referable to the gastrointestinal tract, and therefore suggested some alteration in the physiology of the stomach. One gastric analysis was performed in each of 42 patients (52.5%); two were done in 28 cases (35%), and three were done in 10 of the cases (12.5%). A state of anachlorhydria was encountered in all of them.

ANALYSIS OF THE CASES

Incidence. In the series of cases studied we obtained an incidence of 11.7 per cent, which is in accord with the figures obtained by various authors. The incidence of anachlorhydria in general disease outside of the artificially produced gastric anacidity seems to range from 10 to 15 per cent. Andresen² in a series of 4,000 cases obtained 10 per cent of anachlorhydria; Eggleston,³ 10 per cent in 2,700 cases; Hartfall,⁴ 10.3 per cent in 2,356 cases; Vanderhoof,⁵ 10.5 per cent in 4,281 cases; Hurst,⁶ 15 per cent in 712 cases; Kohiyar,⁷ 15 per cent

1. Received for publication January 24, 1941.

2. A. F. R. Andresen, "Fractional Gastric Analysis with Histamine," *Ann. Clin. Med.*, 5:472-482. Nov., 1926.

3. E. L. Eggleston, "Pathologic Conditions Secondary to Achlorhydria," *J.A.M.A.*, 97: 1216-1221. Oct. 24, 1931.

4. S. J. Hartfall, "Secretion of Gastric Juice in Response to Histamine in Addisonian Anemia," *Guy's Hosp. Rep.*, 83:37-46. Jan., 1933.

5. S. J. Vanderhoof, cited by T. H. Oliver and J. F. Wilkinson, "Critical Review of Anachlorhydria," *Quart. J. Med.*, Vol. 26 (2). 1933.

6. A. P. Hurst, "La Dégénéscence combinée subaigue de la moelle et ses rapports avec l'anémie pernicieuse, l'anachlorhydrie et les intoxications intestinales," *Ann. de Méd.*, 24:5-23. June, 1928.

7. A. J. Kohiyar, "Consecutive Series of 1,080 Gastric Analyses by Fractional Methods," *Guy's Hosp. Rep.*, 76:65-75. Jan., 1926.

in 1,030 cases; Conner,⁸ 15.2 per cent in 5,000 cases; and Friedenwald,⁹ .7 per cent in 1,592 cases.

Sex. Vanzant *et al*¹⁰ in a review of 3,381 fractional gastric analyses in apparently normal gastrointestinal tracts reached the conclusion that in all ages females are more liable to show achlorhydria than males. Apperly and Semmens¹¹ demonstrated achlorhydria to be common in healthy female students (30%). Lerman *et al*¹² in a study of 200 cases of apparently normal individuals found an incidence of 10 per cent in males and 15.4 per cent in females, and concluded that after the age of fifty years there was a tendency toward equal values in both sexes. Hartfall¹³ in an analysis of 2,356 patients found a sex distribution of 13.2 per cent for females and 7.5 per cent for males. Contrary to the findings of the above-cited workers, we have in our series 42 males (52.5%) and 38 females (47.5%) with anachlorhydria.

Age. The age distribution is partially in accord with the age distribution reported in other series of cases, for most of the cases occurred between the second and fifth decades. Most of the reports on anachlorhydria demonstrate an increasing incidence with advancing age. In the tropical and subtropical countries the span of life is shorter than in the temperate zone, and this may explain the small number of cases examined after the fifth decade in our series. Vanzant *et al*¹⁴ found achlorhydria to increase with age, rising from 4 per cent in the second decade to 26 per cent in the sixth decade. He further reports a decrease in incidence after seventy years of age, the highest incidence being in the sixth decade. Seidelin¹⁵ found achlorhydria or hypoacidity in 40 per cent of the working class patients over the age of fifty, and 67 per cent over the age of sixty-seven. Dedichen¹⁶ found 66 per cent of anachlorhydria in 99 healthy old people between the age of sixty-seven and ninety-two years.

8. H. M. Conner, "Hereditary Aspect of Anachlorhydria in Pernicious Anemia. A Study of Gastric Acidity in 154 Relatives of 109 Patients having Pernicious Anemia," *J.A.M.A.*, 94: 606-612. March 1, 1930.

