First progress report / by J.F. Silner, P.E. Garrison and W.J. Macneal.

PELLAGRA

FIRST PROGRESS REPORT

OF THE

THOMPSON-McFADDEN PELLAGRA COMMISSION

OF THE

NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL

BY

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and others

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A SUMMARY OF THE FIRST PROGRESS REPORT OF THE THOMPSON-MCFADDEN PELLAGRA COMMISSION *

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Through the instrumentality of Dr. George N. Miller, at that time president of the New York Post-Graduate Medical School, funds were donated by Col. Robert M. Thompson of New York City and Mr. J. H. McFadden of Philadelphia to support a research expedition for the investigation of pellagra in the United States. It was decided that if possible a commission of three would be formed, one member to be designated by the Surgeon-General of the Army, one by the Surgeon-General of the Navy and one by the authorities of the New York Post-Graduate Medical School. Dr. Jonathan Wright, director of laboratories at the medical school, was requested by the school authorities to act in an advisory capacity. The commission was constituted as follows: Captain J. F. Siler, Medical Corps, U. S. Army, representing the Medical Corps of the U. S. Army; Passed-Assistant Surgeon P. E. Garrison, U. S. Navy, representing the Medical Corps of the U. S. Navy, and Dr. W. J. MacNeal, Professor of Bacteriology and Pathology and Assistant Director of Laboratories, New York Post-Graduate Medical School, representing the New York Post-Graduate Medical School.

It was decided that the investigation should be conducted along two lines: first, an epidemiologic study of pellagra in an endemic area of the South; and, second,

* From the Division of Tropical Medicine, Department of the Laboratories, New York Post-Graduate Medical School and Hospital. Read at the Pellagra Meeting at Spartanburg, S. C., Sept. 3, 1913.

biologic, pathologic and chemical studies in New York City and elsewhere. The epidemiologic studies were undertaken by Passed Assistant Surgeon P. E. Garrison of the U. S. Navy and J. F. Siler, Captain Medical Corps, U. S. Army.

A field headquarters was established in the South early in June, 1912, and the field studies were continued until Oct. 15, 1912. The Bureau of Entomology of the U. S. Department of Agriculture, early in the spring of 1912, detailed Mr. A. H. Jennings and Mr. W. V. King to investigate the possible etiologic relationship between insects and pellagra. These entomologists were in South Carolina when the field headquarters of the commission was established, and through the courtesy of Dr. L. O. Howard, Chief of the Bureau of Entomology, it was arranged that these investigators and this commission should undertake cooperative work in the same territory.

Biologic, pathologic and chemical studies were undertaken in the laboratories of bacteriology, pathology and pathologic chemistry of the New York Post-Graduate Medical School under the supervision of Dr. Jonathan Wright, Director of Laboratories, and Dr. W. J. MacNeal, a member of the commission. The researches along these lines were carried out by Dr. W. J. MacNeal, Dr. O. S. Hillman, Dr. R. M. Taylor, Dr. V. C. Myers and Dr. M. S. Fine. In order to obtain material for these investigations, selected patients were sent to New York from the endemic area, pathologic material was collected in the field, and other material was supplied to the commission through the courtesy of Dr. J. W. Babcock of Columbia, S. C. Studies of the pathologic material are being undertaken by Dr. H. Douglas Singer of the Illinois State Psychopathic Institute.

Several detailed papers constituting a preliminary or progress report have been published during the past year. It is the purpose of this present paper to summarize briefly the observations recorded in these separate reports, to discuss their bearing on the various theories concerning the causation of pellagra and to express in a tentative fashion some of our opinions which are based thereon.

THE FIELD WORK IN SPARTANBURG, S. C.

The epidemiologic studies have led to the accumulation of a very large mass of data concerning the occurrence and distribution of pellagra in Spartanburg County,

S. C., in regard to the cases themselves and their conditions in life. Some of this material has been presented in a preliminary fashion in a paper by Siler and Garrison.[1] They have summarized the matter as follows:

1. Pellagra shows a striking inequality of distribution in ten townships within the county, the township rate of prevalence per ten thousand of population varying from 0 to 71. The city of Spartanburg, with a population of 17,517, gave a rate of 49 per ten thousand against 34 per ten thousand for the remainder of the country.

2. Density of population, while showing a tendency to conform to the relative prevalence of the disease, does not alone offer an explanation of the geographic inequalities of its distribution within the county.

3. The cotton-mill village population gives a rate of prevalence of 104 per ten thousand against 19 per ten thousand for the remainder of the county and against 16 per ten thousand for the rural sections alone.

4. The variations in the rates of prevalence in the ten townships are in a measure proportional to the presence or absence of a large mill-village population. Excluding the mill-village population, there is still a marked discrepancy between the townships, the rate of prevalence in the rural population ranging from 0 to 29 cases per ten thousand of population. The excessive prevalence among the farming classes is found in the townships which have a relatively large mill-village population.

5. The white population of the county gives a prevalence of 45 cases per ten thousand; the negro population a prevalence of 9.5 per ten thousand. Excluding the mill-village population which is practically all white, the remaining white population still gives a rate of prevalence (25.2 per ten thousand) over two and one-half times that among the negroes.

6. The rate of prevalence per ten thousand for males in the county is 17; for females, 50.5. White males give a rate of 22.95 per ten thousand; white females, 87.5 per ten thousand; negro males, 3.9 per ten thousand; negro females, 14.9 per ten thousand.

7. The rate of prevalence among children under 10 years of age and among adults aged 45 years and older, is practically equal in the two sexes.

8. The rate of prevalence drops among males between the ages of 19 and 45 years, whereas for females there is a remarkable excess of prevalence between these ages.

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1. Siler and Garrison: An Intensive Study of the Epidemiology of Pellagra, Report of Progress, Am. Jour. Med. Sc., July, 1913, p. 42, and August, 1913, p. 238.

9. In both males and females there is a striking fall in prevalence between the ages of 10 and 20 years.

10. The most significant fact with regard to occupation is the excessive prevalence of pellagra among women employed in housework.

11. The excessive prevalence of pellagra in the mill-village population is found largely among women and children at home during the day. Among actual mill-workers the rate of prevalence in the two sexes appears to be about equal.

12. One-half of the cases occurred singly in one family; about one-fourth occurred two in one family; the remaining fourth occurred in groups of three, four or five in one family. The question of the possible relative importance of family relationship and household association is still under investigation.

13. Among cases occurring singly in families, the proportion of children of both sexes under 10 years of age is low and that of adult females excessively high. Among cases occurring two or more in one family the proportion of young children is relatively high, especially among males.

14. While apparently authentic sporadic cases of pellagra within the county can be traced back to as early as 1894, the disease does not appear to have occurred in any great number of cases in any year until 1908. Since 1908 the incidence rate appears to have rapidly increased each year to 1911. The number of new cases developing in 1911 appears to have been slightly greater than in 1912.

15. There was no evidence pointing to any spring and fall recrudescence of the disease in the population, so frequently referred to in the literature of pellagra. There is no particularly marked tendency for the seasonal recurrence to appear in an individual during the same month, year after year.

16. Influence of Climate: Climatic conditions appear to influence the development of symptoms of the disease. If during the spring months precipitation is high, temperature low and number of rainy days excessive, the appearance of acute symptoms, more particularly those involving the skin, is delayed.

17. Symptomatology: It would appear that three or four years ago a large proportion of the cases observed in the county presented intestinal and nervous symptoms of great severity. In 1912, in many instances, symptoms were quite mild and sometimes were confined almost exclusively to the cutaneous system, the disease appearing to be of a less virulent type in 1912 than in previous years.

18. Economic Status: In the majority of cases (85 per cent.) economic conditions are poor and the disease is most prevalent among people of insufficient means.

19. Predisposing Diseases: General health conditions in childhood do not appear to warrant consideration as etiologic factors when the disease develops in adult life. In a number of cases the development of pellagrous symptoms in children was preceded by one of the acute exanthematous diseases of childhood. About one-fourth of the cases gave a history of a preceding chronic disease in adult life. In more than one-half of the cases (62 per cent.) the history was that of good health. Among adult females, those most affected were married women (86 per cent.) and 86 per cent. of the married women had borne children. A history of illness immediately preceding the development of pellagra was elicited in 59 per cent. of the cases.

20. Hygiene and Sanitation of Houses and Premises: The most insanitary condition found in the county is the absence of properly constructed privies. Outside of a part of the city of Spartanburg, which is supplied by a water-carriage sewage system, there is no effective provision in the county for the proper disposal of human excreta. A second striking insanitary condition is the almost complete absence of effective screening of dwellings. These two conditions present a situation highly favorable to the transmission of disease organisms eliminated in the excreta, both by direct contamination of food and person and by insects. This situation is naturally aggravated in the mill-villages and small towns by the greater congestion of houses. The absence of effective screening for dwellings gives rise to conditions conducive to the possible transfer of diseases transmitted by biting insects.

21. Dietary: Observations on the habitual use of the more common foodstuffs failed to discover any points of difference between pellagrins and non-pellagrins in the county or any facts which would seem to explain the strikingly greater prevalence of pellagra among certain classes of the population.

The most striking defect in the general dietary of the working classes, appears to be the limited use of fresh meats, the animal protein being supplied largely in the form of cured meats, of which salt pork (especially bacon) is the most important.

Unhygienic preparation of food appears to be a probable important factor in the general health of the population.

Investigation of the kind, quantity and quality of corn and corn products used in the county, failed to bring to light any epidemiologic evidence pointing to the agency of corn as an etiologic factor in the disease. The presence of two cases in our series giving a definite history of no corn consumption within two years prior to the onset of symptoms, together with several other cases in which corn products were eaten, if at all, only in small quantity and at extremely rare intervals, would seem to argue strongly against any hypothesis

that corn products alone are the causative agent of the disease.

In intimate collaboration with the field party of the commission, Mr. A. H. Jennings and Mr. W. V. King, members of the staff of the Bureau of Entomology, U. S. Department of Agriculture, have pursued thorough studies of the insects which seemed worthy of attention as possible carriers of pellagra in Spartanburg County. The results obtained by these investigators have been presented in two papers.[2]

The following is quoted from their conclusions:

Ticks, lice, bed-bugs, cockroaches, horse-flies, fleas, mosquitoes, buffalo gnats *(Simulium)*, house-flies and stable-flies *(Stomoxys)* were under consideration. Of these, horse-flies have nothing and cockroaches little to support them.

Ticks and fleas are excluded on account of their scarcity and the nature of their biting habits. In view of these characteristics, it is doubtful if even the existence of an animal reservoir of infection would bring the groups into prominence.

Lice and bedbugs do not account for the sex or age incidence or the rural nature of the disease; the scarcity of the former species is an additional reason for its exclusion.

The rarity of mosquitoes here and the lack of coincidence between their distribution and that of pellagra for the state in general, together with the night-biting habits of the local species, which fail to account for the sex incidence, seem sufficient cause for their elimination.

House-flies *(Musca domestica)* should be active if the malady is an intestinal infection in which the germ is passed with the feces, with contaminated food acting as the vehicle of infection.

The buffalo gnats *(Simulium)* should be eliminated, principally on account of their biting habits and lack of intimate association with man, also possibly by their comparatively moderate abundance (in our territory). We find that in Spartanburg County they are hardly known as a pest of man and when they do attack him, the nuisance is local and largely confined to field workers. Had Sambon's theory not been advanced, these flies could hardly have attracted suspicion of any connection with pellagra in this country.

The stable-fly *(Stomoxys calcitrans)* displays certain salient characteristics which seem to qualify it for the rôle of a transmitter of pellagra.

The range of this one species covers and exceeds that of pellagra; its seasonal activity, likewise, is coincident with that of the disease and, although its period of greatest abun-

2. Jennings and King: THE JOURNAL A. M. A., Jan. 25, 1913, p. 271; Am. Jour. Med. Sc., September, 1913, p. 411.

dance is somewhat later than the maximum intensity of pellagra, its appearance in spring precedes that of most of the spring recurrences and new cases, at which time it is already abundant; it is an abundant species, its abundance being most manifest in rural districts, thus corresponding with the rural nature of pellagra, its numbers amply fulfilling our conception of those necessary to effective disease transmission; it bites by day only, thereby offering an explanation of the phenomenon of sex incidence and the related one of age distribution; it is intimately associated with man and habitually infests his vicinity and enters his dwellings; it bites man frequently and persistently; its longevity seems sufficient for the development of a hypothetic causative organism; it is readily and frequently carried long distances and might thus account for the occurrence of sporadic cases of the disease.

THE LABORATORY WORK IN NEW YORK

The material for the studies made in New York was obtained by sending patients suffering from pellagra from the field headquarters in South Carolina to the Post-Graduate Hospital in New York City. Altogether fifteen patients were sent to New York during the summer. All these patients showed a typical eruption on the skin and there was considerable variation among them as to the severity of the disease, stage of eruption, general physical vigor and financial status. The detailed observations on these patients have not yet been published. One of them remained under observation in the hospital only two days and was then removed to the house of relatives near New York. The other fourteen patients remained under observation until the acute manifestations of pellagra had disappeared and the physical condition of the patients warranted their return home. No specific medication was employed during the attack of pellagra in any of the cases but arsenic was given to two of the patients, after the acute manifestations of the disease had passed, in the form of sodium cacodylate in one case and as Fowler's solution in the other. The detailed observations on these cases and their subsequent history we hope to present in a later report.

The material for laboratory examination was largely obtained from these patients, but in addition samples of blood-serum, blood-films and some other material were obtained from patients in South Carolina and sent to the laboratory in New York.

The histology of the blood was studied by Dr. O. S. Hillman, Lecturer in Pathology at the New York Post-Graduate Medical School, and his report has already appeared.[3] He found a variable degree of chloranemia—not constituting, however, a prominent feature of the disease—and not infrequently a leukocytosis, apparently inexplicable in the light of our present knowledge of the disease. Lymphocytosis was present in the great majority of cases and may be correlated with the general cachexia of the patients and with the presence of digestive disorders. No characteristic or constant variations were detected in the large mononuclear leukocytes or in the eosinophil cells.

The chemical studies on the patients in New York were carried out by Prof. V. C. Myers and Dr. M. S. Fine and have been reported in detail.[4] The study includes analyses of the gastric juice, quantitative estimation of the food intake and quantitative analysis of the urine and feces of the patients during certain periods of their stay in the hospital. The results of this work have been summarized as follows:

The ability of individuals suffering from pellagra to utilize the various foodstuffs as indicated by our series of fifteen experiments appears to be only slightly if at all below the normal.

The elimination of mineral and nitrogenous constituents in the urine is such as would be anticipated under the dietary and physical conditions of the individuals. A lowered physiologic efficiency is indicated by the low creatinin coefficients and the elimination of small amounts of creatin in the urine. The presence of a few hyaline casts in about 45 per cent. of the cases points to some possible irritation of the kidney.

Anacidity is a condition common in pellagra, found in eight of our fourteen cases. It is generally associated with an entire absence of pepsin, or with pepsin in only very minute quantities.

Individuals suffering from pellagra show a marked indicanuria, which is excessive in the cases with gastric inefficiency. Though the ethereal sulphate hardly parallels the indoxyl-potassium sulphate, the quantities eliminated are much higher where anacidity exists and they furthermore hold a higher ratio to the inorganic sulphates.

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3. Hillman: Some Hematologic Findings in Pellagra, Am. Jour. Med. Sc., April, 1913, p. 507.

4. Myers and Fine: Metabolism in Pellagra, Am. Jour. Med. Sc., May, 1913, p. 705.

The feces contain decidedly abnormal amounts of indol and skatol, especially the latter.

The presence of excessive amounts of indican in the urine, associated with a high elimination of ethereal sulphates, when considered in connection with the abnormal amounts of indol and skatol in the feces, points to some unusual bacterial conditions in the intestine. From the data at hand this putrefaction would appear to take place rather high up in the intestine.

The bacteriologic studies[5] were directed more particularly to the possible relation of intestinal bacteria to pellagra and a large number of agglutination tests were made with various bacterial strains. One of these seemed to react with the blood of pellagrins more frequently than with blood of other individuals, but we have not succeeded in establishing a specific relation of this organism to the disease. The quantitative changes in the bacterial flora of the feces are such as might be expected in irritation of the digestive tract. Numerous attempts to produce the disease in monkeys (*Macacus rhesus*) by the injection of defibrinated blood were without definite result.

RELATION OF THE REPORTED OBSERVATIONS TO THE VARIOUS THEORIES CONCERNING THE ETIOLOGY OF PELLAGRA

The theory that pellagra is due to the ingestion of maize or maize products, either good or spoiled, seems to us wholly inadequate to explain the distribution of the disease actually observed in Spartanburg County, S. C., in 1912, not only because typical severe cases of the disease were observed in those who had abstained from the ingestion of corn for a considerable time, but also because there could be discovered no essential difference in respect to the consumption of corn between those suffering from pellagra and those free from the disease.

The conception that pellagra is an infectious disease in some way transmissible from person to person seems to us to be strongly supported by many of the field observations. The higher incidence of pellagra in the more populous districts and the indications of its occurrence in definite foci are in accord with this idea, and, furthermore, the definite tendency to self-limitation of the attack in the absence of specific therapy and during the

5. MacNeal: Observations on the Intestinal Bacteria in Pellagra, Am. Jour. Med. Sc., June, 1913, p. 801.

continuance of a corn diet bears a very suggestive resemblance to the course of an infectious disease. All the members of the commission and every one of the investigators associated with us in the work have come to regard pellagra as an infection in all probability and many of us would state that as our opinion without any reservation whatever.

Concerning the particular mode of transmission of the disease, the observed evidence does not appear to us to be at all conclusive. The theory of Sambon that pellagra is transmitted by a blood-sucking fly of the genus *Simulium* is based on epidemiologic evidence and apparently to a large degree on the conception that pellagra is a disease of field workers and those who go frequently into the fields. In Spartanburg County pellagra appears to be more especially prevalent in the factory villages and has a higher incidence in the City of Spartanburg itself (population 17,517) than in the less thickly populated remainder of the county. Furthermore, the adult males (the class of the population from which the field workers are largely drawn) show a striking relative freedom from the disease in our statistics. Indeed, one may go farther and say that pellagra in Spartanburg County, although it shows a tendency to attack all classes of the population, is more especially a disease of the women and children in the villages of the cotton-mills. Furthermore, it may be stated that in spite of the abundance and universal occurrence of *Simulium* in the area studied, we have been unable to elicit a history of frequent biting of man by buffalo gnats or black flies in Spartanburg County and this point has been inquired into with special care in the cases of pellagra observed. The experience of the field workers of the commission itself, who have spent day after day in the homes and environs of the pellagrins in Spartanburg County, has failed to note a single instance in which anyone of them personally has been attacked by a fly of the genus *Simulium* during the season of 1912.[6]

A comprehensive consideration of the insect life in the county undertaken by Mr. A. H. Jennings and Mr. W. V. King of the Bureau of Entomology, U. S. Department of Agriculture, has led them to the conclusion that if the distribution of pellagra is to be accounted for by a blood-sucking insect, the observed facts in Spartanburg

6. During 1913 two instances of biting by gnats of the genus *Simulium* have been noted by the investigators.

County point to *Stomoxys calcitrans* as the most probable insect carrier. This opinion is shared by the members of the commission. We do not regard the evidence of transmission of pellagra by a blood-sucking insect in this county as at all conclusive, but we do consider it an important field for further observation.

The possible relation of an insufficient diet to the occurrence of pellagra has received careful consideration and we are inclined to ascribe considerable importance to it, not as the sole or essential cause of pellagra, but as a predisposing factor. The foods rich in animal protein, namely, meat, milk and eggs, although apparently used in abundance by a few individual pellagrins in our series, are, nevertheless, conspicuous by their deficiency in many of the cases. The use of these foods may perhaps be regarded as an index of economic condition and the variation in the incidence of pellagra be explained as due to economic factors in general. We are inclined, however, to regard the relation of nutrition to pellagra as a more direct one. The thesis that deficiency in the quality and quantity of food can be regarded as the essential cause of pellagra seems to us not to be supported by our studies. The fact is that a poorly nourished community generally shows a higher incidence of pellagra than one on a higher plane of nutrition, and, further, that those individuals in a community who are more poorly nourished seem more liable to develop pellagra. There is abundant evidence that other weakening factors, such as exanthematous disease, childbirth and tuberculosis, may play important rôles as predisposing factors. We are inclined to lay stress on the indication apparent in our statistics that poor nutrition or other predisposing cause results in pellagra only when the individual in question has lived in a relatively close association with a previous case of pellagra. The great mass of the population living under the same general conditions of environment and using the same food but living at a greater distance from cases of pellagra escapes the disease.

Our ideas concerning the location of a hypothetic infectious agent in the body of the pellagrin and the exact mode or means by which it gains the body of a new victim are very indefinite. The possibility of transmission by blood-sucking insects has already been considered. This hypothesis calls for the presence of the parasite in the blood or in the superficial tissues of the body.

We are not aware of other important reasons for supposing that the hypothetic parasite exists in either of these situations. The gross and microscopic appearances and the distribution of the skin lesions as well as the histologic changes in the nervous system have been generally regarded by pathologists as reactions to a general intoxication rather than to local infections.[7] No microorganisms have been recognized in these lesions. The possibility that such may exist there cannot, however, be excluded.

The possible localization of the hypothetic parasite in the digestive tract has seemed to us to be worthy of careful consideration. The observed distribution of the disease in Spartanburg County is in accord with the conception that pellagra may be transmitted through contamination of food with the excretions of pellagrins. Its greatest prevalence is in those places without adequate provision for the disposal of human wastes. The agreement between the distribution of the open surface privy close to the unscreened dwellings and the distribution of pellagra is in many instances rather striking. The quite constant presence at necropsy of pathologic lesions in the intestine, acute or chronic inflammation, ulceration and atrophy of the intestinal walls in the later stages, as well as the common occurrence of gastro-intestinal symptoms early in the course of the disease are in accord with this hypothesis, although of course they may also be explained as secondary phenomena. In our opinion the view that pellagra is an intestinal infection, transmitted by contaminated food, to which the individual is rendered more susceptible by malnutrition, poorly selected or poorly prepared food and by the common gastro-intestinal disturbances resulting from errors in diet, is a conception worthy of much further study.

These views are expressed at this time to serve as a general summary and conclusion to the series of papers which constitute the first progress report of this commission. Many, but not all of the observed facts on which it is based have been presented in detail in these separate papers. We hope to supplement and extend the observations during the second year of the investigation and

7. Ormsby and Singer: Clinical and Pathologic Studies, Rep. of Pellagra Commission of State of Illinois, Springfield, Ill., 1911, p. 16; Singer and Pollock: The Histopathology of the Nervous System in Pellagra, THE ARCHIVES INT. MED., June, 1913, p. 565; Mott: The Histologic Changes in the Nervous System of Dr. Box's Case of Pellagra, Brit. Med. Jour., July 5, 1913, p. 4.

expect to present in a later report results of all the work in greater detail, together with ample discusssion.

SUMMARY

1. The supposition that the ingestion of good or spoiled maize is the essential cause of pellagra is not supported by our study.

2. Pellagra is in all probability a specific infectious disease communicable from person to person by means at present unknown.

3. We have discovered no evidence incriminating flies of the genus *Simulium* in the causation of pellagra, except their universal distribution throughout the area studied. If it is distributed by a blood-sucking insect, *Stomoxys calcitrans* would appear to be the most probable carrier.

4. We are inclined to regard intimate association in the household and the contamination of food with the excretions of pellagrins as possible modes of distribution of the disease.

5. No specific cause of pellagra has been recognized.

Twentieth Street and Second Avenue.

Reprinted from The Journal of the American Medical Association
Jan. 3, 1914, Vol. LXII, pp. 8-12

II.

AN INTENSIVE STUDY OF THE EPIDEMIOLOGY OF PELLAGRA. REPORT OF PROGRESS.[1]

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AND

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(From the Laboratory of Tropical Medicine, New York Post-Graduate Medical School.)

I. General Plan of the Work. Although the Thompson-McFadden Pellagra Commission will continue its work in the field during 1913, it is considered advisable and warranted to set forth at this time in a brief preliminary report certain results of the epidemiological study made in 1912.

It was decided that an intensive study of the disease as it occurred among the population of a limited area would yield more valuable epidemiological information than a more superficial investigation over an extended area, conducted by correspondence and by brief studies in a number of different localities. No such intensive epidemiological study within a small area seems to have been previously undertaken in pellagra, while much data gathered by the more general methods are already available in the literature.

For the collection of data a blank booklet was prepared, covering points considered of possible significance regarding the patients themselves, their families, their residences, and the neighborhood in which they lived. In order to secure these data, each patient was visited one or more times in his or her own home.

In this preliminary report only summarized data will be included. The detailed epidemiological data for each case, and certain more intensive studies made in selected localities within the county, will appear in the report to be issued on completion of the investigation.

[1] Reprinted from the American Journal of the Medical Sciences, July and August, 1913 Nos. 1 and 2, vol. cxlvi, pp. 42 and 238.

The problem immediately before the commission in all its work was the etiology of pellagra and not its symptomatology or therapeutics, except as these subjects might throw light upon the essential nature of the disease. In view of the essential importance of diagnosis in our work, the conservative position was taken that a positive diagnosis would be made only when the characteristic skin lesion was evident or its earlier presence could be definitely ascertained by the testimony of patient and physician, though this requirement might, and ultimately did, exclude from our records cases which in all probability were suffering from pellagra without showing evidences of its cutaneous manifestation.

II. Acknowledgments. It is not practicable to make personal acknowledgment in each case to the many physicians to whom we are under great obligations for their interest and coöperation. The Spartanburg County Medical Society supported us in all our work, and we wish to express our high appreciation of its active part in furthering the investigation. Our only way of approaching patients was through their local physicians, and in no case did we find anything but the most ready coöperation on the part of the physicians, while many actively associated themselves in the work at a considerable expenditure of time and effort. In the more intensive studies in selected localities, which will appear in a future report, opportunity will be given us to make acknowledgment of these special services.

We are indebted to Dr. J. W. Babcock for the privilege of consulting with him from time to time during the work, and for many special services, especially for data concerning pellagrins admitted to the State Hospital for the Insane from Spartanburg County and for pathologic material collected at autopsies in that institution.

To Dr. J. A. Hayne, secretary and health officer of the South Carolina State Board of Health, we are under obligations for his interest and coöperation in our investigations, and particularly for furnishing from his office vital statistics concerning pellagra.

III. The Territory Selected. Spartanburg County is situated in the northern or Piedmont section of South Carolina. It is forty miles long in a north-south direction, thirty miles from east to west, and contains 762 square miles. Its surface is hilly and broken by a network of small streams and by four small rivers which, with their tributaries, flow across the county in a southeasterly direction, one of these rivers forming the county line on the south. The elevation above sea level at Spartanburg, the county seat, is 875 feet. To the northwest the slope is upward, the northwest corner of the county being situated at the foot of the Blue Ridge Mountain range, while to the south and east the elevation becomes somewhat lower than at Spartanburg, but with no precipitate fall, the whole county thus resting upon a plateau about 700 feet above sea level.

TABLE I.—Population Spartanburg County Census 1910.

		Total.	One year.	One to four years.	Five years.	Six to nine years.	Ten to fourteen years.	Fifteen to seventeen years.	Eighteen to nineteen years.	Twenty years.	Twenty-one to forty-four years.	Forty-five years and over.	Unknown.
Total population	..	83,465	2,733	10,091	2,370	8,852	10,402	5,710	3,878	1,870	26,239	11,161	159
	M.	41,719	1,425	5,167	1,171	4,490	5,270	2,840	1,903	893	12,822	5,652	86
	F.	41,746	1,308	4,924	1,199	4,362	5,132	2,870	1,975	977	13,417	5,509	73
Native white—native parents	..	56,536	1,918	6,842	1,587	5,834	6,742	3,874	2,576	1,254	17,677	8,149	83
	M.	28,472	991	3,526	793	2,969	3,464	1,907	1,280	612	8,820	4,063	47
	F.	28,064	927	3,316	794	2,865	3,278	1,967	1,296	642	8,857	4,086	36
Native white—foreign parents	..	309	5	28	8	29	31	27	8	6	111	54	2
	M.	150	2	15	6	11	12	14	3	2	55	30	
	F.	159	3	13	2	18	19	13	5	4	56	24	2
Foreign-born white	..	203	..	1	..	1	4	6	7	5	98	80	1
	M.	136	..	...	..	..	3	5	6	5	64	53	
	F.	67	..	1	..	1	1	1	1	..	34	27	1
Black	..	21,944	637	2,675	635	2,445	3,018	1,486	1,098	506	6,910	2,467	67
	M.	10,893	335	1,338	299	1,244	1,489	762	530	236	3,289	1,335	36
	F.	11,051	302	1,337	336	1,201	1,529	724	568	270	3,621	1,132	31
Mulatto	..	4,466	172	544	140	543	607	316	189	99	1,441	409	6
	M.	2,065	97	288	73	266	302	152	84	38	593	169	3
	F.	2,401	75	256	67	277	305	164	105	61	848	240	3
Indian	..	4	1	1	..	..	...	..	..	..	1	1	
	M.	1	..	...	..	..	...	..	..	..	...	1	
	F.	3	1	1	..	..	...	..	..	..	1		
Chinese	..	2	..	...	..	..	...	..	..	..	1	1	
	M.	2	..	...	..	..	...	..	..	..	1	1	
	F.												
Japanese	..	1	..	...	..	..	...	1					
	M.												
	F.	1	..	...	..	..	...	1					

The annual mean temperature, as recorded at Spartanburg, is 60° F. While the winters are mild, killing frosts are apt to occur from November to March inclusive, and the normal mean temperature for the months of December, January, and February is about 42° F.

The total population of the county is 83,465. Spartanburg, with a population of 17,517, is the only city in the county, the remaining population (65,948) being distributed upon farms, in cotton-mill villages, and among eleven small towns, only two of which have over 1000 inhabitants. The density of population, as a whole, is 109 per square mile; for the rural population (that is, outside of Spartanburg City) it is 86.5. While in South Carolina, as a whole, the negroes form 55 per cent. of the total population, in Spartanburg County the whites predominate numerically in the proportion of somewhat over two whites to one negro—there being a white population of 57,055, and 26,410 negroes—the percentage being 68.4 per cent. whites and 31.6 per cent. negroes. The distribution of the population of the county by race, nativity, age, and sex, according

to the United States Census of 1910, is set forth in greater detail in Table I.

The chief industry, and almost the only industry conducted upon a large scale, is that connected with the cotton mills. There are about twenty-eight cotton mills in the county, each mill supporting its mill-village. These mills give employment to approximately 10,000 operatives, representing about 4000 families, and a total mill-village population of about 20,000. As the mill operatives are whites exclusively, it follows that something over 35 per cent. of the white population of the county is found in the mill-villages and is supported by the cotton-mill industry. The mill-village population contains no foreign element, but is drawn altogether from the general native-born population of South Carolina, North Carolina, Tennessee, Kentucky, Georgia, and other nearby States. An effort is made by the mill operators to secure families with the maximum number of individuals capable of employment as operatives. The income of the mill workers ranges from about 75 cents per day to $2 or even more, averaging about $1.25 per day.

The chief agricultural pursuit throughout the county is cotton culture, though in recent years more and more land has been turned over to corn and other grain crops. The average value of farm lands, $36.04[2] per acre, is considerably above that found in many sections of the Southern States.

IV. Prevalence of Pellagra in the County. Altogether, 282 cases of pellagra were studied in detail during the period the commission was working in the county, that is, from June 1 to October 15, 1912, and these 282 cases are the basis for the greater part of our study. For the purposes of certain special lines of inquiry, such as the history of pellagra in the county, the geographic distribution of the disease at different periods, the sequence of cases in different local areas, and the possible increase or subsidence of the malady with regard to both frequency and virulence, records were secured of cases known to the physicians of the county, but which had died or moved beyond the county limits. It should be said also that the 282 cases on our list as present in the county in 1912 represent the minimum figures for the county in this period.

Accepting 282 as the minimum number of cases, we have in Spartanburg County, in 1912, a minimum morbidity rate for the population, as a whole, of 0.35 per cent. or 35 cases of pellagra for each 10,000 of the population.

Including 94 additional cases of which we secured definite knowledge in the county in 1912, but were not able to visit, usually because of their early death or their commitment to the State Hospital, the total number of cases in the county becomes 376, or 44.9 per

[2] United States Census Bureau.

10,000 of population. We believe this rate represents very nearly the actual prevalence of pellagra in 1912 in the territory studied.

In view of the fact that this rate is considerably higher than has previously been reported in any single territory of like area, it should be distinctly understood that in no other territory in the United States has so intensive a study been made and pellagrins so thoroughly sought out. Abundant evidence was gathered that the disease is at least equally prevalent in adjoining counties of South Carolina and in certain parts of adjoining States. Furthermore, in Lavinder's extensive compilations of statistics of pellagra in 9 Southern States, 4 States show a greater number of cases than does South Carolina, and 2 States a higher rate per 10,000 of population. Referring to Spartanburg County, Lavinder justly recognizes the exceptional interest displayed by the physicians of the county in the disease, and considers his reports from this county to be exceptionally complete. He was able to get reports of 226 cases up to the beginning of 1912. Our more intensive search, confined to the one county, discovered a total of 398 cases prior to 1912. The difference of 172 cases might be considered surprisingly small were it not for the unquestionable fact that the reports obtained by Lavinder from Spartanburg County were exceptionally complete. There can be no question that the excessive number of cases for Spartanburg County, which appears in both Lavinder's figures and ours, represents more complete returns, and not a greater prevalence of pellagra than is present in other localities from which reports are less satisfactory.

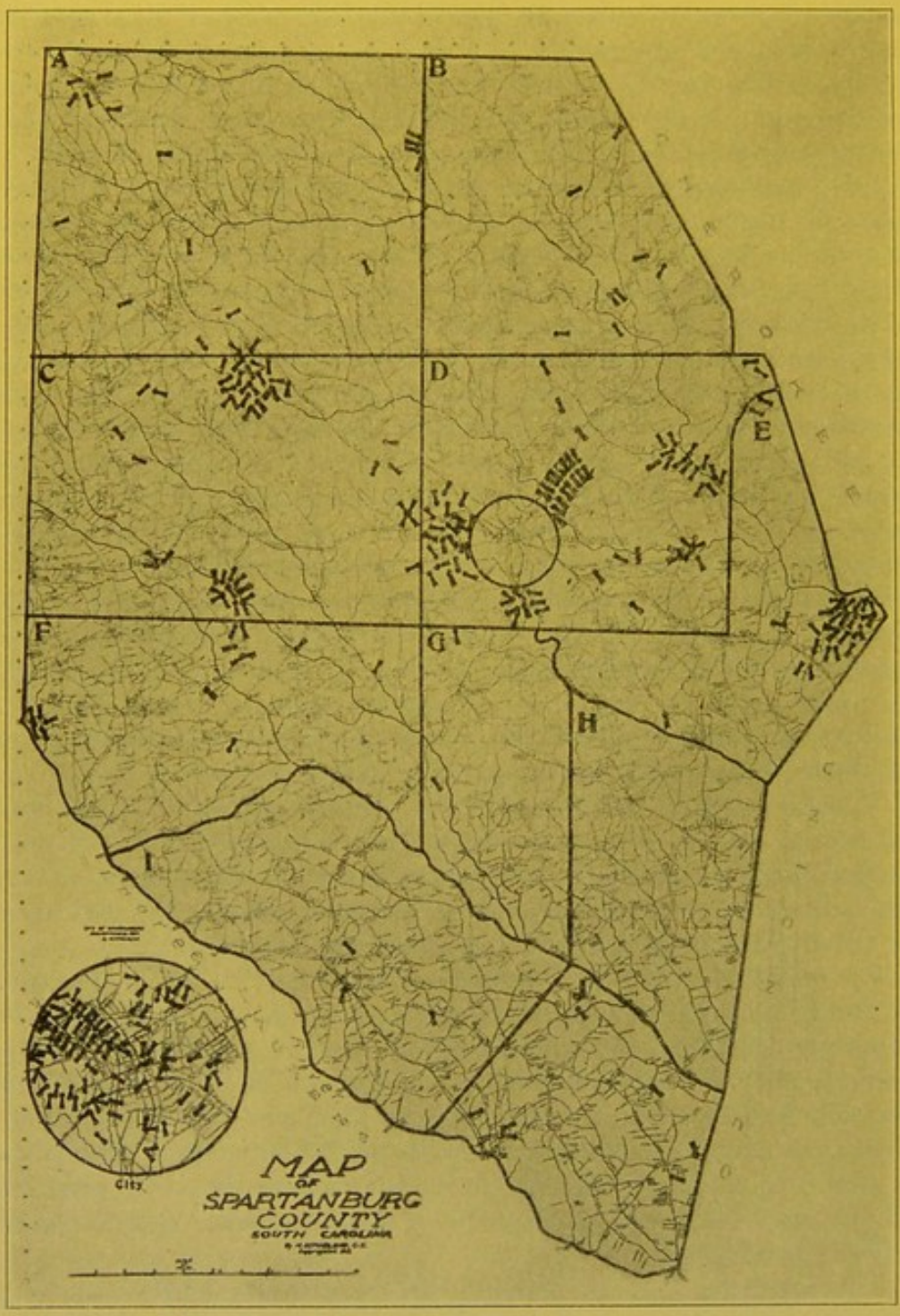
V. Geographical Distribution of Pellagra Within the County. In order first to investigate the possibility of any geographical inequality in the distribution of the disease within the bounds of the county itself, we have considered the incidence of the disease in each of its ten townships separately.

By referring to Map 2 it is seen that the township rate per 10,000 of population ranges from no cases in township H to 71 cases per 10,000 of population in township D. It is noteworthy, further, that the three townships C, D, and E, stretching across the middle of the county, give rates of 43, 71, and 58 cases respectively, or a combined average of 55 per 10,000; while townships A and B to the north and F, G, H, I, and J to the south give 20, 15, 19, 8, 0, 11, and 15 respectively and a combined average of only 14 per 10,000.

The incidence rate of pellagra within the city of Spartanburg was 49 per 10,000, considerably lower than the total rate (58) for township D, in which it is situated. The combined average rate of townships C, D, and E, exclusive of Spartanburg City, is 58 against only 14 in the remaining townships.

The population of the county may be still further divided geographically into three parts: (1) the rural population; (2) the

mill-village population; (3) the urban population of Spartanburg City. The rural population is found upon the farms and in eleven

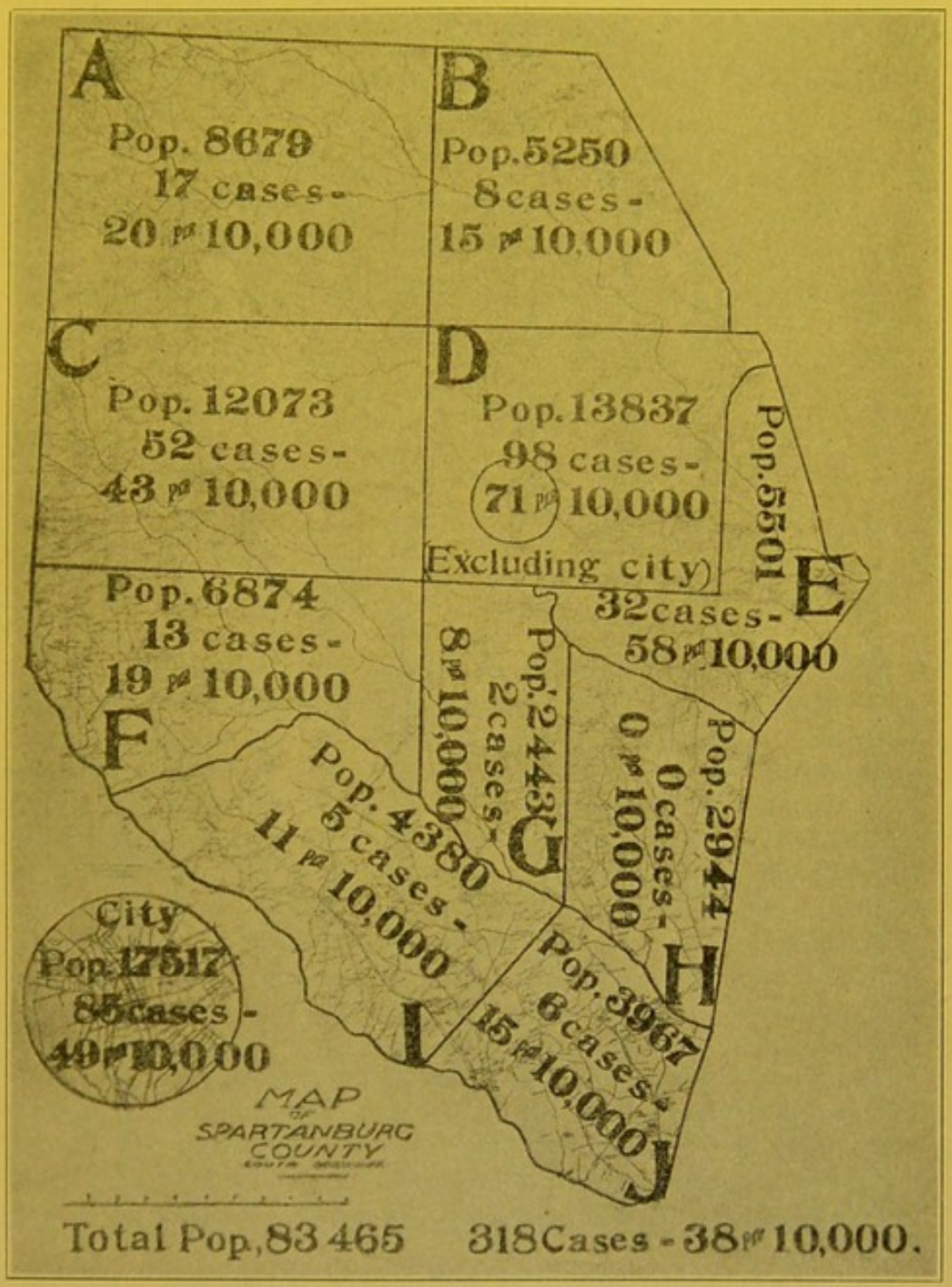


MAP 1.—Geographical distribution of cases in county and city of Spartanburg in 1912.

small towns, one of which has 1880 inhabitants, another 1101, and the remaining nine from 100 to 500 or 600.

Approximately one-fourth of the population of the county live in the cotton-mill villages. There are twenty-eight of these villages

in the county, their individual population ranging from about 200 to about 2000. Within the city of Spartanburg there are two



MAP 2.—Distribution of cases by townships with rate per 10,000 of population.

mill-villages, with a joint population of approximately 2950, the remaining 14,567 constituting the city population proper. Such a distribution of the population affords an opportunity to carry farther the analysis of the geographic distribution within the terri-

tory of each township by considering separately the prevalence of the disease among the rural, urban, and mill-village population respectively. The results of this analysis are shown in Table II and are graphically displayed by Chart 1.

TABLE II.—Rural, Mill-village, and Urban Distribution of Cases by Townships.

Township.	Total population.			Rural population.			Mill-village population.			Excess in mill-village over rural population.
	Population.	Cases of pellagra.	Rate per 10,000.	Population.	Cases of pellagra.	Rate per 10,000.	Population.	Cases of pellagra.	Rate per 10,000.	
A	8,679	17	20	8,179	13	15	500	4	80	65
B	5,250	8	15	4,650	7	13	600	1	17	4
C	12,073	52	43	9,173	17	20	2,900	35	121	101
D[3]	13,837	98	71	7,504	21	28	6,333	77	120	92
E	5,501	32	58	2,751	8	29	2,750	24	87	58
F	6,874	13	19	6,174	8	13	700	5	71	58
G	2,443	2	8	2,443	2	8	0	0	0	
H	2,944	0	0	2,944	0	0	0	0	0	
I	4,380	5	11	3,580	3	8	800	2	25	17
J	3,967	7	18	2,967	4	13	1,000	3	30	23
City	17,517	85	49	(14,567[4])	(43[4])	(29[4])	2,950	42	142	113
County	83,465	319	38	50,365	83	16	18,533	193	104	88

With one exception, in each of the eight townships with a mill-village population, the prevalence of pellagra among the mill-villages is markedly in excess of its prevalence among the rural population, this excess ranging from 17 per 10,000 in township I to 101 per 10,000 in township C, and reaching even a still higher figure (113) in the city of Spartanburg. In the county, as a whole, the mill-village population shows an excess of 50 per 10,000 over the total county average and of 88 per 10,000 over the rural districts alone. The apparent exception presented by township B, in which the excess among the mill-village population was only 4, disappears in view of the fact that the one mill in that township had been in operation only a month or so. The rate per 10,000 in the urban population of Spartanburg City, exclusive of the mill-village population of the city, is about equal to the combined rate among the rural population of townships C, D, and E, exclusive of their mill-village population, while the mill-village population in Spartanburg City (2950) shows 142 per 10,000, the maximum rate in our figures.

Excluding both urban and mill-village population, and considering the rural population alone, we find that the three townships C, D, and E still show a prevalence of pellagra twice that of the remainder of the county, the combined average rural rate for these townships being 24 per 10,000, while for the rural population of the remainder of the county it is only 12.

[3] Exclusive of city.

[4] City population exclusive of mill-village.

There are two factors which may possibly offer an explanation of this difference. In the three townships (C, D, and E) showing the excessive rate, with a total population of 19,428, the mill-village population (9833) makes up 50 per cent. of the total population (excluding the city of Spartanburg), while in the remainder of the

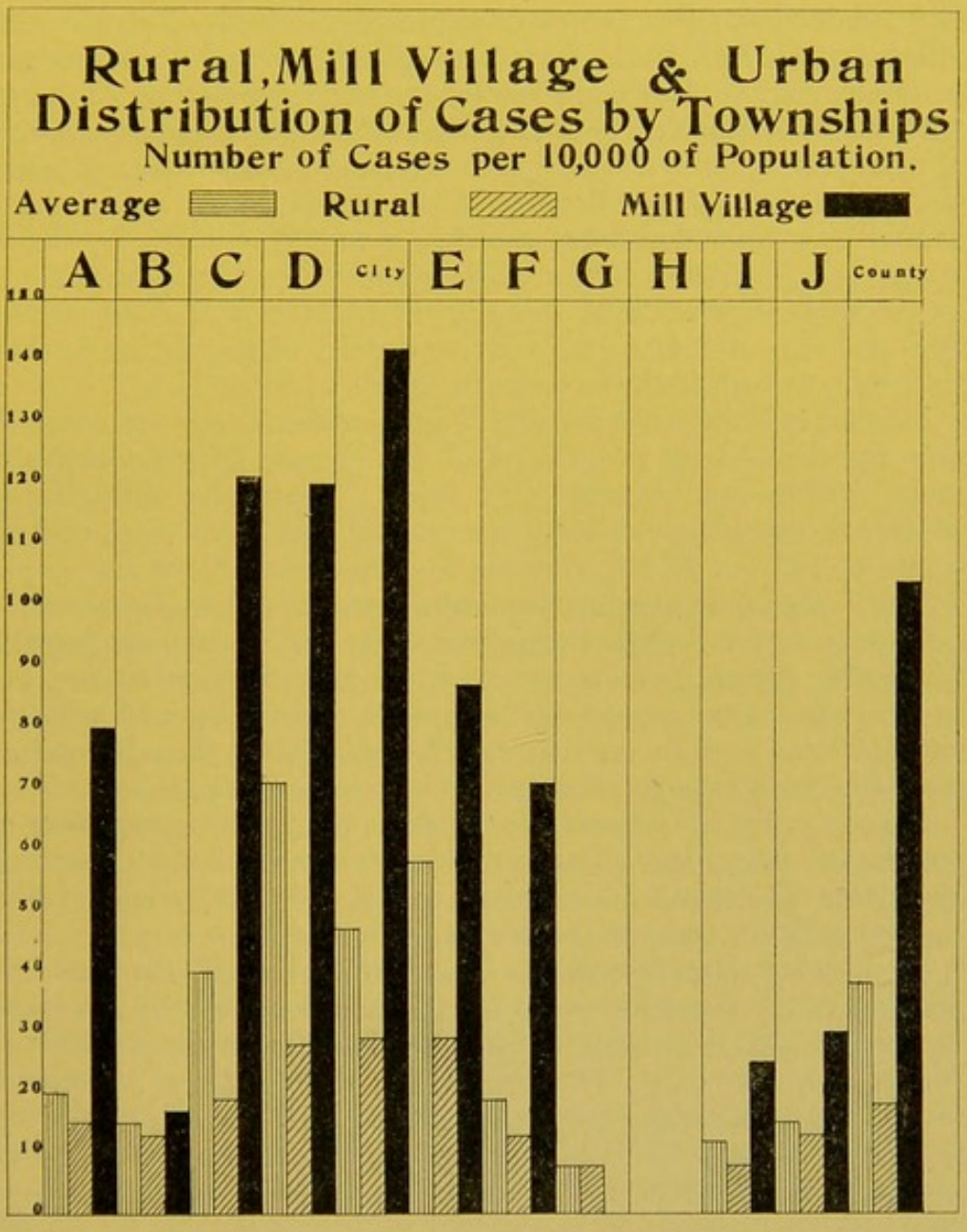


Chart 1.

county, with a total population of 30,937, the mill-villages have a population of only 3600, or 12 per cent. of the whole. It might be supposed that a large mill-village population showing a relatively high prevalence would tend to increase the prevalence of the disease in the surrounding rural districts.