9. J. Friedenwald, cited by T. H. Oliver and J. F. Wilkinson.

10. E. R. Vanzant and others, "Normal Range of Gastric Acidity from Youth to Old Age: Analysis of 3,746 Records," *Arch. Int. Med.*, 49:345-359. March, 1932.

11. F. Apperly and K. M. Semmens, "Fractional Test Meal in Normal Students; Comparison of Results with Those of Other Observers," *Med. J. Australia*, 2:237. 1928.

12. J. Lerman and J. H. Means, "Gastric Secretion in Exophthalmic Goiter and Myxedema," *J. Clin. Investigation*, 11:167-182. Jan., 1932.

13. Hartfall, *op. cit.*

14. Vanzant and others, *op. cit.*

15. H. Seidelin, cited by T. H. Oliver and J. F. Wilkinson.

16. L. Dedichen, cited by T. H. Oliver and J. F. Wilkinson.

Liefschutz¹⁷ reports an incidence of 37 per cent of achylia or anachlorhydria in cases over fifty years of age. Meulengracht¹⁸ noticed an even greater incidence—74 per cent in older people above sixty years of age. Keefer and Bloomfield¹⁹ and Gilford²⁰ made similar observations. Rafsky and Kruger²¹ found only one case of anachlorhydria in 75 old people whose ages ranged from seventy to ninety-one years. Davis and James²² reported a 32 per cent incidence of anachlorhydria in 100 people between the ages of sixty and ninety-five, but only half this number failed to secrete free hydrochloric acid after stimulation with histamine. Boekus *et al*²³ observed a gradually increasing incidence of anachlorhydria with advancing years from 1.3 per cent in the third decade to 15.4 per cent in the seventh decade.

Race. Sixty-eight (88%) of our cases belong to the white race; 7 (8.7%) were full-blooded Negroes, and 5 (6.2%) were mulattoes. Of the first, 34 (50%) were females. Among the full-blooded Negroes 6 (85.7%) were females, and among the mulattoes 3 (60%) were females.

Symptoms and signs. The most common symptoms encountered were: flatulence in 65 cases (81.25%), loss of weight in 53 (60.6%), diarrhea in 44 (55%), epigastric distress after meals in 42 (52.5%), and nervousness in 38 (47.5%). The most prominent signs, by far, were undernourishment in 48 cases (60%) and epigastric tenderness in 22 cases (28.5%).

Oliver and Wilkinson²⁴ classify the symptoms of anachlorhydria as functional, related to the gastrointestinal tract or to other organs and symptoms associated with organic disease. Symptoms classified as functional are flatulence, diarrhea, vomiting, nausea, heartburn, loss of weight, epigastric fullness, and oppression post coenum, and sometimes, pain. The most common symptoms, according to these authors, are flatulence and bowel disturbances.

17. M. J. Liefschutz, cited by T. H. Oliver and J. F. Wilkinson.

18. E. Meulengracht, cited by T. H. Oliver and J. F. Wilkinson.

19. C. S. Keefer and A. L. Bloomfield, "Quantitative Study of Effect of Sodium Bicarbonate on Gastric Function," *Bull. Johns Hopkins Hosp.*, 39:379-388. Dec., 1926.

20. H. Gilford, "Addison's Anemia," *Lancet*, 1:64-66. Jan. 13, 1923.

21. H. A. Rafsky and D. R. Kruger, cited by T. H. Oliver and J. F. Wilkinson.

22. D. T. Davis and T. G. I. James, "Investigations into Gastric Secretion of 100 Normal Persons over Age of 60," *Quart. J. Med.*, 23:1-14. Oct., 1930.

23. H. L. Boekus, J. Bank and J. H. Willard, "Achlorhydria with a Review of 210 Cases in Patients with G. I. Complaints," *Am. J. Med. Sc.*, 184:185-201. Aug., 1932.