The apparent fact that cases of pellagra are excessively prevalent in the mill-villages where the population is congested, suggests the question whether the congestion of population itself may not have an important influence upon the incidence of the disease. The average density of population for the county as a whole is 109 per square mile, while for the rural districts, exclusive of Spartanburg City, it is 86.5. For the rural population, exclusive of the mill-villages, it is 60.3. In the three townships C, D, and E, which show a striking excess of pellagra among the rural population compared with the rural population of the eight other townships, the density of rural population is 72 per square mile, and in the remaining townships it is only 56, a difference in density of 16 per square mile. While the greater density of population in townships C, D, and E might be a causative factor in the greater prevalence of pellagra in the rural population of those townships, the rate of prevalence does not vary strictly as the relative density of population in each township, though it shows some tendency to do so.

Further evidence that density of population alone is not accountable for the greater prevalence of the disease in mill-villages is found within Spartanburg City itself. There the mill-villages, which are continuous with and an integral part of the city, present a rate of 142 per 10,000, whereas the remainder of the city population, living under approximately the same condition of congestion, gives only 29 per 10,000. Furthermore, the non-mill-village population within the city, with a density which is certainly over 3000 per square mile, shows almost exactly the same prevalence of pellagra per 10,000 as does the strictly rural population of the surrounding township, with only 90 inhabitants per square mile.

These figures would seem to indicate that while congestion of population may play a part in the prevalence of the disease, it alone does not explain the marked inequality of distribution between the mill-villages and the strictly rural population.

VI. Racial Distribution. The distribution of the cases of pellagra in the county between the races presents a second marked inequality. While in South Carolina as a whole the number of whites and negroes is about equal, the negroes being slightly in excess, in Spartanburg County the whites predominate numerically in about the proportion of two to one, the actual figures being, whites 57,055, negroes 26,410 (Table III). The 57,055 whites gave 257 cases of pellagra, or at the rate of 45 per 10,000; the 26,410 negroes gave 25 cases of pellagra, or at the rate of 9.5 per 10,000. In other words, while whites are present in the population in the proportion of two whites to one negro, there are ten white pellagrins to one negro pellagrin.

One fact of fundamental importance in the racial comparison is the practical absence of negroes from the mill population. It follows that a more accurate comparison between the races can be

made by comparing the rate of prevalence among negroes with the rate among whites, exclusive of the mill population. We have seen that the rate among the total population, exclusive of the mill-villages, was 18 per 10,000. Subtracting the negro population and the negro pellagrins we have remaining a white population, exclusive of mill-village population, of 38,522, which gave 97 cases of pellagra, or 25.2 per 10,000 against 9.5 per 10,000 among the negroes. In other words, in Spartanburg County the disease appears to be 4.7 times as prevalent among all whites as among negroes, and 2.6 times as prevalent among whites, exclusive of the cotton mill-villages.

TABLE III.—Distribution of Pellagrins among Whites and Negroes.

	Population.	Cases of pellagra.	Rate per 10,000.	Excess of whites over negroes per 10,000 of population.
All whites	57,055	257	45.0	35.5
Whites outside of mill-villages	38,522	97	25.2	15.7
Negroes	26,410	25	9.5	

The racial incidence was carefully investigated with a view to determine whether the racial variation might be due to failure to discover cases of pellagra among negroes as readily as among whites. The practising physicians throughout the county were questioned as to the comparative prevalence among the negroes in their particular section, and as to its comparative prevalence in this race in the past. Without exception we were informed that pellagra in negroes was of comparatively infrequent occurrence. In this connection it is well to state that many of these physicians have lived and practised medicine in the same place for many years; that they are personally acquainted with practically the entire population in their particular field of work, both whites and negroes, and that they are in general thoroughly capable of correctly diagnosticating the disease.

The two colored physicians in Spartanburg were closely questioned as to the occurrence of pellagra in their practice at present and in the past, and the cases cited by them are included in our statistics. Furthermore, the information furnished by them relative to the occurrence of cases in the past is in accord with these statistics. When negroes suffering with pellagra were visited a particular effort was made to secure from them information as to the occurrence of the disease in others of their own race. A number of names were secured in this way, and many negroes suspected of having the disease were visited. Many of the planters owning large plantations and having as tenants or laborers a large

number of negroes were closely questioned as to the prevalence of the disease, and in some instances canvasses were made. Notwithstanding the efforts made to discover the disease in negroes, it was impossible to find more than twenty-five cases.

It is not believed that the number of cases overlooked could materially alter the relative incidence of nearly five cases in whites to one in negroes, and the racial variation is evidently a real one, though it may possibly be explained in part by the absence of negroes from the mill-village population, which, as we have seen, shows a marked excess of pellagra compared with the remainder of the white population.

TABLE IV.—Racial Distribution of Population and Racial Distribution of Pellagra with Percentages.

State.	Population statistics.[5]				Pellagra statistics.					
	White.		Negro.		White.		Negro.		Pellagra per 10,000 of population.	
	Number.	%	Number.	%	No.	%	No.	%	W.	N.
Virginia	1,389,809	67.4	671,096	32.6	476	76	152	24	3	2
North Carolina	1,500,513	68.0	697,843	31.6	1744	81	407	19	12	6
South Carolina	697,162	44.8	835,843	55.2	1129	71	471	29	16	6
Georgia	1,431,816	54.9	1,176,987	45.1	3127	80	741	20	22	6
Kentucky	2,027,951	88.6	261,656	11.4	442	92	39	8	2	4
Alabama	1,228,832	57.5	908,282	42.4	1138	58	813	42	9	9
Mississippi	786,119	43.7	1,009,487	56.6	1387	55	1156	45	18	11
Louisiana	941,086	56.8	713,874	43.1	338	56	269	44	4	4

Table No. IV is an analysis of population by race, and of the incidence of pellagra by race for eight Southern States. The pellagra statistics in this table were secured by correspondence and, as Lavinder states, are very incomplete.

In Spartanburg County there is a marked difference in racial incidence, but any suggestion that this depends upon the factor of race alone may seriously be questioned. In Table IV it may be seen that the case incidence in the two races in the States of Alabama and Louisiana shows little difference; while in South Carolina and Georgia, and to a less extent in North Carolina, there is a marked preponderance in whites. It is possible that industrial conditions in these States account largely for this variation.

VII. SEX DISTRIBUTION. The population of the county is divided practically equally between males and females, the females being only 27 in excess. The total male population of 41,719 gave 71 cases of pellagra, or at the rate of 17 per 10,000. The female population gave 211 cases, or at the rate of 50.5 per 10,000 (Table V). In other words, pellagra appears nearly three times more frequently

[5] Population statistics are those of the Thirteenth Census (1910). The pellagra statistics were compiled from those reported by Lavinder in reprints from Weekly Public Health Reports, No. 106.

among females than among males. Among the white population alone this proportion between males and females remains about the same, while among the negroes the relative prevalence among males and females is nearly four females to one male. This inequality between the sexes is brought out more strikingly and in greater detail if the figures are analyzed by dividing the population according to age.

TABLE V.—Distribution by Sex.

		Number in population.[6]	Cases of pellagra.	Rate per 10,000.	Excess per 10,000 among females.
Whites:	Male	28,758	66	22.95	
	Female	28,290	191	67.5	44.5
Negroes:	Male	12,958	5	3.9	
	Female	13,452	20	14.9	11.0
Both races:	Male	41,716	71	17.0	
	Female	41,742	211	50.5	33.5
Total population		83,458[6]	282	33.8	

TABLE VI.—Age Distribution of Two Hundred and Eighty-two Cases.

Age.	Total population.[7]	Cases of pellagra.	Rate per 10,000.
0 to 5	15,194	21	10.8
6 to 9	8,852	22	24.9
10 to 19	21,860	28	12.8
20 to 44	26,239	158	60.2
45+	11,161	53	47.5

VIII. AGE DISTRIBUTION. First, considering the prevalence of pellagra according to age, without reference to sex, we find the inequalities shown in Table VI, and graphically presented in Chart 2.

In this and the following tables dealing with age distribution, in which the prevalence of pellagra is expressed in rate per 10,000 of the population, our age groups are necessarily made to conform to the age statistics for the population of Spartanburg County which could be secured from the United States Census Bureau—namely, the population of the county under six years of age, from six to nine years, ten to nineteen years, twenty to forty-four years, and forty-five years or older. The actual number of cases in these groups means little because of the wide difference in the size of the groups, both with regard to the number of years and the number of individuals concerned. A striking excess in the rate of prevalence is apparent in the group twenty to forty-four years of age (60.2 per 10,000). The rate among those over forty-four years of age is much higher than in any other group excepting that between

[6] Exclusive of 4 Indians, 2 Chinese, and 1 Japanese.
[7] Exclusive of 159 persons of unknown age.

twenty and forty-four years. These two groups taken together, that is, the entire population over nineteen years of age compared with the entire population under twenty years of age gives the following result: Twenty years and older, 211 cases, or 56.4 per 10,000; nineteen years and younger, 71 cases, or 15.5 per 10,000.

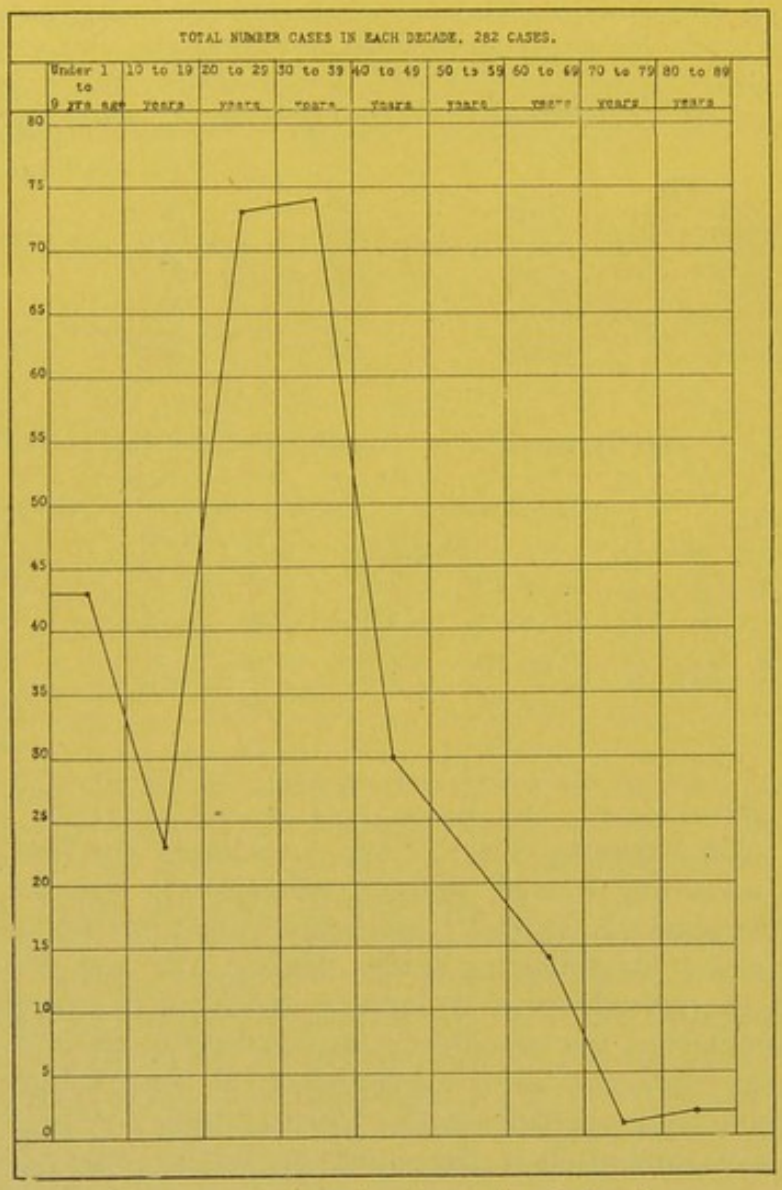


CHART 2.—Total number of cases in each decade.

Dividing the younger group we find that children under ten years of age gave a total of 43 cases, or 17.9 cases per 10,000; those from ten to nineteen years of age gave 28 cases, or 12.8 per 10,000. Furthermore, this higher prevalence for children under ten years is found entirely among the children between the ages of five and ten years who alone gave a rate of 24.9 per 10,000, while the younger group under five years of age gives only 10.8 per 10,000, the lowest rate found in any group.

In Chart 2 the distribution of pellagra by the number of cases in each age group is shown, dividing the cases into age decades. By comparing this chart with Table VI it is evident that the curve would be considerably modified if it expressed the rate per 10,000 of population instead of the actual number of cases in our figures. The prevalence among children under ten years would not be quite so high compared with that in other groups. The relative prevalence in groups over forty years would be higher. The two groups of from twenty to forty years would still show a striking excess over all other decades. It may be said here that the marked fall in the prevalence of pellagra in the groups ten to nineteen years appears throughout our statistics, and will come out strikingly in the consideration of the family distribution of the disease.

IX. Distribution by Age and Sex. It is important to ascertain whether the excessive prevalence of pellagra among females holds in all ages of the population, and whether the excessive prevalence found in certain age groups, notably those from twenty to forty-five years, is to be found among both males and females. Referring to Table VII it may be seen that the excess among females is not the same among all ages of the population, but is confined largely to those between the ages of twenty and forty-four years. Further, under ten years of age males and females show practically the same prevalence of pellagra. From ten to nineteen years the females show a rate a little over twice that of the males; in the large group of from twenty to forty-four years the females show a rate per 10,000 over nine times greater than the male rate. Among the population of forty-five years and over the distribution between the sexes is again nearly equal.

These cases have been further analyzed by decades, with the result as represented graphically by curves in Chart 3. These curves express actual number of cases.

Table VII.—Distribution by Age and Sex.

Age.	Sex.	Population.	Number of cases.	Rate per 10,000.	Excess per 10,000.
Under 5	M.	7,763	10	12.9	
	F.	7,431	11	14.8	1.9
5 to 9	M.	4,490	12	27.0	
	F.	4,364	12	27.5	0.5
10 to 19	M.	10,906	7	6.4	
	F.	10,954	16	14.6	8.2
20 to 44	M.	12,822	16	12.5	
	F.	13,417	148	110.3	97.8
Over 44	M.	5,652	25	44.2	
	F.	5,509	27	49.0	4.8

The fall in the curve in the second decade of life is present for both sexes, but is more marked for males. Thereafter the male curve continues to fall, whereas the female curve rises to its highest

point in the following decade (twenty-one to thirty years), drops slightly among women of thirty-one to forty years, then falls abruptly in the next decade (forty-one to fifty years) to a point somewhat below both males and females under ten years. In the decade of from fifty-one to sixty years the female curve continues to fall, and for the first time descends below the male curve, which shows a slight rise. Thereafter the number of cases is small and the two curves fall together.

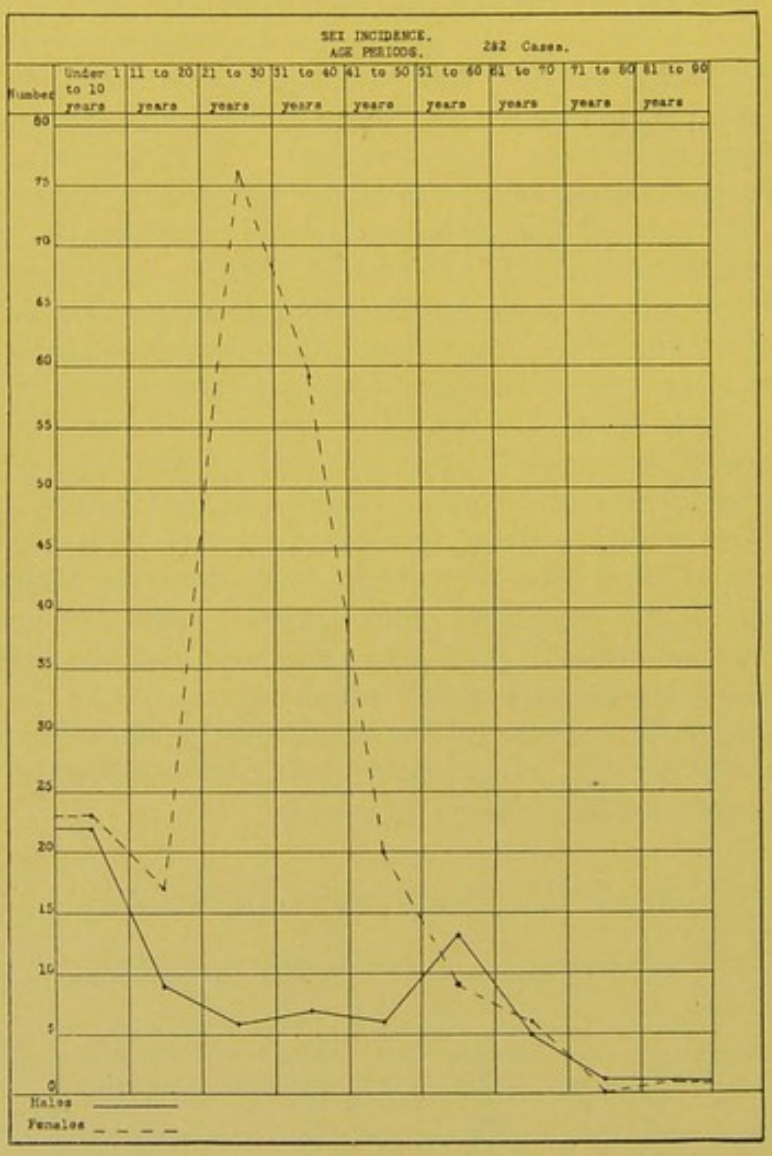


CHART 3.—Distribution by age and sex.

The data expressed in Table VII and Chart 3 may be summarized as follows: Pellagra appears to be about equally prevalent among males and females under ten years of age and over forty-five years. Males alone show the highest prevalence in children under ten years. Females show a strikingly higher prevalence in the two

decades of twenty to thirty and thirty to forty years than does either sex in any other decade.

Table VIII indicates in a general way that both whites and negroes separately show practically the same inequalities in the distribution of pellagra between the sexes in the different age groups, as has been shown in considering both races together. Any closer analysis of the figures for the two races is unsatisfactory, owing to the small number of negro cases in each age group.

TABLE VIII.—Race, Age, and Sex Incidence (Two Hundred and Eighty-two Cases).

Age.	Whites, 257 cases.		Negroes, 25 cases.	
	Male.	Female.	Male.	Female.
Under 1 to 5	9	11	1	0
Under 6 to 10	12	11	0	1
Under 11 to 20	9	14	0	3
Under 21 to 30	4	65	2	11
Under 31 to 40	6	56	1	3
Under 41 to 50	6	20	0	0
Under 51 to 60	14	9	0	0
Under 61 to 70	4	5	1	1
Under 71 to 80	1	0	0	0
Under 81 to 90	1	0	0	1
Totals	66	191	5	20

While it is not proposed to enter into any extensive comparative studies in this preliminary report, there are certain data upon the age and sex distribution of pellagra in this country which present an interesting parallel with the figures for Spartanburg County.

Chart 4 represents by curves based on actual number of cases the age and sex distribution of 164 cases of pellagra, 99 of which were reported by Mizell,[8] of Georgia, and 65 by Tucker,[9] of Virginia.

Chart 5 shows mortality rates for the State of Texas. This chart was furnished to us by Dr. H. K. Beall, of Fort Worth, Texas,[10] who first directed attention to the inequalities of distribution by age in males and in females.

Chart 6 is based upon death reports of pellagra in Alabama between June, 1909, and December, 1912. These reports cover a total of 1148 cases during this period. The data were kindly supplied by Dr. W. H. Sanders and Dr. H. G. Perry, of the Alabama State Board of Health.[11]

Chart 7 presents a graphic representation of mortality rates for pellagra in the State of North Carolina for 1911 and 1912. We have to thank the health authorities of North Carolina for the information on which this chart is based.[12]

[8] From paper read at the Second Triennial Meeting of the National Association for the Study of Pellagra, Columbia, S. C., October 3, 1912.

[9] Beverley R. Tucker, M.D., A Discussion of Pellagra, with Remarks on Sixty-six Cases Occurring Outside of Institutions, Old Dominion Jour. Med. and Surg., April, 1911, vol. xii, No. 4.

[10] Personal communication. [11] Ibid. [12] Ibid.

The data from these five sources are all the statistics available to us at the present time which lend themselves to a comparison with our own figures regarding age and sex distribution. It should be noted that the curves in Chart 4, like our own, are based on morbidity statistics, while Charts 5, 6, and 7 are based upon death reports.

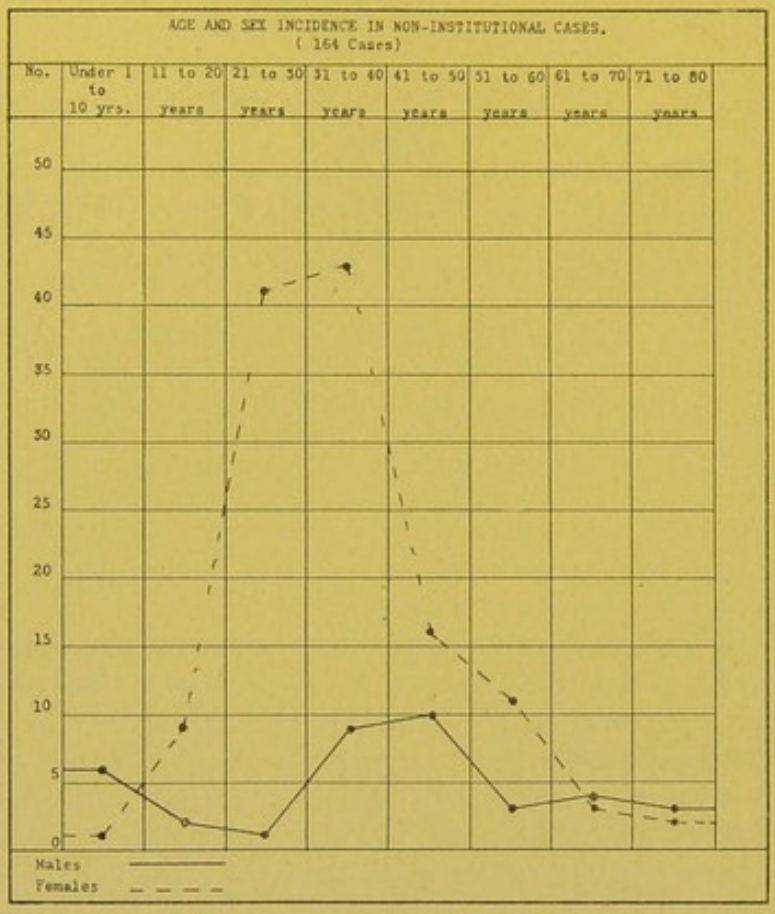


Chart 4.—Age and sex incidence in non-institutional cases.