24. T. H. Oliver and J. F. Wilkinson, "Critical Review of Anachlorhydria," *Quart. J. Med.*, Vol. 26 (2). 1933.

Eggleston²⁵ believes that constipation is a more frequent symptom than diarrhea. Eusterman²⁶ is of the opinion that with the exception of those cases simulating ulcer, there is no proof that the symptoms referable to the stomach are due to achlorhydria by itself, the majority of the symptoms being of neurogenic origin. Moore²⁷ has observed pylorospasm in some of the cases with achlorhydria, and says that rapid emptying of the stomach with increased motility is the rule. According to Oliver and Wilkinson²⁸ disturbances of the tongue have been found to be another complaint. This may vary from an intermittent sensation of discomfort without any physical signs whatsoever, to soreness of the anterior two-thirds with atrophy of the papillae or to frank ulceration. However, they draw attention to the fact that this finding may occur in a state of hyperacidity also. Keefer *et al*²⁹ believe that the changes in the tongue are due to a deficiency state, since they clear up under proper dietary regime. Physical findings, according to Oliver and Wilkinson,³⁰ are usually negligible; vague abdominal tenderness, chiefly over the descending colon, succussion splash and gurgling over the bowel, being most commonly encountered. In a recent study of chronic atrophic gastritis by Schindler and Murphy³¹ 13 out of 44 cases studied suffered from anachlorhydria. In every one of these, epigastric discomfort was an important complaint, described as distress, fullness, heaviness, or burning sensation of the stomach. In 46 per cent of the cases epigastric distress came on shortly after meals; in 38 per cent, one to four hours after meals; and in the remainder, the distress was permanent or at any time. Contrasting the symptomatology of atrophic gastritis with peptic ulcer, they stressed the absence of sharp or severe pain, of night pain, and, moreover, the relief obtained from food and alkalis was not as common in the former as in the latter. Bloating and belching were frequently encountered, the latter being a complaint in about 50 per cent of the cases. One

25. Eggleston, *op. cit.*

26. G. B. Eusterman, "Achlorhydria; Practical Consideration of its Clinical Significance," *Northwest Med.*, 30:249-256. June, 1931.

27. H. Moore, "Remarks on Clinical Study of Achlorhydria," *Brit. M. J.*, 1:363-368. Feb. 27, 1932.

28. Oliver and Wilkinson, *op. cit.*

29. C. S. Keefer, K. K. Huang, and C. S. Yang, "Anemia Associated with Chronic Dysentery, Clinical Considerations with Special Reference to Cause and Treatment," *Arch. Int. Med.*, 47:436-466. March, 1931.

30. Oliver and Wilkinson, *op. cit.*

31. R. Schindler and H. M. Murphy, "Symptomatology of Chronic Atrophic Gastritis," *Amer. J. Digest. Dis. & Nutrition*, 7:7-13. Jan., 1940.

patient complained of periods of diarrhea; in other words, there was almost a complete absence of the so-called "gastrogenic diarrhea." Several authors³² have stressed the importance of the nervous symptoms associated with achlorhydria or with chronic atrophic gastritis. Depression, sleeplessness, migraine, chronic fatigue, intolerance to cold, intense weakness brought on by even the slightest exertion, and a feeling of exhaustion, are many of the symptoms which make the differential diagnosis between these conditions and psychoneurosis extremely difficult at times.

Achlorhydria and organic diseases. The association of achlorhydria with diseases of the gastrointestinal tract, hematopoietic system, central nervous system, endocrine system, as well as with disease of joints and those of allergic origin, is well known. The relationship of achlorhydria and gastric carcinoma has been a question of great interest during the past years. Some authorities believe that free HCl in the stomach contraindicates a diagnosis of malignancy. Lately, however, many authors—among them Hurst,³³ Hartman and Sager,³⁴ Friedenwald,³⁵ Apperly and Norris,³⁶ and Arafa,³⁷ have reported cases of gastric carcinoma with the presence of free HCl in the stomach contents. The association of duodenal ulcer with achlorhydria has been disputed by many authors: Kohn,³⁸ Bockus *et al*,³⁹ and Horner.⁴⁰ Palmer and Nutter⁴¹ have lately reviewed the literature and have concluded that duodenal ulcer has never been encountered in the presence of achlorhydria. In our series of cases, the most common diagnoses were macrocytic hyperchromic anemia (tropical macrocytic anemia?), 20 cases (25%); sprue, 16 cases (20%); uncinariasis in 9 cases (11.25%); cholecystitis, 7 cases (8.9%); and secondary anemia (cause unknown) in 8.9 per cent of the cases.