A comparison of the four charts shows considerable variation in both the male and the female curves in different age groups. They all agree, however, in showing a strikingly excessive prevalence among females of middle age and a comparative equality of distribution between males and females in childhood and among people of advanced age.

X. Distribution by Occupation. The consideration of the relationship between occupation and the incidence of pellagra in Spartanburg County resolves itself almost entirely into a discussion of the relative prevalence of the disease among field laborers, workers in the cotton-mills, and those engaged in housework. Only a few scattered cases gave other employment. The actual data with regard to occupation obtained from 234 cases of pellagra is set forth in Table IX: 110 (47 per cent.) gave housework as their occupation exclusively; 14 others (6 per cent.) gave house-

work as their chief employment; 16 (6.8 per cent.) were employed in housework part of the time, working the remainder of the

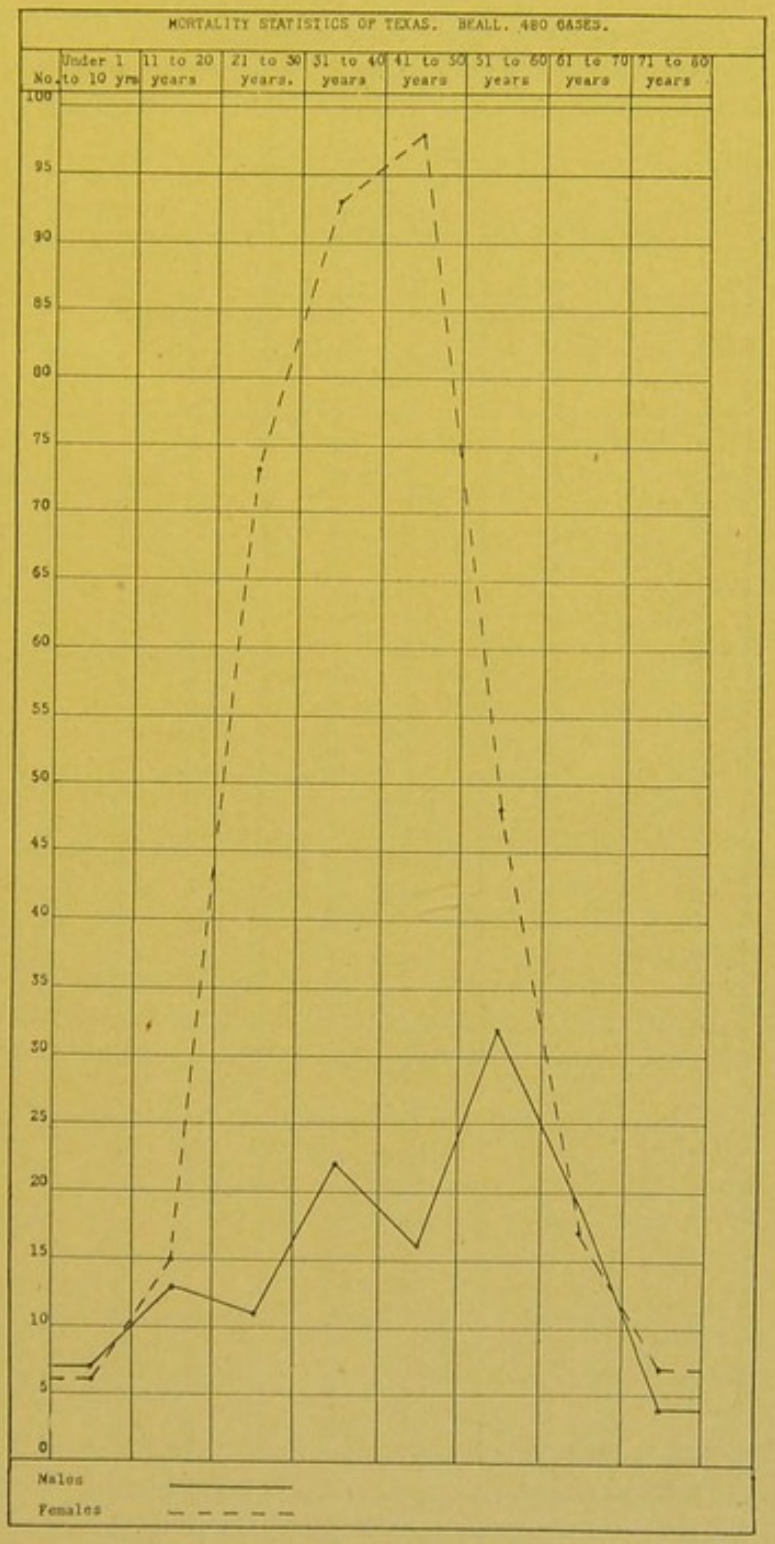


CHART 5.—Mortality statistics of Texas.

time in the mills; 18 (7.7 per cent.) worked alternately about the house and in the fields. Thus a total of 158 (67.5 per cent.) of

the 234 cases, were employed in household work within the home for at least a fair portion of their time. These figures mean little

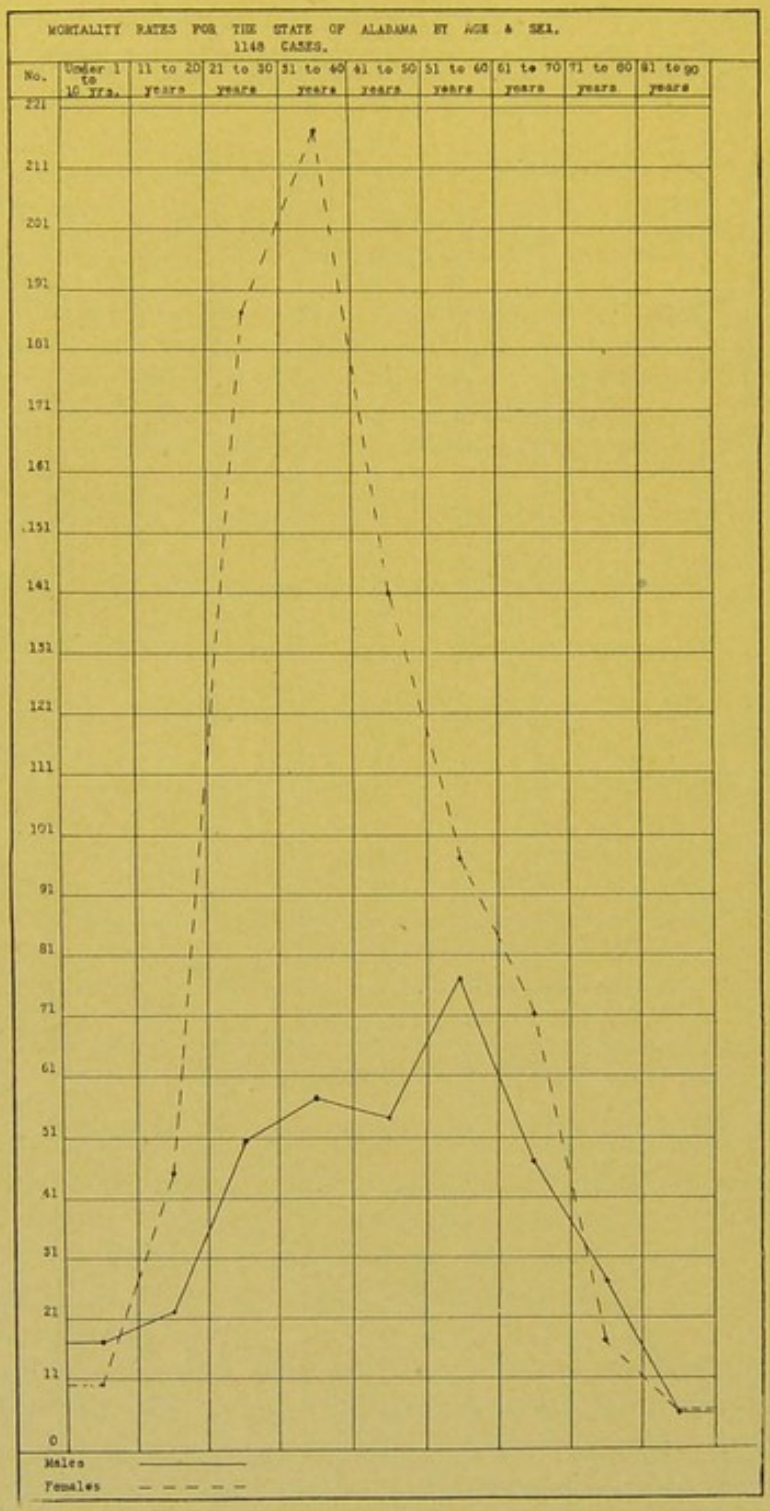


CHART 6.—Mortality rates for the State of Alabama by age and sex.

more than what has already been shown by the age and sex distribution of the disease—namely, that it is excessively prevalent among adult females the great majority of whom are employed in

housework. There is one further indication, however, that pellagra has a much higher prevalence among the adult females of the mill-villages who are occupied as housewives than among those who work in the mills, and this point may be more closely examined by considering the occupational distribution of pellagra in the mill population alone.

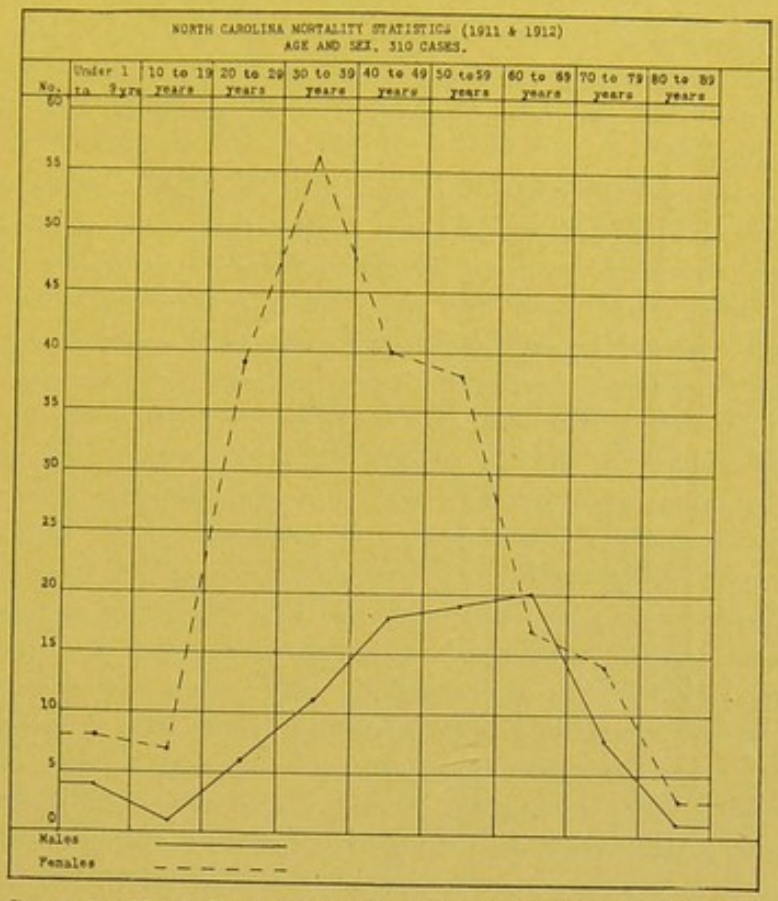


CHART 7.—North Carolina mortality statistics during 1911 and 1912.

TABLE IX.—Distribution of Two Hundred and Thirty-four Cases of Pellagra by Occupations.

Occupation.	Males.	Females.	Both sexes.	Per cent. of total.
Farmers	14	..	14	6.0
Field work and housework	..	18	18	7.7
Mill work exclusively	21	20	41	17.5
Mill work, some housework	..	16	16	6.8
Housework exclusively	..	110	110	47.0
Housework chiefly, some mill work	..	14	14	6.0
Scattering[13]	9	3	12	5.1
No occupation	2	7	9	3.8

There are available for this study 121 cases of pellagra of working age residing in mill-villages. Of these, 24 were males and 97

[13] Two patients were merchants, two dressmakers, one was employed in each of the following occupations: insurance, student, carpenter, butcher, clerk, railroad fireman, day laborer, school teacher.

females; 21 (87.5 per cent.) of the 24 males were mill operatives. Of the 97 females, 12 (only 12.37 per cent.) worked in the mills exclusively; 16 additional female cases worked in the mills the greater part of the time, making a total of 28 female mill workers (or 28.86 per cent.) of the 97.

46, or very nearly half (47.42 per cent.) of the 97 women did no mill work, devoting themselves to housework exclusively; while 14 others were chiefly employed in housework, going to the mills only occasionally, making a total of 60 houseworkers, or 68.85 per cent. of the female pellagrins of working age living in the mill-villages.

We have no actual statistics regarding the proportion of males and females among mill operatives. It would seem perfectly safe to say that there are at least as many females as males, the probabilities being that they are in a considerable majority. As a rule, female operatives are preferred by the mill operators. Assuming equality between the sexes among mill workers, as may surely be done with safety, the data above presented has a highly important significance, in that it shows a nearly equal prevalence of pellagra in males and females who are employed in the mills as operatives—namely, 17 males and 12 females—if we include only those women doing mill work exclusively, and 28 females if we include the 16 who gave mill work as their chief but not exclusive occupation. This comparative equality as regards the prevalence of pellagra between the sexes among mill operatives is in striking contrast to the inequality between adult males and females in our sex statistics for the population as a whole, and is very closely in harmony with what is known of sex distribution in institutional cases where a difference in prevalence between the sexes is absent or slight.

In comparing the mill-village population with the rural population as regards the prevalence of pellagra, we found the disease nearly seven times as prevalent in the mill-villages as in the rural districts, the actual rate of prevalence in the mill population being 104 per 10,000. Out of the total mill-village population of approximately 19,000, about one-half, or 9500, are actually employed in the mills. Among these mill operatives we have 57 cases of pellagra, including those patients who gave mill work as their chief but not exclusive occupation. These 57 cases give a rate of 60 per 10,000 among actual mill operatives, against 104 per 10,000 for the total mill-village population. The 41 patients giving a history of mill work exclusively present a rate of only 43.2 per 10,000. These figures seem to indicate that the excessive prevalence of pellagra in the mill-village population is not found among those who actually work in the mills, but among the women engaged in the day about the houses, and the children who are at home with them.

While children under working age do not form a part of an occu-

pational study, it may well be noted in this connection that 30 mill-village children under ten years of age had pellagra. These cases added to the 60 adult females in the mill-villages engaged in house-work exclusively make a total of 90 cases of pellagra in the mill-village population of the county, which by occupation were about the dwellings during the day, against 57 cases among the population engaged in mill work. The 57 operatives give a rate of 60 per 10,000 for the half of the mill-village population which works in the mills. The 90 houseworkers and children give a rate of 94.7 per 10,000.

XI. Distribution of Cases in Families. 316 cases of pellagra are available in our data for a study of family and household relationships, and these cases represent 223 families, an average of 1.42 cases of pellagra per family. An analysis of the family distribution is given in Table X. About half the total number of cases occurred singly in families, and about one-fourth of the total number occurred two to a family. Of the total number of families with pellagra (223) nearly three-fourths (160) had but one case, and nearly one-fifth gave but two cases. Nearly one-tenth of the families gave 3, 4, or 5 cases.

Table X.—Distribution of Pellagra in Families.

	Number of families.	Number of cases.	Percentage of total number of families.	Percentage of total number of cases.
One case to one family . .	160	160	71.7	50.6
Two cases to one family . .	42	84	18.8	26.6
Three cases to one family .	14	42	6.3	13.3
Four cases to one family .	5	20	2.3	6.
Five cases to one family . .	2	10	0.9	3.2
Total with more than one case to one family . .	63	156	28.3	49.4

In view of the inequalities found in the prevalence of pellagra in the two sexes, and at different ages, an attempt has been made to discover whether the sex and age distribution differs among cases which occur singly in families from the distribution among cases occurring two or more to a family—in other words, to determine whether cases developing singly in families are apt to be of any particular age or sex, and to differ in these respects from multiple family cases. For this purpose, 294 cases for which age and sex statistics are available have been charted (Chart 8) by age periods of five years each—cases occurring singly in families being represented by a solid line, and cases occurring two or more to a family by a broken line. The upper two curves represent male

cases alone; the middle curves, females alone; and the lower curves, the two sexes combined. The curves represent the percentage of the total 294 cases and not the actual number of cases in each group. Accordingly, the solid line and the broken line would coincide wherever the same condition of distribution exists between single cases and cases occurring two or more to the family.

The Age and Sex Distribution of Pellagra in Families with a single case and in Families with two or more cases

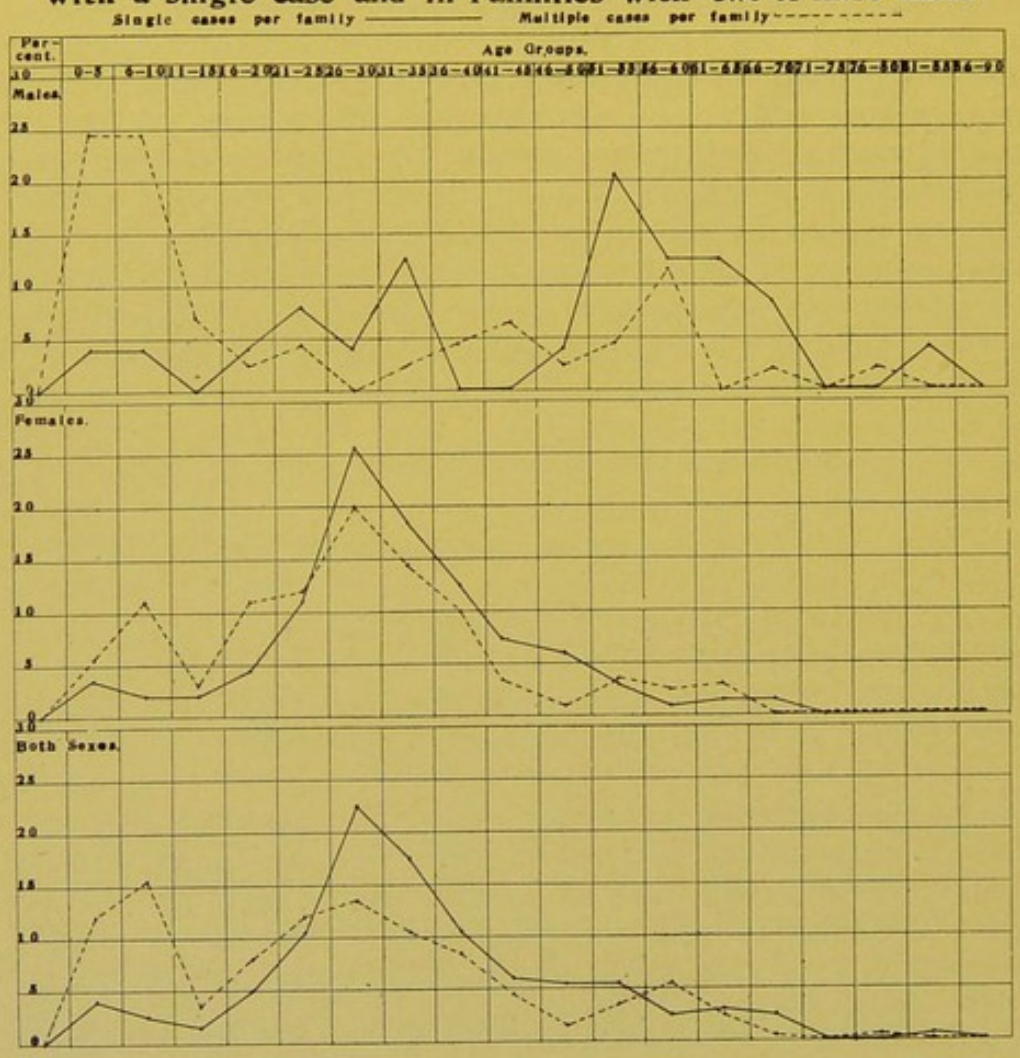


CHART 8.

The most striking inequality between the two curves is present among children under ten years of age. Not only is the curve for multiple family cases higher than the curve for single cases in both males and females, but for males alone and for the combined sexes it goes higher among children under ten years than in any other age group. In this respect it presents a striking contrast to the

curve for single family cases and to our general age distribution. It is remarkable, further, that this excessive prevalence in multiple family cases is much greater among males than among females, especially in the younger group of children under six years of age. Among cases occurring singly in families the curve never goes above 5 per cent. in any age group under twenty years among males, females, or the sexes combined. These facts seem to show that where single cases of pellagra occur in families it is rarely children under ten years who are the ones attacked. Among families with more than one case, however, children under ten years form a higher percentage of the cases than does any other decade. Among families with but one case it would appear that the two decades from twenty-one to forty years give the great majority of cases among females, while among males more single cases occur among those over fifty years.

When considering the subject of age and sex distribution, attention was called to the striking fall of prevalence apparent among persons from eleven to twenty years old. Inspection of the curves in Chart 8 shows this fall to be confined almost entirely to cases which occur two or more per family, the indication being that isolated cases in families are as apt to arise among individuals from eleven to twenty years of age as among children under eleven years.

It is not considered advisable to proceed farther at the present time in an analysis of the family relationships of pellagrins. Such further investigation would carry us into a study of each individual family, the actual sequence of cases in each family, and, furthermore, would introduce the whole subject of household association and its significance with regard to the family relationship. As yet our data are not sufficiently complete to make such a study in a satisfactory manner. It may be said, however, that while there is some evidence in our preliminary investigation that family relationship *per se* does seem to have some influence upon the incidence of pellagra, there are stronger indications that household association is a more important factor in the distribution of the disease.

XII. Relative Prevalence, Severity, and Mortality Rates in Recent Years. Pellagra is not a reportable disease in the State of South Carolina, nor do the State laws require notification of deaths from pellagra to the health authorities.

The data to be analyzed were obtained from a number of sources. The 282 cases studied in detail by the Commission afforded one source. In the City of Spartanburg, official records are on file covering deaths from all causes within the city, and thus it was possible to secure accurate mortality statistics for the city. There are some five or six undertaking establishments in the county,

as a whole, and the two establishments in the city of Spartanburg sell very nearly all the coffins used throughout the county. These two establishments keep on file the names, causes of death, and other information concerning the deceased for whom coffins are furnished, and they very courteously permitted us to make abstracts from their records. From these records we obtained information of importance. From the members of the medical profession throughout the county we secured much valuable information relating to prevalence and mortality rates for 1912 and previous years. From pellagrins themselves and from others we were able occasionally to obtain information concerning individual cases. Dr. Babcock, of South Carolina, kindly furnished us with information covering the cases admitted to the State Hospital for the Insane from Spartanburg County.

Although we availed ourselves of all these sources of information, we wish to emphasize the fact that this study is still far from complete. We hope, however, to make it more comprehensive and complete during the course of our studies in the same county in the summer of 1913.

The opinion was expressed by many physicians in Spartanburg County, that pellagra was not so prevalent in 1912, as was the case in 1911. We might say, further, that a like impression prevailed in many other parts of South Carolina and in other Southern States.

The statistical data at hand for Spartanburg County are subject to analysis in several ways:

1. From the information available we have determined as nearly as possible the actual number of cases of the disease existing in the county each year, without consideration of the year in which the disease was contracted and without reference to recurrences.

In 1912	there were 376 cases (minimum).
In 1911	there were 285 cases (minimum).
In 1910	there were 115 cases (minimum).
In 1894 to 1910	there were 114 cases (minimum).

It is quite evident that pellagra was not recognized as such, to any extent, until the year 1909.

We have endeavored to secure from the practising physicians in the county accounts of the first and other early cases occurring in their practices. As yet this information is incomplete, but it establishes the fact that the disease has existed in the county sporadically for a number of years. Dr. Fike of Spartanburg, has the record of a patient dying of pellagra in 1894, although not at the time recognized as such. The patient was an adult female, and three other members of her family are said to have died of the disease. One of the first cases which developed in the city of Spartanburg

was that of a young woman in a well-to-do family. She contracted the disease and died of it in 1902. Dr. Jefferies, of Spartanburg, has the record of a patient who died of pellagra, in November, 1903, but the disease was unrecognized as such until years afterward.