32. Eggleston, *op. cit.*; Bockus, Bank and Willard, *op. cit.*; and Schindler and Murphy, *op. cit.*

33. A. F. Hurst, "Schorstein Lecture on Precursors of Carcinoma of Stomach," *Lancet*, 2:1023-1028. Nov. 16, 1929.

34. H. R. Hartman and W. W. Sager, "Statistical Study of Diagnostic Value of Anacidity," *Med. J. and Record*, 124:96-97. July 21, 1926.

35. J. Friedenwald, cited by T. H. Oliver and J. F. Wilkinson.

36. F. L. Apperly and J. H. Norris, cited by T. H. Oliver and J. F. Wilkinson.

37. M. A. Arafa, cited by T. H. Oliver and J. F. Wilkinson.

38. E. Kohn, cited by T. H. Oliver and J. F. Wilkinson.

39. H. L. Bockus *et al*, cited by T. H. Oliver and J. F. Wilkinson.

40. C. B. Horner, cited by T. H. Oliver and J. F. Wilkinson.

41. W. L. Palmer and P. B. Nutter, "Peptic Ulcer and Achlorhydria. Further Study of Role of Acid. Gastric Juice in Pathogenesis of Peptic Ulcer," *Arch. Int. Med.*, 65:499-509, March, 1940.

Blood picture. Among 77 cases in which complete blood work was done, the red blood cell count varied from 880,000 to 6,250,000 per c.mm. In 54 cases (70%) the red blood cell counts varied between 3 and 4½ millions; in 14 (18%) it was over 4½ millions, and in 7 cases (9%), above 5 millions; in 9 (11%) there was a profound anemia with counts below 3 millions. The hemoglobin percentage oscillated between 2.9 gm. (20%) and 17.4 gm. (120%). In 14 cases (18%) the hemoglobin was below 5.8 gm. (60%), and in 56 cases (72%) the values varied between 5.8 gm. (60%) and 14.5 gm. (100%). In 9 cases the hemoglobin was above 14.5 gm. (100%). White blood cell counts in 53 (66%) cases ranged between 5,000 and 8,000 cells per c.mm. In 14 cases (17%) a leukopenia was encountered, while in 5 cases (6%) the count was over 10,000. Eosinophilic leukocytes were seen in the smears of 45 cases (56.25%). In 24 cases (53%) there was eosinophilia percentage ranging from 5 to 18.

Alvarez and Vanzant⁴² have expressed the idea that when hemoglobin drops to a point below 12 grams (72%) there is a corresponding fall in the gastric acidity with a rapid rise in the incidence of gastric anachlorhydria. Apperly and Cary⁴³ assert that when the hemoglobin approximates an average of two-thirds of the normal value, anachlorhydria frequently occurs, i.e., anemia can bring about anachlorhydria; but Bloomfield and Keefer⁴⁴ and Hurst and Bell⁴⁵ believe that anemia causes no impairment whatsoever to gastric secretion. Keefer and Young⁴⁶ have shown that in treatment of cases of hypochromic anemia, free hydrochloric acid can return concomitantly with improvement in the gastric function. Wintrobe and Beebe⁴⁷ state that free HCl acid is frequently found in idiopathic hypochromic anemia. Among 24 cases they found a normal secretion in 2 cases (8%), hypochlorhydria in 10 cases (41%), and the remaining 12 cases (51%) showed histamine anachlorhydria.

42. W. C. Alvarez and F. R. Vanzant, "Relations between Hemoglobin and Gastric Acidity," *Proc. Staff Meet., Mayo Clin.*, 11:385-391. June 17, 1936.

43. F. L. Apperly and M. K. Cary, "The Relation of Gastric Acidity to the Erythrocyte Count of Blood," *Am. J. Dig. Dis. & Nutrition*, 3:466. Sept., 1936.

44. A. J. Bloomfield and C. S. Keefer, "Gastric Acidity; Relation to Various Factors," *J. Clin. Investigation*, 5:285. Feb., 1928.

45. A. F. Hurst and J. R. Bell, "The Pathogenesis of Subacute Combined Sclerosis," *Brain*, 45:266. Oct., 1922.

46. C. S. Keefer and C. S. Young, "Value of Liver and Iron in Treatment of Secondary Anemia," *J.A.M.A.*, 93:575-578. Aug. 24, 1929.