While there is no doubt that pellagra has existed in this section for a number of years, information obtained from the medical profession throughout the county indicates very clearly that the cases must have been more or less sporadic until within recent years. The general impression is held that sporadic cases occurred until about 1909, at which time there was a marked increase in the number of cases; that during 1910 and 1911 the disease became more prevalent; while in 1912 there was a slight decrease in incidence. The perceptible increase of cases in 1909 may be accounted for in part by the fact that the disease was not until then generally recognized as pellagra. We have consulted with many medical men in Spartanburg County and in other parts of South Carolina, and in other States, and it is our belief that the large number of cases recognized in 1910 and 1911, as compared with the number recognized previous to that time, cannot alone be explained on a basis of general failure to recognize the disease in earlier years. Non-recognition unquestionably explains some of the increase, but we are thoroughly convinced that there has been an actual and quite perceptible increase in the number of cases within the past three or four years.

2. A second analysis of our data shows that the minimum number of cases of pellagra in Spartanburg County from 1894 to October, 1912, was 495. This is obviously a conservative estimate, as prior to 1911 our data are made up largely of cases in which the disease terminated in death.

3. We have endeavored to determine the actual number of new cases of the disease occurring each year. It is possible to determine this with a reasonable degree of accuracy for 1912 and with a fair degree of accuracy for 1911, but prior to that time the incidence rates (annual) are altogether a matter of conjecture. We have seen that there were at least 376 cases of pellagra in Spartanburg County in 1912. Of the cases seen during our study in 1912 (282), 97 contracted pellagra in 1912, and of 94 others not included in our series we have knowledge of the fact that 16 contracted the disease in 1912. The minimum total of new cases for 1912 is thus 113. In 1911 the total number of cases in the county was 285. Among the cases included in our series (282), 100 contracted pellagra in 1911, and we have record of 20 other cases contracting it in 1911, making a total of 120. Of the remaining 165 cases existing in the county in 1911 the information at hand is more or less indefinite, but unquestionably some of this number contracted the disease in 1911.

Prior to 1911 definite statistics are too meagre to warrant analysis.

Our statistics suggest that pellagra, so far as new cases are concerned, was somewhat more prevalent in 1911 than in 1912.

The annual case death-rate among pellagrins was as follows:

Year.	No. of deaths.		No. of cases.	Per cent. of deaths.
Unknown	8			
1894	1			
1898	1			
1899	1			
1901	2			
1902	2	25	114	22
1903	1			
1904	1			
1908	2			
1909	14			
1910	32		115	28
1911	54		285	19
1912	47		376	12

It should be understood that these mortality statistics are of pellagrins who have died from all causes, not deaths from pellagra alone. In a number of these cases the pellagrous symptoms were of but little moment, the actual causes of death being other factors, among which may be mentioned tuberculosis and senility. The morbidity and mortality statistics for 1910 and the years preceding are not sufficiently complete to warrant any deductions. Those for 1911, showing 19 per cent. deaths, and for 1912, showing 12.5 per cent. deaths, represent more nearly the relationship between the morbidity and mortality rates as they exist at present.

Death during the initial attack is not uncommon. In the series of 282 cases studied by this Commission, 97 contracted the disease in 1912, and 5 of these cases died during the initial attack.

Summary. The following general statements concerning relative prevalence and mortality seem to be warranted:

Sporadic cases have been observed in Spartanburg County since 1894. During the past three or four years there has been an alarming increase in the number of cases. The number of new cases developing in 1911 was somewhat greater than in 1912, although the difference was but slight. When the disease first appeared in Spartanburg County the symptoms were frequently severe and the death-rate appears to have been high. The number of cases in the county is increasing while the death-rate appears to be decreasing.

XIII. Clinical Observations on Pellagra. A. *Chronicity and Periodicity, with a Study of the Influence of Climatic Conditions.* 1. *Chronicity.* We have observed no differences in the symptomatology, and more particularly in the chronicity, of the disease as it exists in this country and in Italy, except the fact that the mortality rates in this country two or three years ago were apparently much higher than those obtaining in Italy at the same time.

A few of the cases in the present series died during the initial attack in 1912, while others presented a wide gradation of symptoms ranging from those involving the cutaneous, gastrointestinal, and nervous systems to those in which the cutaneous system alone was involved.

Original Attack and Annual Recurrences.

Early history indefinite; recurrence, 1912	1
1904.	
First attack, 1904; recurrences, 1905, 1906, 1907, 1908, 1909, 1910, 1911, 1912	1
1905.	
Indefinite history, 1905 to 1911 inclusive; recurrence 1912	1
First attack, 1905; recurrences, 1906, 1907, 1908, 1909, 1910, 1911, 1912	1
1906.	
First attack, 1906; recurrences, 1907, 1908, 1909, 1910, 1911, 1912	1
1907.	
First attack, 1907; recurrences, 1908, 1909, 1910, 1911, 1912	1
First attack, 1907; no clear history, 1908, 1909, 1910; recurrences, 1911, 1912	1
1908.	
First attack, 1908; recurrences, 1909, 1910, 1911, 1912	2
First attack, 1908; recurrences, 1909, 1910; no recurrence, 1911; recurrence, 1912	1
First attack, 1908; no recurrences, 1909, 1910; recurrences, 1911, 1912	1
First attack, 1908; recurrence, 1909; no recurrence, 1910, 1911, 1912	1
1909.	
First attack, 1909; recurrences, 1910, 1911, 1912	11
First attack, 1909; indefinite history, 1910, 1911; recurrence, 1912	1
Indefinite history, 1909, 1910, 1911; recurrence, 1912	1
First attack, 1909; no recurrence, 1910; recurrence, 1911; no recurrence, 1912	1
First attack, 1909; no recurrences, 1910, 1911, 1912	1
First attack, 1909; recurrences, 1910, 1911; no recurrence, 1912	1
First attack, 1909; no recurrences, 1910, 1911; recurrence, 1912	1
First attack, 1909; recurrence, 1910; no recurrence, 1911; recurrence, 1912	1
1910.	
First attack, 1910; recurrences, 1911, 1912	30
First attack, 1910; no recurrence, 1911; recurrence, 1912	3
First attack, 1910; recurrence, 1911; no recurrence, 1912	12
Indefinite history, 1910; recurrences, 1911, 1912	1
First attack, 1910; no recurrence, 1912	3
First attack, 1910; no history, 1911, 1912	1
1911.	
First attack, 1911; recurrence, 1912	69
First attack, 1911; no recurrence, 1912	29
Indefinite history, 1911; no recurrence, 1912	1
Indefinite history, 1911; recurrence, 1912	1
1912.	
First attack, 1912	97
Total	277

It will be noted that in some of these cases the disease was contracted originally in 1904; in others, in 1905 and every year thereafter to 1912, inclusive. Occasionally the history of previous attacks was indefinite, and such cases are so classified.

In this series there are 55 cases of pellagra recognized from one to five years ago by the attending physicians in which the annual recurrence has failed to appear in one or more seasons. In some of these cases the disease has reappeared after an intermission of one or two years, while in other instances symptoms have been present for one or more seasons, and have never since recurred. The following cases illustrate this point:

First attack, 1908; recurrence, 1909; no recurrences, 1910, 1911, 1912	1
First attack, 1909; no recurrences, 1910, 1911, 1912	1
First attack, 1910; no recurrences, 1911, 1912	3

In addition to these five cases we have records of a few other cases in Spartanburg County, not included in this series, in which patients have been without symptoms for a period of two, three, or more years and appear to be cases of recovery from the disease.

Our individual case histories show that a number of adult females have borne children since contracting pellagra, but in only 22 cases is the relationship of the pregnancies to the development of symptoms sufficiently definite to warrant analysis. In 16 of these cases (75 per cent.) there were no symptoms of pellagra during pregnancy. These observations cover only a small number of cases, and this subject will be investigated more in detail in this series and in additional ones during the summer of 1913. Pregnancy seems to show a tendency to inhibit the development of pellagrous symptoms.

2. *Periodicity.* A study of the literature of pellagra gives one the impression that there is a definite seasonal periodicity. We are led to believe that the disease appears in the spring; that there is a relative decrease in the number of cases in midsummer; that a fall recrudescence occurs, and that there is a tendency for symptoms to reappear at the same time each year.

Sambon cites the spring and fall periodicity as a strong argument in favor of his hypothesis that the disease is of protozoal origin and transmitted by a blood-sucking insect, a species of Similium.

We have undertaken some studies bearing on this phase of the subject. It is evident that these observations, except for the year 1912, must be based on the statements of patients suffering with pellagra. We have endeavored to control such statements and to add to their reliability by information obtained from other members of the household, and more particularly by that obtained from the attending physician. The cases will first be considered by month of onset of symptoms. Chart 9 represents graphically the month of onset of symptoms arranged by years. It is understood, of course, that this chart represents not only the month of original

onset in each case, but includes also the recurrences in each case year by year.

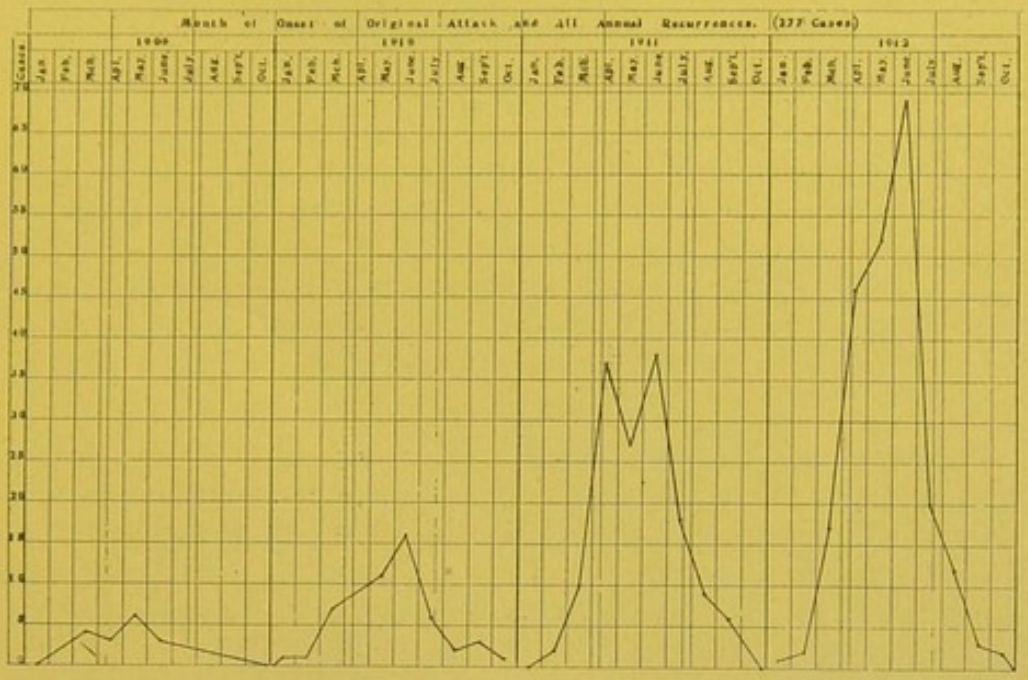


CHART 9.—Month of onset of original attack and all annual recurrences (277 cases).

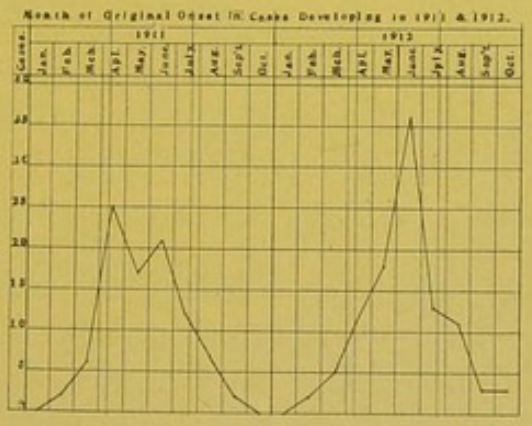


CHART 10.—Month of original onset in cases developing in 1911 and 1912.

In Chart 10 we have analyzed further the 1911 and 1912 cases from the standpoint of original onset of symptoms when the disease was contracted. It is evident from these charts that cases begin to show symptoms in the early spring, that there is a gradual increase in the number showing symptoms until the month of June, when the incidence curve reaches its highest point, and that after the month of June the incidence-rate falls quite rapidly. It is also evident that there are no spring and fall recrudescences of pellagra in Spartanburg County. On the contrary, cases begin to show symptoms in the spring, increase in number until midsummer, and then rapidly decrease.

We have analyzed the recurrent attacks with a view of determining whether or not there was any marked tendency in each individual case for active symptoms to appear during the same month year after year, with the following results:

INTERVAL BETWEEN ONSET OF SUCCESSIVE ATTACKS.

	11½ to 12½ months.	11 to 11½ months or 12½ to 13 months.	Less than 11 or more than 13 months.
Cases contracting pellagra in 1909	4	2	5
Cases contracting pellagra in 1910	12	17	10
Cases contracting pellagra in 1911	21	20	24
	37	39	39

We have analyzed still further the uniformity of recurrences, first by ascertaining the date of appearance of symptoms in individuals who contracted the disease in 1910 and comparing these dates with date of recurrence of symptoms in the same individuals in 1911, and second, by tabulating the same facts for cases developing originally in 1910 and 1911 and recurring in 1912.

Among the cases showing symptoms originally in 1910 the recurrence in 1911 was a month or more earlier in 14 cases, during the corresponding month in 27 cases, and a month or more later in 17 cases. Among the cases contracting the disease in 1910 and 1911 the recurrence in 1912 was at least a month earlier as compared with the appearance of symptoms in 1911 in 36 cases, during the same month in 48 cases, and at least a month later in 33 cases.

It is evident from this analysis that there is no particularly marked tendency for the seasonal recurrences to reappear during the same month year after year.

3. *Influence of Climate.* Climatic conditions are said to influence the periodicity of the disease. If during the spring months the precipitation is high, temperature low, and number of rainy days excessive, there is said to be a delay in the appearance of acute symptoms, more particularly those involving the skin. One of us had occasion to observe this influence in the spring of 1910 while investigating conditions in northern Italy. In March and April of that year the weather conditions in the provinces of Milan and Bergamo were quite unsettled, precipitation was excessive, there were many rainy days, but little sunshine, the temperature was low and the atmosphere was damp and chilly. At this time there were but few cases showing active symptoms of pellagra. The delay in appearance of active symptoms was attributed to unsettled weather conditions. We were informed, further, that it had been observed for many years that unsettled weather conditions in the spring always delayed the appearance of active

symptoms of the disease. We have been able to compare this general impression as regards conditions in Italy with similar conditions in the South. Early in May, 1912, we investigated the prevalence of pellagra in different sections of South Carolina, in North Carolina, and in Georgia. The physicians consulted informed us that there was a delay in appearance of cases showing active symptoms, and that whereas in April, 1911, they had observed many such cases, in April, 1912, they had seen but few. We were informed that spring and settled weather conditions were present much earlier in 1911 than was the case in 1912. This general impression is confirmed by the fact that farmers in the states mentioned were able to get their crops under way quite early in 1911 while in 1912 they were delayed for from three to six weeks. In Spartanburg County it was possible to secure much more detailed information covering weather conditions. The general information given us is in agreement with that outlined above.

In order that these general impressions may be controlled, we have obtained from the United States Weather Bureau its reports on weather conditions in Spartanburg County, South Carolina. The available information from this source, which includes monthly precipitation, monthly mean temperature, and number of rainy days, is presented in Charts 11, 12, and 13.

It is evident from an analysis of the monthly precipitation curves for 1911 and 1912 that in 1912 during the months of January to June inclusive, except for the month of April, the monthly precipitation was greatly in excess of that for the like period in 1911.

Analysis of the monthly mean temperature curve for 1911 and 1912 shows that in 1912 for the months of January to June inclusive the temperature was, in general, appreciably lower than was the case for like months in 1911.

A study of Chart 13 (number of rainy days) shows that for the first six months in 1912, except for the months of March and April, the number of rainy days per month was in excess of the number for the like period in 1911. While there were more rainy days in March and April, 1911, than for the same months in 1912, the amount of precipitation for these two months in 1912 was in excess of that for 1911.

These charts, considered as a whole, indicate quite clearly that settled weather conditions with relatively high temperature and low precipitation existed in Spartanburg County at an earlier date in 1911 than was the case in 1912.

The relationship between climatic conditions existing in 1911 and 1912 and the appearance of acute symptoms of pellagra can be determined by referring to Charts 9 and 10. There was quite a definite tendency for symptoms to appear at an earlier date in 1911 than was the case in 1912. The incidence-rate in both charts was high for the month of April, 1911, while in 1912 the incidence-

rate for April was comparatively low, especially in respect to new cases, and the maximum rate was not attained until the month of June.

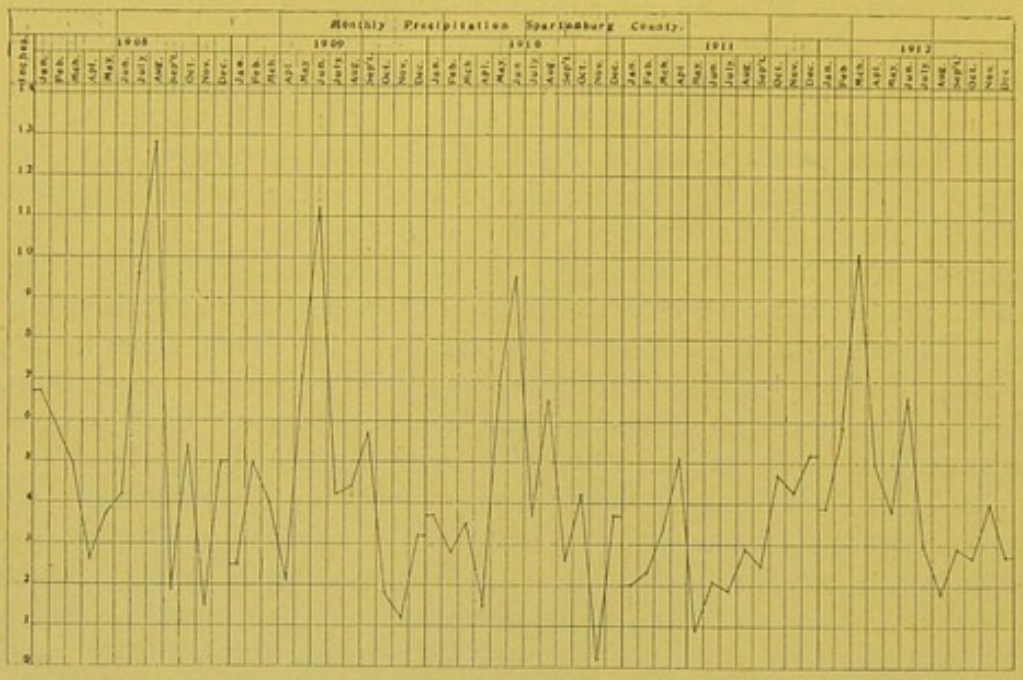


CHART 11.—Monthly precipitation, Spartanburg County.

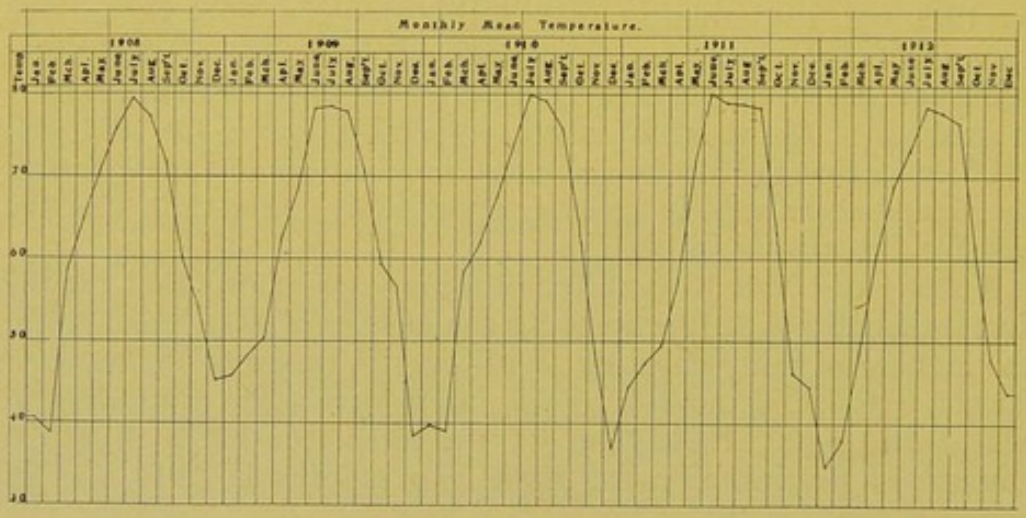


CHART 12.—Monthly mean temperature.

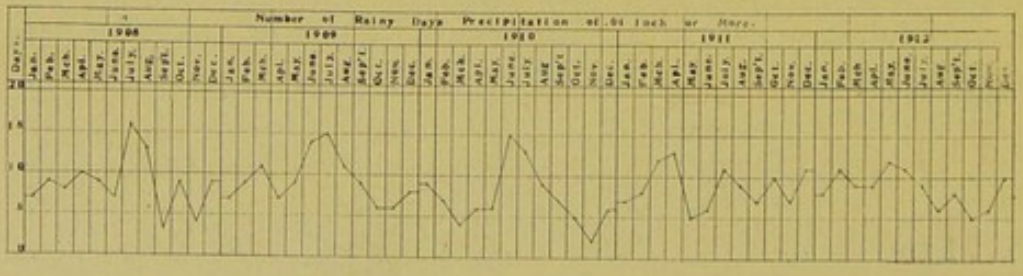


CHART 13.—Number of rainy days, precipitation 0.01 inch or more.

SUMMARY. 1. *Chronicity.* In a large proportion of the cases in this series the disease exhibited marked chronicity. In 20 per cent. the annual recurrences had failed to appear in one or more seasons. Pregnancy seems to show a tendency to inhibit the development of pellagrous symptoms. In 2 per cent. of the cases no symptoms had been present for from two to three years, and these appear to be cases of recovery from pellagra.

2. *Periodicity.* Cases begin to show symptoms in the early spring, increase in number until midsummer, and then rapidly decrease. There was no evidence whatever pointing to any spring and fall recrudescences, so frequently referred to in the literature of pellagra. There is no particularly marked tendency for the seasonal recurrences to appear during the same month, year after year, in the same individual.

3. *Influence of Climate.* Climatic conditions appear to influence the development of symptoms of the disease. If during the spring months precipitation is high, temperature low, and number of rainy days excessive, the appearance of acute symptoms, more particularly those involving the skin, is delayed.

B. *Symptomatology of* 1912 *Attacks.* A considerable amount of information has been collected in reference to symptomatology, but a discussion of this phase of the subject will not be undertaken until we have followed these cases through their 1913 recurrences.

The following general statements are warranted: While three or four years ago it was quite the usual thing to see patients showing a combination of severe skin lesions, severe stomatitis, intractable diarrhea or dysentery, mental derangement, and physical exhaustion, comparatively few patients exhibiting this symptomatology in a marked degree were observed in Spartanburg County during the summer of 1912. In many of the cases observed the symptoms were quite mild, and frequently they were confined almost entirely to the cutaneous system. This apparent indication of a decreasing virulence of the disease is strengthened by certain facts which appear in the study of mortality rates of pellagra in Spartanburg County for 1912 and earlier years.

XIV. CLINICAL OBSERVATIONS UPON ECONOMIC STATUS AND PREVIOUS HEALTH OF PELLAGRINS. It is believed by many who are brought into contact with pellagra that predisposition plays an important part in its development and that the disease most frequently affects the poorer classes, who live under unfavorable hygienic conditions and who subsist on a diet of low nutritive value and of limited variety. Some detailed studies were undertaken covering these points. The general hygienic conditions and dietary will be discussed elsewhere, and this section will be confined to a consideration of financial circumstances and health conditions as possible predisposing factors.

A. *Economic or Financial Circumstances.* In recording the data relating to the economic conditions under which the patients lived, the following classification was adopted: squalor, poverty, necessities, comfort, affluence. These terms are somewhat arbitrary and necessitate some brief explanation.

Squalor. Cases so classified are confined to those living in wooden huts in poor repair and without out-houses. Their diet was extremely poor and without variety, living rooms squalid, clothing filthy and in rags.