47. M. M. Wintrobe and R. F. Beebe, "Idiopathic Hypochromic Anemia," *Medicine*, 12:187. May, 1933.

Faber and Gram,⁴⁸ nevertheless, have shown that in the majority of cases anacidity is principally the result of a disorder of the gastric mucosa or some type of gastritis; mainly, a diffuse gastritis tending to atrophy. Faber and Hurst believe that anacidity is a precursor of gastric carcinoma, pernicious anemia, combined sclerosis, and "less clearly defined" disabilities featuring sore mouth and diarrhea. Hartfall and Witts⁴⁹ draw attention to the association of achlorhydria and hypochromic anemias among certain families. Faber and Gram⁵⁰ state that the anemia associated with achylia gastrica is a secondary phenomenon produced by the absence of gastric secretion. Among 201 cases of achylia gastrica he found 59 (29%) with a hemoglobin below 80 per cent, 22 (10.9%) were examples of Addison's anemia, and 37 (18%) were cases of simple anemia. Twenty-two of the cases of simple anemia were very severe, with hemoglobin below 65 per cent. Among 60 cases of gastric anacidity analyzed by Hunter,⁵¹ 7 (11.6%) had a moderate or severe secondary anemia, and most of the patients had chronic diarrhea. Faber and Gram⁵² reported 96 cases of achlorhydria, 41 of them with anemia. Schneider and Carey⁵³ encountered 7 cases of anachlorhydria with a high color index and 7 with a secondary anemia, in a series of cases totaling 51. Borgbjoerg and Lottrup⁵⁴ report 41 per cent of 134 cases of anachlorhydria with a secondary anemia of mild degree and several of them with a color index above 1. Bloomfield⁵⁵ stresses the fact that various degrees of anemia may be associated with anacidity and that all types of gastric secretion may be associated with anemia. Ivy *et al*⁵⁶ have collected a total of 36 cases of pernicious anemia preceded by anacidity.

Color Index. The color index varied from .45 to 2. Thirty-nine (50.6%) out of 77 hemoglobin and red blood cell estimations showed a color index above 1. Twenty-nine (37.7%) were below 1, and in

48. K. Faber and H. C. Gram, cited by T. H. Oliver and J. F. Wilkinson.

49. S. J. Hartfall and L. J. Witts, cited by T. H. Oliver and J. F. Wilkinson.

50. Faber and Gram, *loc. cit.*

51. C. Hunter, "Analysis of 60 Cases of Gastric Anacidity Associated Mainly with Chronic Diarrhea and Pernicious Anemia," *Canad. M. Arc.*, 13:38-43. Jan., 1923.

52. K. Faber and H. C. Gram, "Relations between Gastric Achylia and Simple and Pernicious Anemia," *Arch. Int. Med.*, 34:658-668. Nov., 1924.

53. J. P. Schneider and J. B. Carey, "Clinical Significance of Primary Achlorhydria," *J.A.M.A.*, 91:1763-1768. Dec. 8, 1928.

54. A. Borgbjoerg and M. C. Lottrup, "Examinations of Blood in Gastric Achylia, with Special Regard to Pernicious Anemia," *Hospitalstid.*, 72:745-764. July 11, 1929.

55. A. L. Bloomfield, cited by T. H. Oliver and J. F. Wilkinson.

56. A. C. Ivy, J. E. Morgan, and J. L. Farrel, "Effects of Fatal Gastrectomy; Experimental Achylia Gastrica in Dogs with Occurrence of Spontaneous Anemia and Anemia of Pregnancy," *Surg., Gynec. & Obst.*, 53:611-620. Nov., 1931.

8 cases (11.7%) the color index was 1. Only one case showed a color index of 2. Fourteen cases (18.3%) had a color index below .9; 7 (9%), below .8; 4 (5.2%), below .7; and 4 (5.2%), below .6; while only 2 cases (2.6%) were found to have a color index below .5. In the light of the above figures and according to the interpretation given to a color index above 1, we have to assume that 50.6 per cent of our cases had a hyperchromic blood picture. Twenty-two (28.7%) cases had a normal color index (.9 to 1). Sixteen cases (20.7%) had a hypochromic blood picture.

Incidence of syphilis in our series. Among the 80 cases presented there were six luetics: five white patients and one colored patient, two females and four males. The colored luetic was a male.