Poverty. Cases of this class lived in cabins usually without out-houses, rather isolated, ordinarily on large plantations. Food consisted largely of bacon, molasses, corn-bread, and biscuit. Negroes of the poorer tenant class form this group very largely.

Necessities. This class included those instances in which the family had a fairly regular cash income sufficient to provide for actual needs. It is made up largely of mill operatives and their families. They live in cottages, with some land about them, but rather closely aggregated to form mill-villages.

Comfort. Cases classified in this group are made up largely of farmers who own their own plantations and stock, have a good diet, and are in comfortable financial circumstances.

Affluence. In this group are included patients who live under the best of hygienic and financial conditions. Their houses are well-constructed, usually screened, and their diet is well balanced.

The cases so classified number 277 and are divided as follows:

Squalor	2
Poverty	28
Necessities	200
Comfort	41
Affluence	6

It will be seen that in 83 per cent. of the cases (squalor, poverty, necessities) the economical conditions were poor; that in 15 per cent. (comfort) the economical conditions were within the average, and in 2 per cent. (affluence) the financial circumstances were well above the average.

In connection with the "affluence" group, it may be said that the members of the Commission have personal knowledge of a number of other instances in which pellagra has developed in persons living under the best of hygienic and economic conditions.

Grouping the cases under two general subdivisions, we find that in 83 per cent. of the cases the economic conditions are poor, while in 17 per cent. they are good.

B. *Diseases of Childhood and General Health in Childhood. Diseases of Childhood.* In considering the diseases of childhood the cases were divided in two groups: (1) those giving a history of one or more of the following diseases: measles, mumps, chickenpox,

and whooping cough; (2) those giving a negative history for the diseases of childhood. The data covered 270 cases.

DISEASES OF CHILDHOOD.

Cases giving a history of one or more of the following diseases of childhood: measles, mumps, whooping cough, and chickenpox	252
No history of diseases of childhood	18
Total	270

As permanent injury to the heart and kidneys not infrequently follows attacks of scarlet fever, this disease was considered separately. In 20 cases a history of scarlet fever was elicited.

General Health in Childhood. The classification adopted in the consideration of general health in childhood was the following: Good, fair, and poor. Inquiries covering this point were made in 270 cases. Of this number, 232 (86 per cent.) gave a history of good health during childhood; in 28 cases it was fair, and in 10 cases it was poor.

C. *Diseases of Adult Life and General Health during Adult Life. Diseases of Adult Life.* The total number of cases considered is 198. The diseases peculiar to female adult life will be considered in a separate table. The following summary shows the prevailing diseases in some detail:

	No. of cases
Gastric disturbance	14
Dysentery, acute or chronic	28
Typhoid fever	46
Tuberculosis	7
Other diseases, unclassified	36
No history of ill health	67
Total	198

An analysis of diseases of adult life shows that 34 per cent. (67) of the total number of cases gave no history of ill-health. In 25 per cent. of the cases, those giving history of gastric disturbances, dysentery, and tuberculosis, a chronic disease was present.

General Health in Adult Life. In considering this point the classification adopted was that of good health, fair health, and poor health.

GENERAL HEALTH DURING ADULT LIFE.

Good	134
Fair	66
Poor	18
Total	218

An analysis of the data concerning general health conditions during adult life shows a history of good health in 62 per cent., fair health in 30 per cent., and poor health in 8 per cent.

D. *Obstetrical and Gynecological History.*

Social Status.

Married	150
Widowed	9
Single	25
	184

Obstetrical History.

Married females who have borne children	136
Unmarried females who have borne children	2
Married females who have not borne children	23
Unmarried females who have not borne children	23
	184

Number of females who have borne 1 child	28
Number of females who have borne 2 children	20
Number of females who have borne 3 children	21
Number of females who have borne 4 children	25
Number of females who have borne 5 children	16
Number of females who have borne 6 children	8
Number of females who have borne 7 children	10
Number of females who have borne 8 children	4
Number of females who have borne 9 children	3
Number of females who have borne 10 children	1
Number of females who have borne 11 children	2
	138

Average number of children borne = 3.8.

Menstruation during Period of Acute Pellagrous Symptoms.

Normal	95
Irregular	53
Excessive	6
Suppressed	10
Menopause	11
No information	9
	184

Diseases of Women.

Number of females giving more or less definite history of ovarian, uterine, or other pelvic disease	49

From this summary it will be noted that among the females who had attained the age of puberty, 86 per cent. of the cases occurred in married women, and that 86 per cent. of these married women had borne children. The greatest number of children borne by an individual is 11. The average number borne is 3.8. We have collected some statistical information in reference to the average size of families in mill-villages in Spartanburg County, from the standpoint of children borne by each woman, and it is not significantly different from the average number shown among pellagrous women.

The amount of time at our disposal and the relative importance of the subject did not warrant examinations of sufficient thoroughness to classify in detail the diseases of women. Of the 49 cases

giving history of such diseases the following were noted: tubal and ovarian inflammation, pus-tubes, cystic ovary, endometritis, uterine fibroid, carcinoma of the uterus, displacement of the uterus, and pelvic inflammation. In a number of cases, symptoms referable to the genital tract were quite indefinite.

The feature of most interest and relative importance in the consideration of predisposing factors is the chronologic relationship of previous illness to the development of pellagrous symptoms. The following summary gives in some deatil the information secured:

RECENT ILLNESS POSSIBLY PREDISPOSING TO PELLAGRA.

Gastric disturbance (including chronic gastric indigestion)	15
Dysentery (chronic during summer)	23
Diarrhea	6
Hookworm disease (moderate infection)	1
Ovarian cyst (large)	1
Uterine disease	4
General poor health (usually following childbirth)	30
Nephritis	3
Ascites (probably due to nephritis)	1
Valvular disease of the heart	1
Asthma	1
Pulmonary tuberculosis	7
Malarial fever	1
Alcoholism	1
Morphine habit	1
Infantile paralysis	1
Whooping cough	2
Measles	12
Chickenpox	1
No history of recent illness, 156 Health better than usual, 2	158
	270

In 15 of the cases a history of chronic indigestion was obtained. In explanation of these cases it may be said that symptoms of gastric disturbance preceded the active cutaneous symptoms of pellagra by a period of several months to several years. In 11 per cent. (30) of the cases no history of illness immediately preceding the development of pellagra could be obtained other than the fact that the general health was poor. Quite frequently this history of poor health followed confinement. One history of hookworm disease is included. This case showed objective clinical evidence of hookworm infection, which was uncommon for Spartanburg County. Malarial fever does not appear to be endemic in this county, and the one case included in this table was contracted in one of the "low country" counties. We were impressed with the fact that children not infrequently contracted pellagra during convalescence from acute infectious diseases, or very soon thereafter. It will be noted that 15 such observations were made: whooping cough, 2; measles, 12; chickenpox, 1. Of the 43 cases in children under ten years of age, 11 (approximately 23 per cent.) gave a

history of measles. In most of these the attack of pellagra occurred soon after recovery from measles.

Summary. In the large majority of these cases (83 per cent.) economic conditions were poor, and the disease is most prevalent among people of insufficient means. We would, however, invite attention to the fact that 17 per cent. of these cases occurred in patients living in comfortable circumstances. This is not in agreement with Italian conceptions of the disease, where it presumably is confined altogether to the poorer element of the general population.

An analysis of general health conditions during childhood shows that in 86 per cent. of the cases the history was that of good health. So-called congenital diseases and inherited constitutional defects were of no apparent significance.

An analysis of diseases of adult life shows that in 25 per cent. of the cases, those giving a history of gastric disturbances, dysentery, and tuberculosis, a chronic disease was present, and it might be inferred that there is evidence of existing predisposition. During adult life the general health conditions were good in more than half the cases (62 per cent.).

An analysis of the obstetrical and gynecological data shows that among females who had reached the age of puberty, those most affected were married women (86 per cent.). As 86 per cent. of the married women had borne children and the average number of children borne was 3.8, it might be inferred that childbearing is an important predisposing factor. We know, however, that the average number of children borne by married women in the general population of the South is equal to or even greater than this.

Recent illnesses do appear to be worthy of serious consideration as predisposing factors, and it is our opinion that they frequently do influence not only the development of pellagra but also the severity of the attacks. It will be noted, however, that 59 per cent. of the cases in this series gave no history of illness immediately preceding the development of pellagra.

XV. Studies upon Hygienic and Sanitary Conditions of Houses and Premises. A. *Houses.* The prevailing type of home in this county is a frame dwelling. The site usually is well drained, and there is always more than sufficient space between houses to afford free circulation of air.

In this study the dwelling houses are considered in three groups: brick, frame, and cabin.

Brick Dwellings. Dwellings of brick construction are relatively few in number. The mercantile houses in the larger centres are usually of brick construction, one or more stories in height, and the upper stories occasionally are used for living quarters. One of the cases included in this series was occupyiug such quarters.

Frame Dwellings. The mill-village dwellings are of the same general type, usually one story, sometimes two (Figs. 1, 2, 3, and 4).

The houses are almost always double. The single-story houses consist of a combination sitting and bed room, dining room, and

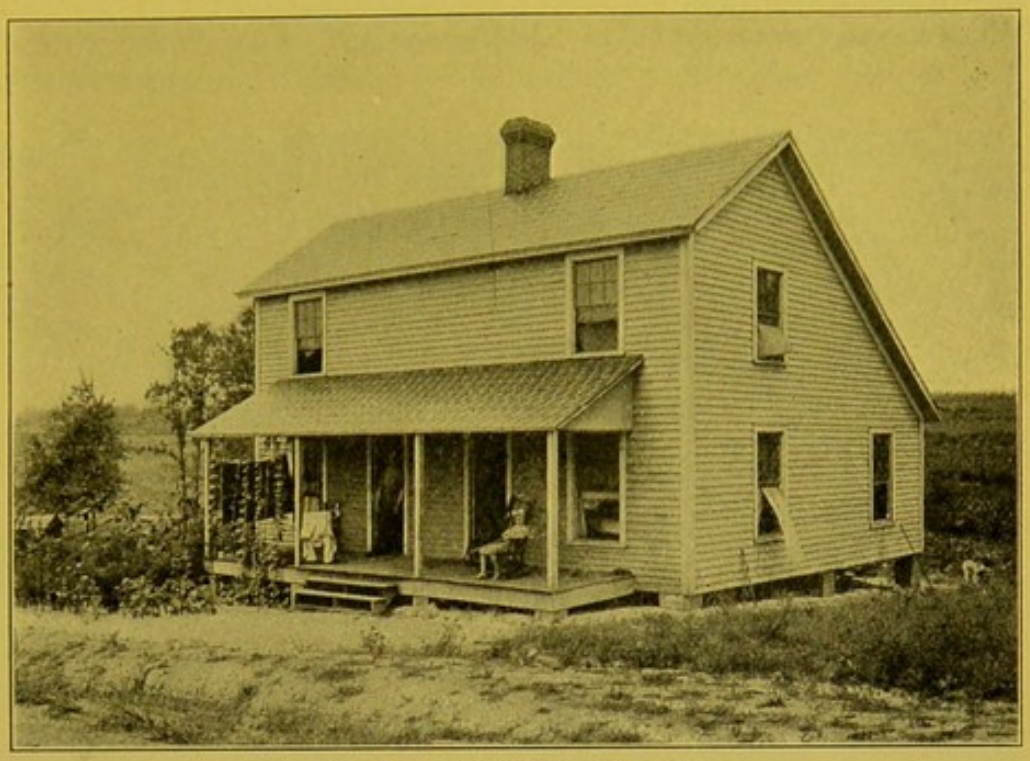


FIG. 1.—Typical mill-village house.

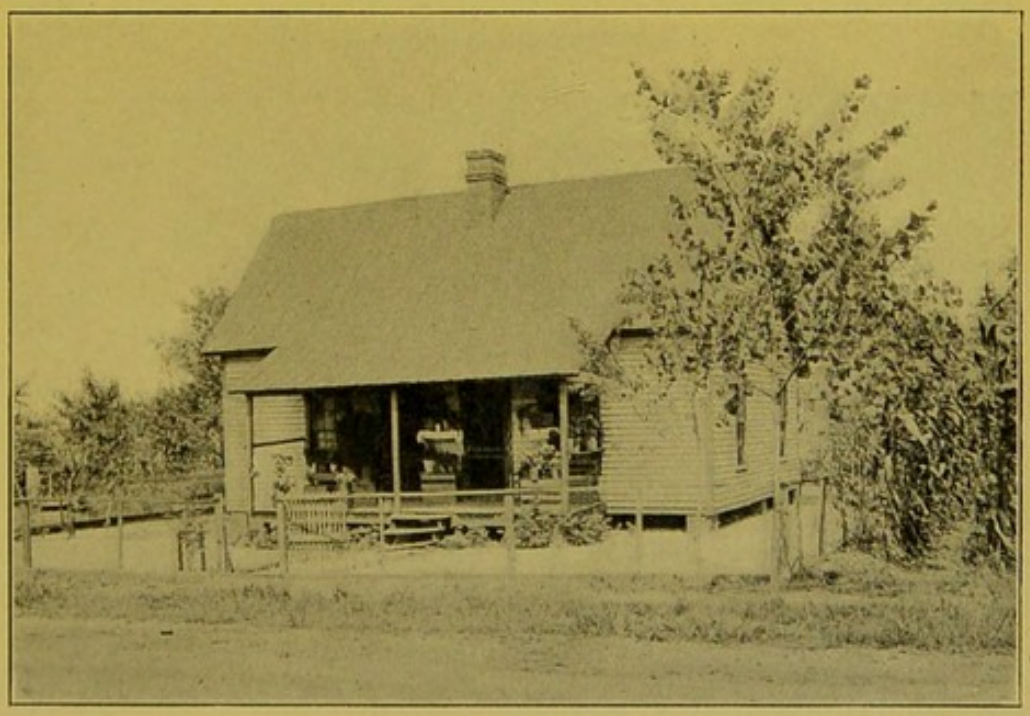


FIG. 2.—Typical mill-village house

kitchen (Fig. 5). In the two-story houses there is in addition a bed room on the second floor. Small families occupy one-half

of a double single-story house, and large families live in either a two-story house or both sides of a double one-story house. There are two or three windows in each room and a small porch in front. These houses have no cellar, the foundation is brick, the ground floor is well above the ground, and the space between the ground

FIG. 3.—Typical mill-village house

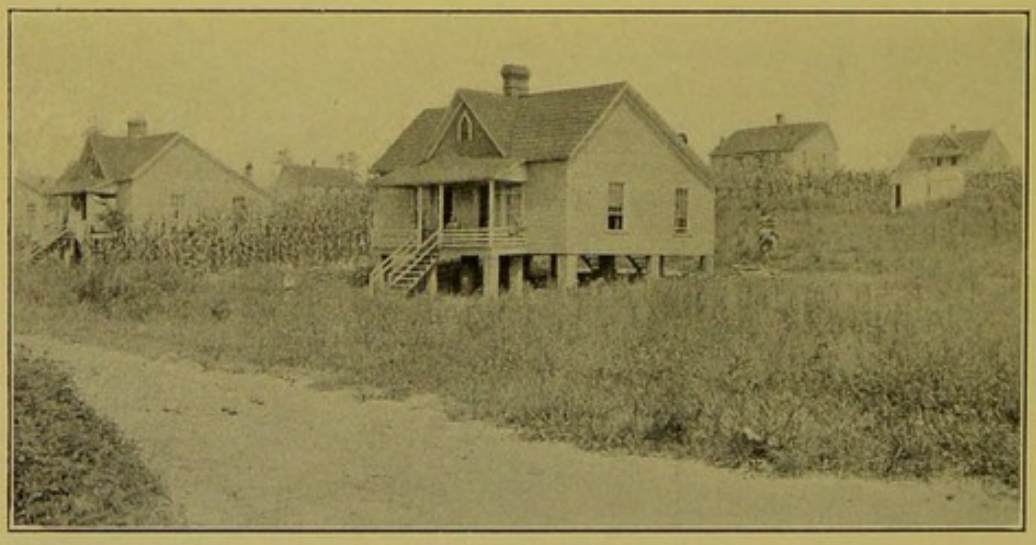


FIG. 4.—Typical mill-village house.

and ground floor is left open, permitting free circulation of air. Doors are placed directly in line from front to rear of the house, permitting free and unobstructed passage of fresh air. Rooms are sealed, both walls and ceiling. The timber used for this purpose is sometimes matched, sometimes not. The roof has a good pitch

with a large attic, permitting circulation of air, and the bed rooms have open fireplaces which further improve ventilation.

These houses are practically all infested with *Cimex*, and the grooves between the boards used in sealing the rooms afford an ideal place for the hatching out of broods of these insects.

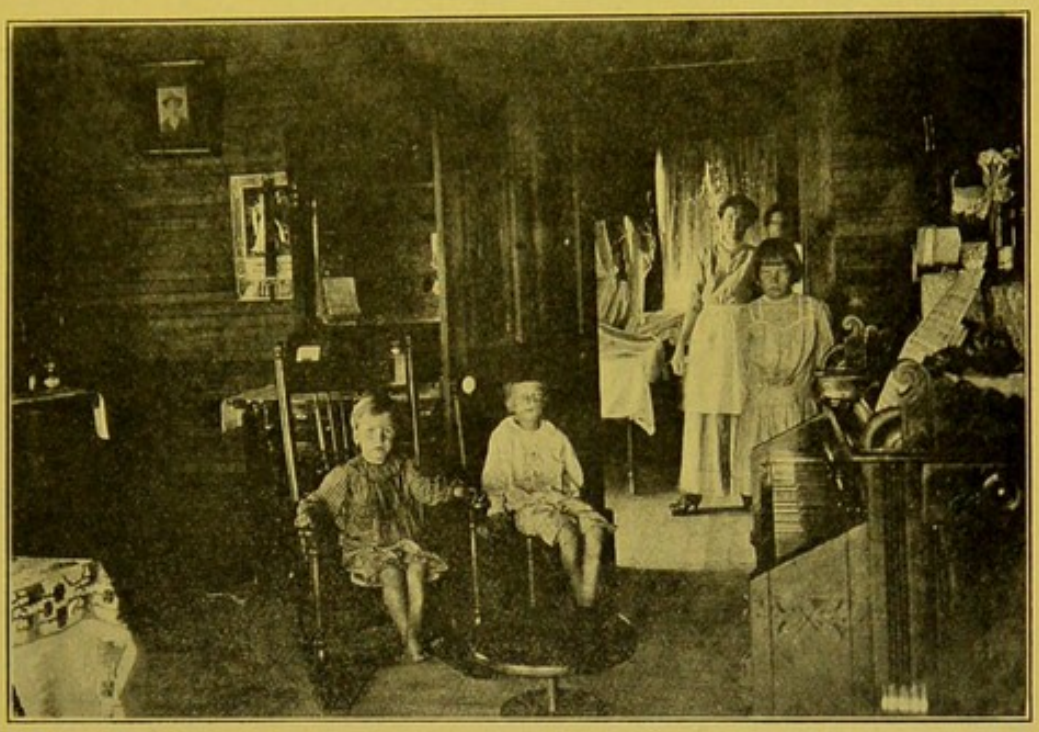


FIG. 5.—Interior view, mill-village house.

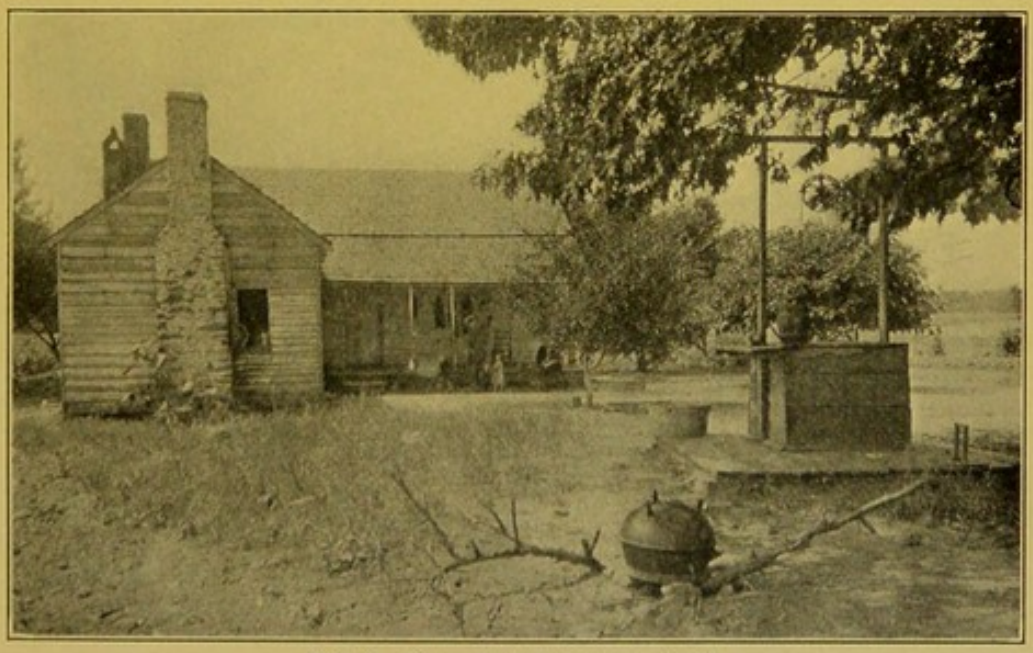


FIG. 6.—Type of farm-house and well.

The dwelling houses in the farming section are practically always frame houses (Fig. 6). Many of the farm-houses, more particularly

those occupied by owners, are well-constructed, roomy, and superior to the mill-village dwelling-house. On the other hand the usual tenant-house is inferior in many respects to that found in mill-villages.

Cabins. In this group are included the small frame or log dwellings, poorly constructed and ill-ventilated (Fig. 7). The negroes of the farming class usually occupy such houses.

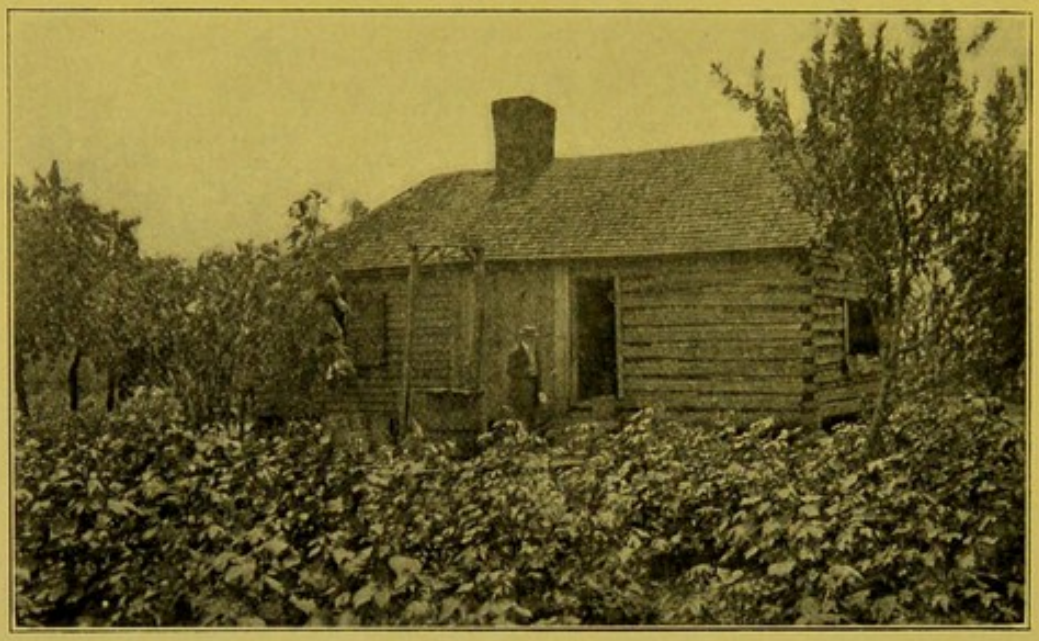


Fig. 7.—Type of cabin occupied by negro tenants on farms.

Hygienic and Sanitary Condition of Houses.

Brick		2
Frame		236
Cabin		19
		257
Repair:	Good	212
	Poor	38
		250
Screened:	Yes	21
	No	229
		250
Ventilation:	Good	155
	Fair	86
	Poor	8
		249
General cleanliness:	Good	142
	Fair	92
	Poor	12
		246

Summary. 92 per cent. of the cases lived in frame houses of fairly good size, and 85 per cent. of the houses investigated were in fairly good repair. Nine per cent. of the houses were screened, but in many instances the screening was more or less unsatisfactory. In only a small proportion of the screened houses did the screening afford satisfactory protection against the ingress of insects. *Musca domestica* was present in all, and *Stomoxys calcitrans* was present in many unprotected houses.

Ventilation. In 62 per cent. of the houses investigated, ventilation of the bed rooms was good, in 36 per cent. only fair, and in 3 per cent. poor. The number of persons occupying each bedroom averaged about three, and the available allowance of air space did not, in general, suggest overcrowding. Poor ventilation and overcrowded conditions were more in evidence in the negro population.

Summary. We have failed to find anything of significance in connection with the houses from the standpoint of overcrowding and ventilation. It was observed that *Mucosa domestica* was always more or less abundant, and that of the blood-sucking insects, *Stomoxys calcitrans* and *Cimex lectularius* were of common occurrence. A detailed study of the observations on insects will be considered in the entomological section of this report.

B. *Water Supply.* The sources of water supply for drinking purposes among the general population of Spartanburg County are similar to those considered in this study. For analytical purposes the sources of supply are divided into three groups, wells, springs, and city water.

Source of Water Supply.

Wells: Dug well, with bucket	162		
Artesian well, with pump	30	192	
Springs	13	13	
City water, hydrant	36	36	241

Protection of Water-supply with Reference to Contamination by Surface Water or by Seepage at Point from Which Supply is Drawn.

Protection satisfactory (water-supply drawn from hydrants, from artesian wells with concrete base, or from deep wells with concrete base)	65
Partly protected (water-supply drawn from wells with wooden base, either covered or uncovered, or from isolated springs)	176
	241

Wells. The wells are of several types. The type most common in rural districts and in some of the mill-villages is the ordinary dug well, about five feet in diameter (sometimes round and sometimes square), from thirty to sixty or more feet in depth, and protected at the top by a wooden frame. Though a few wells could be classified as "shallow wells," it was quite the usual thing to

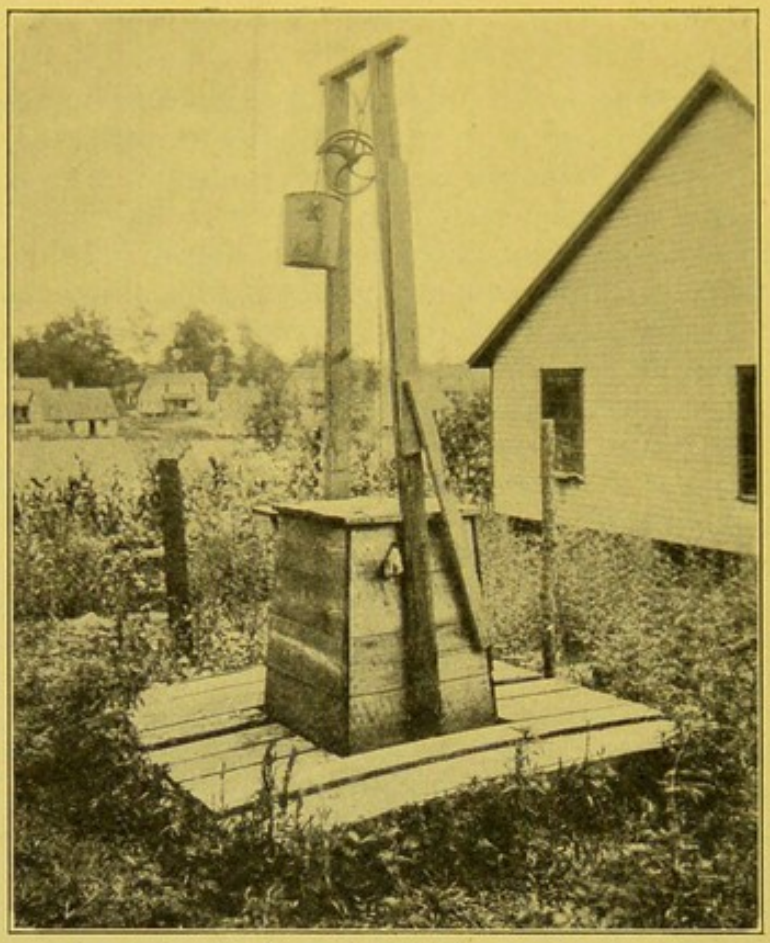


FIG. 8.—Typical dug well with bucket. Wooden base.

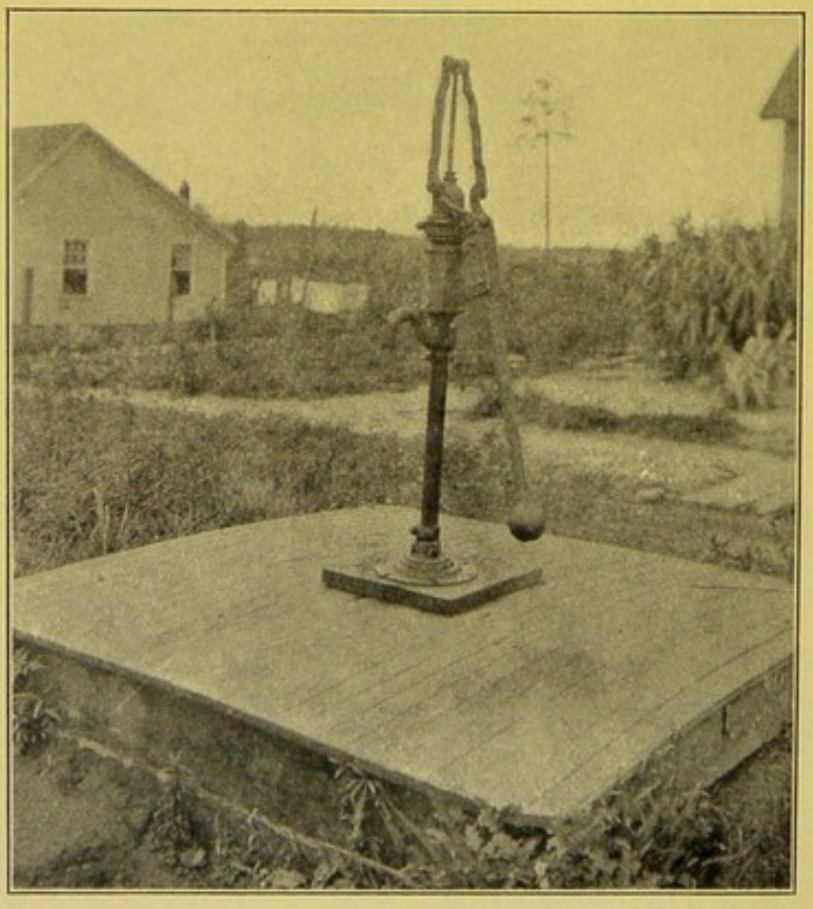


FIG. 9.—Type of driven pump well, wooden base.

find that the supply was obtained from a sufficient depth to insure that an impermeable stratum supervened, preventing contamination by surface water.

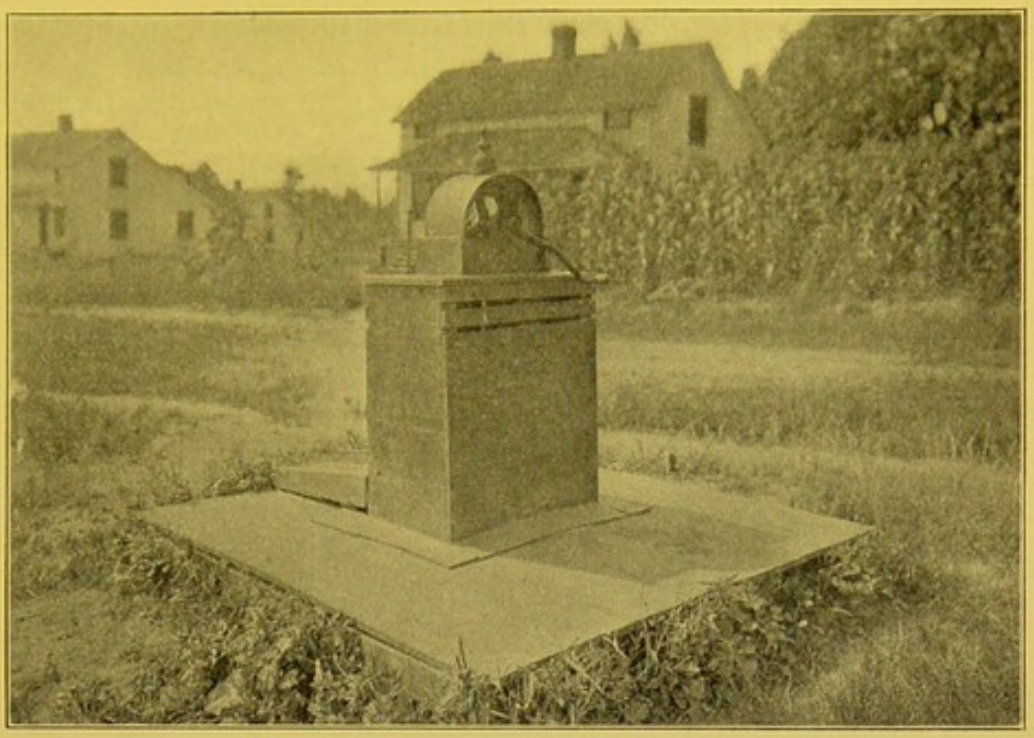


FIG. 10.—Type of bucket well, wooden base

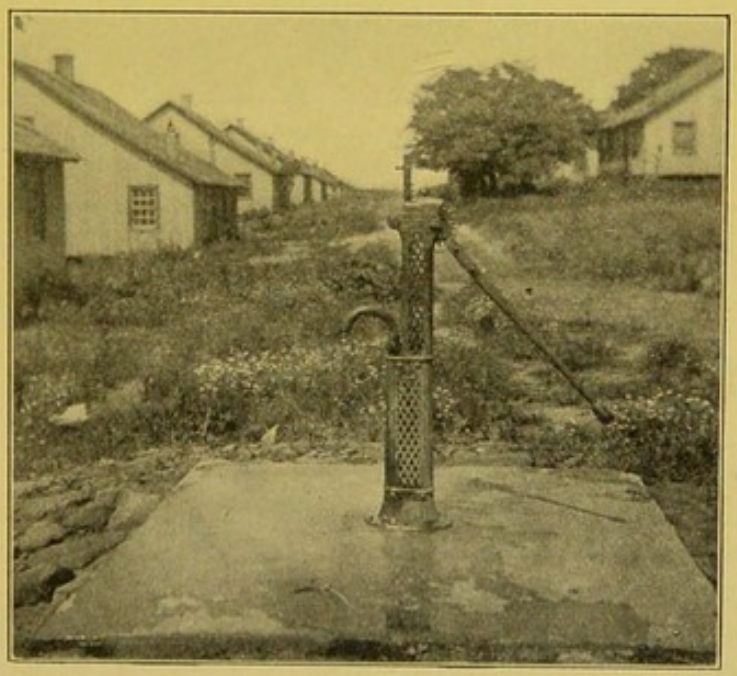


FIG. 11.—Type of driven well with pump. Sloping concrete base

The water was usually drawn by means of the well-known bucket and windlass arrangement, but in a number of instances pumps were

in use. In the farming districts, ordinarily, no effort was made to guard against contamination at the immediate source of supply, but in some of the mill-villages these wells have concrete bases, sloping outward. The various types of wells can be better understood by reference to Figs. 8, 9, 10, 11, and 12.

In some of the mill-villages, artesian wells are in use. These artesian wells are usually quite deep, and the water is drawn by pump.

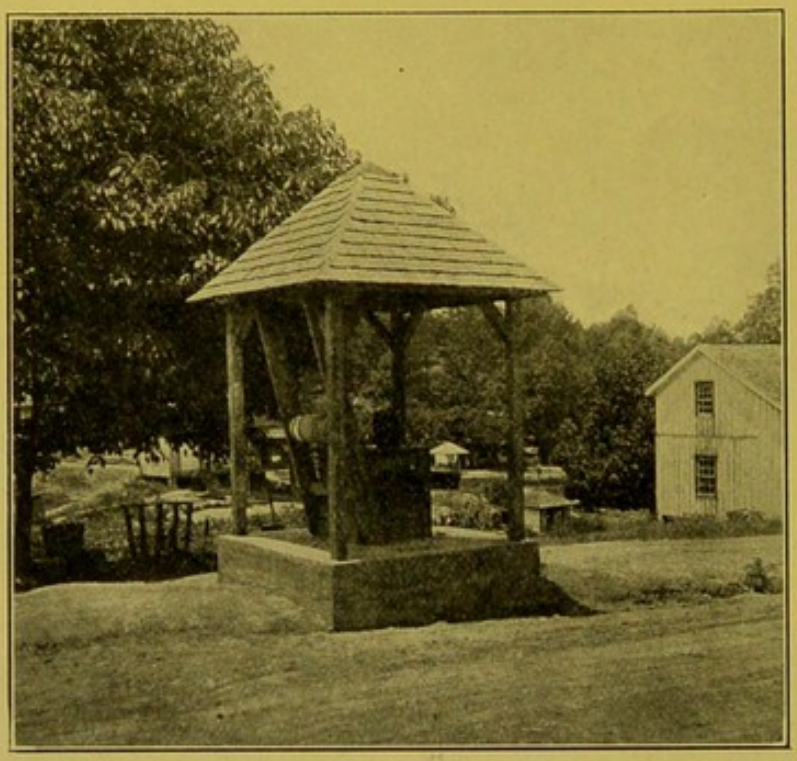


FIG. 12.—Dug well with bucket. Concrete base.

Springs. The use of spring water was, with one or two exceptions, confined strictly to the farming population living in comparative isolation. Usually drainage from the house was not in the direction of the spring, and the possibility of contamination was not a factor of importance.

City Water. This source of supply was confined to the city of Spartanburg. Bacteriological and chemical examinations are made from time to time, with no evidence of contamination.

SUMMARY. It will be noted that 80 per cent. of the cases used well water; 15 per cent. used city water; and 5 per cent. used spring water.

In 27 per cent. of the total observations (241) the water supply was perfectly protected from contamination. The remaining 73 per cent. are classified as partly protected, but this group requires some further explanation, as otherwise an erroneous inference might be drawn. We have included in this group all springs, all shallow wells, and all wells without a concrete base. As a matter

of fact, there were few shallow wells, and the probability of contamination in this group, considered as a whole, was but slight.

We realize that the water-supply is not considered to be of any importance as a factor in the etiology of pellagra. In this study, however, we have endeavored to investigate, as far as was possible, all probable factors concerned in the epidemiology of the disease, and for this reason have considered the water-supply. We have found nothing of any apparent significance in this connection.

C. *Disposal of Excreta.* In making a general survey of sanitary conditions, a study of the disposal of excreta was included. In classifying privy types we have adopted, for the sake of convenience, the classification used by the Rockefeller Sanitary Commission in its hookworm investigations in the Southern States.

INDEX OF PRIVY TYPES ADOPTED BY THE ROCKEFELLER SANITARY COMMISSION.

		Per cent.
Class A.	Water carriage or Marine Hospital Barrel (L. R. S.)	100
Class B.	Water-tight and rigidly fly-proof privy	75
Class C.	Water-tight, closed-in back	50
Class D.	Closed-in back, surface privy	25
Class E.	Ordinary open-in-back surface privy	10
Class F.	No privy	00

We encountered in this study one type of privy not falling strictly in any of these groups. The type in question (Fig. 14) was found in three or four of the mill-villages, and consisted of an out-house open in front and behind. The excreta were collected in square metal pails, supposedly water-tight. These pails were emptied at intervals. No attempt was made to keep out flies, the pails were frequently battered, and not water-tight, and usually were extremely filthy. It was not possible to include these privies in Class C, nor was it fair to put them in Class E. We have therefore placed them in Class D.

The following tables will show the facts observed:

PRIVY TYPES.

Class A	11
Class B	0
Class C	0
Class D	51
Class E	152
Class F	29
Total	243

SANITARY INDEX FOR ALL PRIVIES.

Class A.	11 at 100 per cent.	1100
Class B.	00 at 75 per cent.	00
Class C.	00 at 50 per cent.	00
Class D.	51 at 25 per cent.	1275
Class E.	152 at 10 per cent.	1520
Class F.	29 at 0 per cent.	00
Total		3895

Sanitary index = 16.

DISTANCE OF PRIVY FROM HOUSE.

10 yards	4
15 yards	9
20 yards	35
25 yards	25
30 yards	75
35 yards	4
40 yards	9
45 yards	1
50 yards	31
60 yards	2
70 yards	1
75 yards	1
100 yards	2
200 yards	1
Water-carriage system (Class A)	11
No privy (Class F)	29
Total	240

DISTANCE OF PRIVY FROM WELL.

10 yards	5
15 yards	5
20 yards	13
25 yards	7
30 yards	27
35 yards	7
40 yards	12
50 yards	45
60 yards	5
70 yards	6
75 yards	9
80 yards	1
85 yards	1
100 yards	5
110 yards	1
250 yards	1
Water-carriage system (Class A)	11
No privy (Class F)	29
Total	190

The cases in which the disposal of excreta was by water carriage (5 per cent.) were confined to the city of Spartanburg. No privy of the Marine Hospital type (L. R. S.) was observed. Between 30 and 40 cases of pellagra developed in the city of Spartanburg in other than mill-village sections. Only 8 of these cases used a water-carriage system of disposal of excreta. There were no privies of Class B or C. In 21 per cent. the privies were arbitrarily included in Class D. In 63 per cent. of the cases the method of disposal was that of the unhygienic and insanitary open surface privy, and in 12 per cent. of the cases no privy was used.

The method of disposal of excreta in the mill-villages, located in Spartanburg County falls under two classes, D and E (Figs. 13, 14, 15, 16, and 17): In some villages the pail system is in use, but beneficial results are negatived by the fact that no effort is made to screen the closets properly either in front or behind. In other

villages the unhygienic open surface privy is in use, and flies have free access to large collections of excreta in close proximity to the dwelling-houses. In some mills the privies are cleaned weekly;

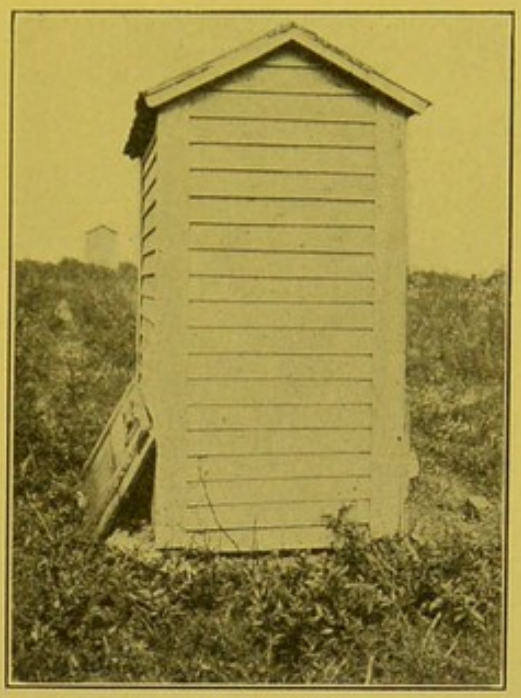


FIG. 13.—Privy, Type E. Surface, unscreened.

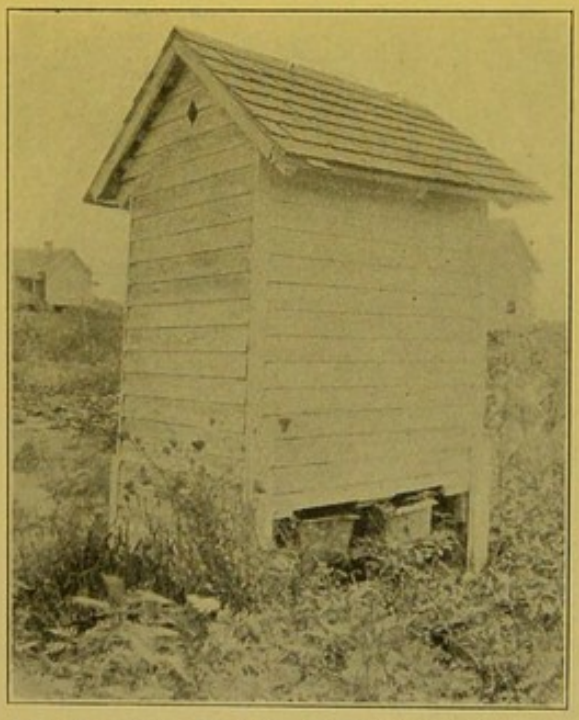


FIG. 14.—Privy, Type D. Pail system, unscreened.

in others, at greater and more irregular intervals. In some villages the sanitary condition around the privies is extremely poor, while in others some attempt is made to keep things relatively clean.

In the farming districts the methods of disposal fall in Classes E and F (Fig. 18). The open-surface privies on farms usually are

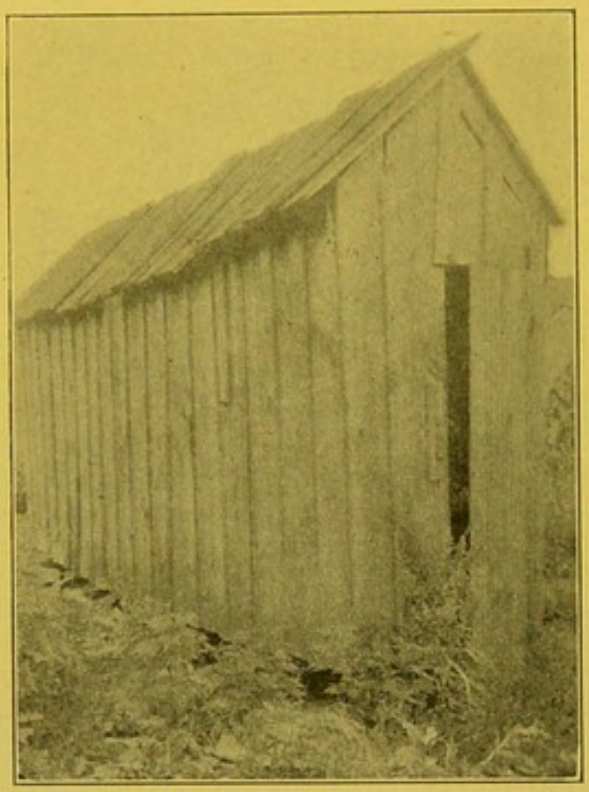


FIG. 15.—Privy, Type E. Surface, unscreened.

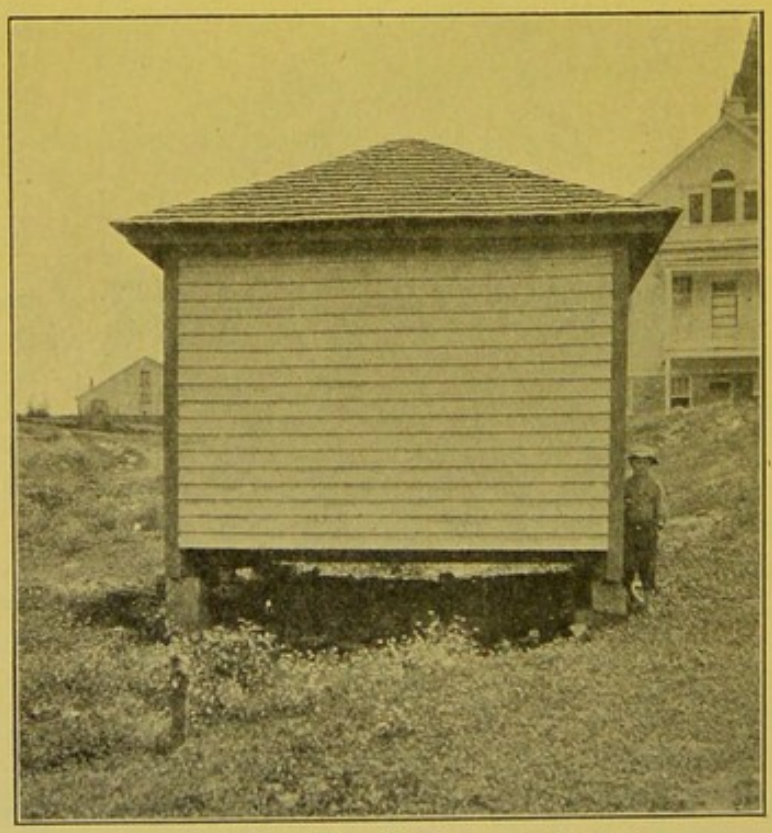


FIG. 16 —Privy, Type E. Surface, unscreened

poorly constructed and filthy, and the excreta are seldom removed, poultry being relied upon as scavengers. Negroes in the farming

FIG. 17.—Privy, Type E. Surface, unscreened.