Parasitic infestation. The concomitance of parasitic infestation and anachlorhydria is quite remarkable in our series. There were 9 (11.2%) cases of hookworm disease; 5 (6%) cases with *E. histolytica*; 2 (2.5%) with *Schistosoma mansoni*; 13 (16%) with *E. coli*; 5 (6%) with whipworm; and 4 (8%) with *E. nana*. In 3 (3.7%) cases two or more intestinal parasites were found. In 35 cases (43.75%) parasitic infestation was discovered on routine fecal examinations.

Time of attendance and treatment. This varied anywhere from twenty-one days to ten years. In 52 cases dilute HCl acid and pepsin was given with each meal; in 31 cases liver extract was administered. The liver extract used was prepared from Lilly's liver extract powder 341, in which 1 cc. of the solution is equivalent to 2 grams of liver. These medications constituted by far the most important therapeutic means. In the cases showing a hypochromic blood picture, either ferrous sulphate or ferric ammonium citrate was used. Out of the 80 cases studied, improvement in the general condition of the patients was noted in 51 (63.7%); 10 (12.5%) were only slightly improved; and in 19 (23.9%) of them, treatment was of no avail. So far as the anachlorhydria *per se* is concerned, no improvement was noticed in those cases in which the gastric analysis was repeated. Whether this lack of response was due to improper treatment or to the extensive alteration in the glandular element of the gastric mucosa is difficult to ascertain. Recent studies by Schindler and Serby⁵⁷ in pernicious anemia and chronic atrophic gastritis tend to demonstrate some degree of improvement in the gastric mucosa, as observed through the gastroscope after the administration of massive doses of liver extract and vitamin B₁.

SUMMARY AND CONCLUSIONS

1. Among 684 analyses, 80 (11.7%) showed anachlorhydria. All cases were comprised of Puerto Rican indigents. The percentage of occurrence of anachlorhydria is in accord with other results reported by different workers in all parts of the world.

2. The incidence among males was a little higher than among females, which is contrary to the results obtained by other authors.

3. The age distribution is partially in accord with other series, for most of the cases occurred between the second and fifth decades. This may be explained by the shortened span of life in the tropics.

4. Among the 80 cases reported, 68 belonged to the white race, 7 were full-blooded Negroes, and 5 were mulattoes.

5. The most common symptoms encountered were: flatulence, loss of weight, diarrhea, epigastric distress after meals, and nervousness. The most prominent physical signs were undernourishment in 60 per cent of the cases and epigastric tenderness in 27.5 per cent.

6. Organic diseases associated with achlorhydria in our series of cases were: tropical macrocytic anemia; sprue; uncinariasis; cholecystitis; and idiopathic microcytic anemia.

7. The blood picture among 77 cases in which the blood work was completed was as follows: red blood cell counts varied from 880,000 to 6,250,000 per c.mm. In 54 cases the red blood cell count varied from 3 to 4½ millions; in 7 cases, above 5 millions; in 17 cases it was over 4½ millions; while in 9 there was a profound anemia with counts below 3 millions. Hemoglobin percentage oscillated from 20 to 120 per cent; in 14 cases the hemoglobin was below 60 per cent; in 56 cases it varied between 60 and 100 per cent; and in 9 cases it was above 100 per cent.

8. Color index varied from .45 to 2. Out of 77 cases, 39 (50.6%) had a color index above 1, while 8 cases had a color index of 1. One case showed a color index of 2. Thus 50.6 per cent of our cases revealed a hyperchromic blood picture.

9. Fourteen cases showed a leukopenia, while in 5 cases only a leukocytosis was demonstrated.

10. Eosinophilia was encountered in 56.25 per cent. In 24 cases (31%) it ranged from 5 to 18 per cent.

11. Lues was encountered in 6 (7.5%) of the cases.

12. The concomitance of anachlorhydria with parasitic infestation was quite remarkable. In 35 cases (43.75%) parasitic infestation was discovered in routine fecal examinations.

57. R. Schindler and A. M. Serby, "Gastrosopic Observations in Pernicious Anemia," *Arch. Int. Med.*, 63:334-356. Feb., 1939.

13. The most important medications used were crude liver extract and dilute HCl acid and pepsin. The time of attendance varied from twenty-one days to ten years. Out of the 80 cases, 51 showed some general improvement; 10 were very slightly improved; and in 19, treatment was of no avail.