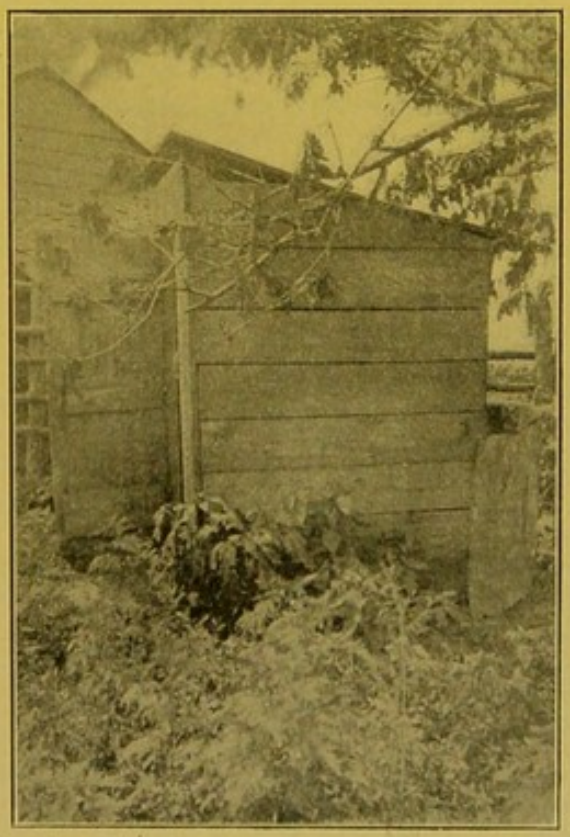


FIG. 18.—Privy, Type E. Surface, unscreened, on farm.

districts seldom have privies, and we were greatly surprised to find that farmers of the better classes sometimes had no privies.

The methods of disposal of excreta observed by us among the families of pellagrins in the different groups of the population are similar to the methods of disposal adopted by the general population in these groups.

Many of the mill authorities are well aware of the importance of good sanitation, and it is their constant endeavor to improve conditions. Even now plans are under way for the installation of a water-carriage system of disposal in one or two of the larger and better mills.

SUMMARY. The average general sanitary index for all the privies studied is only 16, on a basis of 100 for perfect disposal. So far as population groups are concerned the methods of disposal in use by the general population are not different from those observed among pellagrous families. Between 30 and 40 cases of pellagra developed in the city of Spartanburg more or less away from mill districts, and only 8 of these cases used a water-carriage system of sewage disposal. In general the methods of disposal of excreta observed in this series are insanitary, and many of the diseases of the intestinal canal transferred by mechanical means, flies, etc., would find conditions most favorable for such transfer.

D. *Premises.* The following table covers the observations made relative to the sanitary conditions of the premises of pellagrins:

LOCATION OF HOUSE RELATIVE TO MOISTURE AND DAMPNESS.

Air and soil:	Dry		242
	Damp		6—248
Drainage:	Good		242
	Poor		6—248
General cleanliness of premises:	Good		146
	Fair		90
	Poor		12—248
Stagnant water:	Yes		7
	No		239—246
Shade:	None		145
	Little		62
	Much		38—245
Undergrowth or shrubbery:	None		207
	Little		36
	Much		2—245
Barns:	Number of houses having barns		90
	Number of houses having no barns		145—235
Animal:[14]	Dogs		76
	Cats		79
	Horses or mules		54
	Cows		93
	Goats		6
	Fowl		158
	Rats		88
	Mice		124

[14] Number of observations, 237.

SUMMARY. In 98 per cent. of the cases the dwelling-houses were well located and the drainage was good. Stagnant water was noted on the premises in only 3 per cent. of the houses investigated (246). But few mosquitoes were observed. The entomological section of this report will deal with permanent streams and collections of water, with the blood-sucking insects breeding therein, and with other biting insects found in the houses, on the premises, and in the neighborhood.

XVI. GENERAL OBSERVATIONS UPON THE DIETARY. The data analyzed in this study are necessarily of a general nature, based on information obtained from statements of patients, physicians, storekeepers, millers, and others.

In order to determine the relative frequency with which the more important foodstuffs were used, patients and their families were closely questioned as to how often certain articles of food would appear upon the family table, and with regard to the patient's particular fondness for any particular dish. Replies to these questions were recorded under the following heads: Daily, one or more times a day; habitually, one or more times a week, but not daily; rarely, at irregular intervals of more than a week; never.

With a view to discovering any significant differences in the habitual dietary of the three groups in the population which show the greatest disparity in the prevalence of pellagra, the results of this inquiry are summarized for the rural population, urban population, and the mill-village population, separately. These results are set forth in the following tables, which represent the actual number of pellagrins and the percentage of the total number of pellagrins from whom the particular information in question was obtained.

TABLE XI.

FRESH MEATS:			Daily.	Habitually.	Rarely.	Never.
Fresh beef in season	Mill population	Number	1	51	84	11
		Per cent.	1	35	57	7
	Urban population	Number	3	27	16	0
		Per cent.	7	59	34	0
	Rural population	Number	2	20	40	12
		Per cent.	3	27	54	16
Fresh pork in season	Mill population	Number	9	68	60	10
		Per cent.	6	46	41	7
	Urban population	Number	1	33	12	0
		Per cent.	2	72	26	0
	Rural population	Number	4	45	18	5
		Per cent.	5	63	25	7
Fresh fish in season	Mill population	Number	0	32	79	34
		Per cent.	0	22	55	23
	Urban population	Number	0	14	29	2
		Per cent.	0	31	64	5
	Rural population	Number	0	7	44	21
		Per cent.	0	10	61	29

TABLE XI.—Continued.

			Daily.	Habitually.	Rarely.	Never.
FRESH MEATS:						
Fresh fowl in season	Mill population	Number	1	59	81	6
		Per cent.	1	40	55	4
	Urban population	Number	1	30	14	2
		Per cent.	2	64	30	4
	Rural population	Number	2	45	23	2
		Per cent.	3	62	32	3
CURED MEATS:						
Cured beef	Mill population	Number	1	0	25	94
		Per cent.	1	0	21	78
	Urban population	Number	0	1	10	26
		Per cent.	0	3	27	70
	Rural population	Number	0	1	3	66
		Per cent.	0	1	4	95
Cured pork	Mill population	Number	92	40	10	2
		Per cent.	64	28	7	1
	Urban population	Number	25	9	9	2
		Per cent.	56	20	20	4
	Rural population	Number	49	12	8	1
		Per cent.	70	17	12	1
Cured fish	Mill population	Number	1	6	45	95
		Per cent.	1	4	31	64
	Urban population	Number	1	5	15	22
		Per cent.	2	12	35	51
	Rural population	Number	1	3	14	53
		Per cent.	1	4	20	75
Canned beef	Mill population	Number	0	14	80	51
		Per cent.	0	10	55	35
	Urban population	Number	0	3	20	20
		Per cent.	0	7	47	46
	Rural population	Number	0	2	25	46
		Per cent.	0	3	34	63
Canned pork	Mill population	Number	0	7	39	88
		Per cent.	0	5	29	66
	Urban population	Number	0	2	14	24
		Per cent.	0	5	35	60
	Rural population	Number	0	1	7	58
		Per cent.	0	2	11	87
Canned fish	Mill population	Number	0	20	90	30
		Per cent.	0	14	64	22
	Urban population	Number	1	7	28	8
		Per cent.	2	16	64	18
	Rural population	Number	0	5	38	29
		Per cent.	0	7	53	40
EGGS, BUTTER, AND MILK:						
Eggs	Mill population	Number	10	36	13	2
		Per cent.	16	59	22	3
	Urban population	Number	7	8	0	0
		Per cent.	47	53	0	0
	Rural population	Number	11	12	17	3
		Per cent.	25	28	40	7
Butter	Mill population	Number	114	16	12	4
		Per cent.	78	11	8	3
	Urban population	Number	33	6	8	0
		Per cent.	70	13	17	0
	Rural population	Number	51	8	9	6
		Per cent.	69	11	12	8
Milk	Mill population	Number	83	21	29	12
		Per cent.	57	15	20	8
	Urban population	Number	16	14	16	9
		Per cent.	29	25	29	17
	Rural population	Number	41	15	18	9
		Per cent.	49	18	22	11

TABLE XI.—Continued.

VEGETABLES, FLOUR, LARD:			Daily.	Habitually.	Rarely.	Never
Fresh vegetables in season	Mill population	Number	120	21	3	3
		Per cent.	82	14	2	2
	Urban population	Number	36	6	4	0
		Per cent.	78	13	9	0
	Rural population	Number	61	11	1	0
		Per cent.	84	15	1	0
Canned vegetables	Mill population	Number	4	41	70	29
		Per cent.	3	28	49	20
	Urban population	Number	2	17	25	2
		Per cent.	4	37	54	5
	Rural population	Number	3	8	25	37
		Per cent.	4	11	34	51
Wheat flour	Mill population	Number	142	1	0	0
		Per cent.	99	1	0	0
	Urban population	Number	45	0	0	0
		Per cent.	10	0	0	0
	Rural population	Number	71	1	0	0
		Per cent.	99	1	0	0
Leaf lard (pork)	Mill population	Number	30	16	2	0
		Per cent.	62	34	4	0
	Urban population	Number	10	2	0	0
		Per cent.	83	17	0	0
	Rural population	Number	28	4	0	0
		Per cent.	87	13	0	0
Compound lard	Mill population	Number	101	2	23	5
		Per cent.	77	2	18	3
	Urban population	Number	37	5	2	1
		Per cent.	82	11	5	2
	Rural population	Number	62	1	7	1
		Per cent.	87	1	10	2

TABLE XII.

CORN PRODUCTS. CORN MEAL USED.

		Daily.	Habitually.	Rarely.	Never.
Mill population	Number	85	21	40	0
	Per cent.	58	14	28	0
Urban population	Number	23	12	10	2
	Per cent.	49	26	21	4
Rural population	Number	47	13	11	0
	Per cent.	66	18	16	0

SOURCE OF SUPPLY OF MEAL. SHIPPED MEAL GROUND IN NEARBY STATE

		Exclusively.	Mostly.	Rarely.	Never.
Mill population	Number	84	8	22	4
	Per cent.	71	7	19	3
Urban population	Number	29	2	5	1
	Per cent.	78	5	14	3
Rural population	Number	16	9	13	4
	Per cent.	38	21	31	10

LOCAL CORN GROUND LOCALLY.

		Exclusively.	Mostly.	Rarely.	Never.
Mill population	Number	30	22	2	0
	Per cent.	56	40	4	0
Urban population	Number	7	7	0	0
	Per cent.	50	50	0	0
Rural population	Number	32	19	4	0
	Per cent.	58	35	7	0

TABLE XII.—Continued.

QUALITY OF MEAL.

		Good.	Musty.
Mill population	Number	41	49
Urban population	Number	13	12
Rural population	Number	34	18

USE OF HOMINY OR GRITS.

		Daily.	Habitually.	Rarely.	Never.
Mill population	Number	9	47	53	19
	Per cent.	7	37	41	15
Urban population	Number	9	16	7	5
	Per cent.	24	43	19	14
Rural population	Number	5	14	23	11
	Per cent.	10	26	43	21

		Syrup.	Corn-starch.	Whisky.
Mill population	Number	47	5	19
	Per cent.			
Urban population	Number	23	5	9
	Per cent.			
Rural population	Number	27	3	6
	Per cent.			

Meats. The following meats were used to a greater or less extent in these three subdivisions of the population: fresh meat, fresh pork in season, fresh fish in season, fresh fowl, dried or chipped beef, bacon, cured fish, canned beef, canned sausages, and canned salmon. Fresh beef is not a staple article of diet of any of these population groups during the summer months. By far the greater number of individuals among the mill-village and rural population groups used it but rarely, and some never, while the urban group used it more extensively. The actual percentages of those eating fresh meat, either rarely or never, are as follows: Rural cases, 70 per cent.; mill-village cases, 64 per cent.; urban cases, 34 per cent. Fresh pork in season was used approximately equally in the three groups, but rather more generally in the rural group, the actual percentages of those using it daily or habitually being as follows:

Urban cases, 74 per cent.; rural cases, 68 per cent.; mill-village cases, 52 per cent.

Fresh fish is not a common article of diet in Spartanburg County, and was but rarely used in any of the three groups. This statement applies more particularly to the mill-village and rural population. The percentages of those using fresh fish either rarely or never are as follows: urban cases, 59 per cent.; rural cases, 90 per cent.; mill-village cases, 78 per cent.

Fresh fowl was used quite extensively in all three groups particularly during the summer months; most extensively by the rural

cases; less so by the urban group, and least extensively by the mill-village group. The actual percentages of those using fowl, either daily or habitually, are as follows: urban cases, 66 per cent.; rural cases, 65 per cent.; mill-village cases, 41 per cent.

Cured beef is used but rarely in any of the three groups. In 95 per cent. of the rural group, 78 per cent. of the mill-village group, and in 70 per cent. of the urban group it was never used.

Bacon (cured pork) is a common article of diet in all groups, being used either daily or habitually by 92 per cent. of the mill-village group, 87 per cent. of the rural group, and 76 per cent. of the urban group.

Cured fish is little used in any of the three groups, though somewhat more frequently in the city population than by the the other two classes.

Canned beef is not used extensively. In 63 per cent. of the rural cases, 46 per cent. of the urban cases, and 35 per cent. of the mill-village cases it is never used. When used it appears to be eaten neither daily nor habitually.

Canned sausages (pork) are quite extensively used although seldom with any great frequency or regularity. The farming population uses them least.

Canned Fish. Canned salmon, while quite generally used, is not a staple article of diet in any of the groups. In 93 per cent. of the rural cases, 86 per cent. of the mill-village cases, and 82 per cent. of the urban cases it is rarely or never used.

Eggs, Butter, and Milk. These farm and dairy products are used with great frequency and regularity in all three groups of the population. Eggs were used either daily or habitually by 100 per cent. of the urban cases, 75 per cent. of the mill-village cases, and 53 per cent. of the rural cases. Butter was used daily or habitually by 89 per cent. of the mill-village cases, 83 per cent. of the urban cases, and 80 per cent. of the rural cases. Milk was used either daily or habitually by 72 per cent. of the mill-village cases, 67 per cent. of the rural cases, and 54 per cent. of the urban cases. The use of eggs and butter is not so common in the rural group as in the other two. It must be remembered, however, that a greater number of negroes are included in this group, and their diet is probably below that of the whites, more particularly from the standpoint of variety. For example, Table XI shows that in 3 cases among the rural population, eggs were never used; 2 of these cases were negroes. Of 6 cases that never used milk, 3 were negroes. Our data are not sufficiently extensive to draw a careful comparison between the average dietary of whites and negroes at the present time. Further information on this subject will be sought, the coming season.

Vegetables. Fresh vegetables were used in season, to a very large extent, by all the groups. They were used either daily or habitually

by 99 per cent. of the rural cases, by 96 per cent. of the mill-village cases, and by 91 per cent. of the urban cases. Among the vegetables most commonly used may be mentioned cabbages, green corn, beans, potatoes (Irish and sweet), peas, tomatoes, and squash. During the winter months the available vegetables were confined largely to Irish potatoes, cabbage, peas, and beans. Canned vegetables were seldom used habitually. In 85 per cent. of the rural cases, 69 per cent. of the mill-village cases, and 59 per cent. of the urban cases they were either rarely or never used.

The lards used consisted of pure leaf lard, the compound lards, and pure vegetable (cotton-seed) lards. In 7 cases pure leaf (hog) lard was used exclusively. In many instances, particularly so in the rural cases, sufficient lard was rendered from the pork killed at home to supply all needs for from two to eight months of the year or longer. Others used compound or pure vegetable lards exclusively. Inquiry among 50 non-pellagrous families in one mill-village showed the use of compound lards to be quite as extensive as among pellagrins.

Some of the grocers catering to the well-to-do classes of the population in Spartanburg informed us that some customers preferred the pure leaf lard, while others preferred and used constantly the pure vegetable lards.

Wheat Flour. Bread made of wheat flour was used daily by 99 per cent. of the cases in each group, and was used habitually by the remaining 1 per cent.

Corn Products. Among the corn products used are included corn meal, hominy, grits, syrup, corn-starch, and whisky. Corn-meal is a staple article of diet in all classes of the population in the area studied. In this series, 84 per cent. of the rural cases, 75 per cent. of the urban cases, and 72 per cent. of the mill-village cases used corn-meal either daily or habitually. Two cases had not used corn-meal for a period of two years prior to the development of pellagra. These cases were two children whose mother had contracted pellagra in 1910, at which time she was advised by her physician to discontinue the use of corn products absolutely. She states that she had done so and that there had been no corn products in the house for the past two years. The children, aged six and thirteen years respectively, developed the disease in 1912.

The meal was obtained from different sources. Many of the families used no meal other than that grown locally and ground at a local mill; others used such meal the greater part of the time; others used, exclusively, meal shipped in from a near-by state; and still other used such meal the greater part of the time, but used more or less meal made from local corn, locally ground. The cases in which both local and shipped meal was used are included in both tables, which accounts for the apparent excess in numbers.

Some families raised sufficient corn to supply them with meal,

locally ground, for from six to eleven months of the year, the remainder being purchased from a grocer. The quality of the meal varied. When meal was made from the home-raised corn it was the usual custom to grind it up in small amounts at frequent intervals, and such meal was said to be fresh and sweet. The meal purchased from grocers was sometimes musty, but such meal usually was fed to the chickens. The use of hominy and grits was not so common in these groups as had been expected. Among the rural cases 64 per cent., the mill-village cases 56 per cent., and the urban cases 33 per cent. rarely or never used either.

Comparative dietary studies on the normal non-pellagrous population under like conditions are desirable in any attempt to determine the possible influence of the dietary on the development of pellagra. We have made some comparative studies with this object in view, but our data are not sufficiently complete at this time to warrant any definite conclusions.

The diet to which most of these cases were accustomed is of fairly good variety, but it is probable that in many instances the methods of preparation and cooking of the food are subject to criticism. This matter likewise is to be made a subject of further investigation. We are quite certain, from personal observation, that the average dietary of the poorer classes of the population in the county studied is much superior both in its variety and actual nutritive value to the dietary of the peasants in the North of Italy. Another striking difference may be mentioned, namely, that corn-meal in the form of polenta constitutes the chief bread component of the diet of the peasant of Northern Italy, whereas in Spartanburg County, among all classes of the population, wheat flour, in the form of bread or biscuit, is the principal bread-stuff, and corn-meal, while extensively used, is not nearly so staple an element of the dietary as wheat flour.

XVII. Synopsis. The epidemiological study of pellagra as it exists in Spartanburg County, South Carolina, is still in progress and will be continued during the spring and summer of 1913. The work done in 1912 constituted a more or less general preliminary survey of the field, and the results of that work as set forth in this report are tentative and will be further tested by continued observations and study.

The results of the work in 1912 tend to strengthen the belief that a satisfactory knowledge of the epidemiology of pellagra is best to be gained by intensive studies, of the behavior of the disease in selected communities, and of the prevailing conditions which influence its local prevalence and distribution. It is hoped that a study conducted with sufficient care and thoroughness along these lines will yield valuable evidence either for or against the possible infectious nature of the disease and its possible communicability.

The epidemiological data presented in the present report are summarized below:

PART I. 1. Pellagra shows a striking inequality of distribution in the ten townships within the county, the township rate of prevalence per 10,000 of population varying from 0 to 71. The city of Spartanburg, with a population of 17,517 gave a rate of 49 per 10,000 against 34 per 10,000 for the remainder of the county.

2. Density of population while showing a tendency to conform to the relative prevalence of the disease does not alone offer an explanation of the geographical inequalities of its distribution within the county.

3. The cotton-mill-village population gives a rate of prevalence of 104 per 10,000 against 19 per 10,000 for the remainder of the county, and against 16 per 10,000 for the rural sections alone.

4. The variations in the rates of prevalence in the ten townships are in a measure proportional to the presence or absence of a large mill-village population. Excluding the mill-village population, there is still a marked discrepancy between the townships in the rural population alone, ranging from 0 to 29 cases per 10,000 of population. The excessive prevalence among the farming classes is found in the townships which have a relatively large mill-village population.

5. The white population of the county gives a prevalence of 45 cases per 10,000; the negro population a prevalence of 9.5 per 10,000. Excluding the mill-village population which is practically all white, the remaining white population still gives a rate of prevalence (25.2 per 10,000) over two and one-half times that among the negroes.

6. The rate of prevalence per 10,000 for males in the county is 17; for females, 50.5. White males give a rate of 22.95 per 10,000; white females, 87.5 per 10,000, negro males, 3.9 per 10,000; negro females, 14.9 per 10,000.

7. The rate of prevalence among children under ten years of age and among adults aged forty-five years and older is practically equal in the two sexes.

8. The rate of prevalence drops among males between the ages of nineteen and forty-five years, whereas for females there is a remarkable excess of prevalence between these ages.

9. In both males and females there is a striking fall in prevalence between the ages of ten and twenty years.

10. The most significant fact with regard to occupation is the excessive prevalence of pellagra among women employed in housework.

11. The excessive prevalence of pellagra in the mill-village population is found largely among women and children at home during the day. Among actual mill-workers the rate of prevalence between the two sexes appears to be about equal.

12. One-half of the cases occurred singly in one family; about one-fourth occurred two in one family; the remaining fourth occurred in groups of three, four, or five in one family. The question of the possible relative importance of family relationship and household association is still under investigation.

13. Among cases occurring singly in families, the proportion of children of both sexes under ten years of age is low and that of adult females excessively high. Among cases occurring two or more in one family the proportion of young children is proportionately high, especially among males.

PART II. 14. While apparently authentic sporadic cases of pellagra within the county can be traced back to as early as 1894, the disease does not appear to have occurred in any great number of cases in any year until 1908. Since 1908 the incidence-rate appears to have rapidly increased each year to 1911. The number of new cases developing in 1911 appears to have been slightly greater than in 1912.

15. There was no evidence pointing to any spring and fall recrudescence of the disease in the population so frequently referred to in the literature of pellagra. There is no particularly marked tendency for the seasonal recurrence to appear in an individual during the same month, year after year.

16. *Influence of Climate.* Climatic conditions appear to influence the development of symptoms of the disease. If during the spring months precipitation is high, temperature low, and number of rainy days excessive, the appearance of acute symptoms, more particularly those involving the skin, is delayed.

17. *Symptomatology.* It would appear that three or four years ago a large proportion of the cases observed in the county presented intestinal and nervous symptoms of great severity. In 1912, in many instances, symptoms were quite mild, and sometimes were confined almost exclusively to the cutaneous system, the disease appearing to be of a less virulent type in 1912 than in previous years.

18. *Economic Status.* In the majortiy of cases (83 per cent.) economic conditions are poor and the disease is most prevalent among people of insufficient means.

19. *Predisposing Diseases.* General health conditions in childhood do not appear to warrant consideration as etiological factors when the disease develops in adult life. In a number of cases the development of pellagrous symptoms in children was preceded by one of the acute exanthematous diseases of childhood. About one-fourth of the cases gave a history of a preceding chronic disease in adult life. In more than one-half of the cases (62 per cent.) the history was that of good health. Among adult females, those most affected were married women (86 per cent.), and 86 per cent. of the married women had borne children.

A history of illness immediately preceding the development of pellagra was elicited in 59 per cent. of the cases.

20. *Hygiene and Sanitation of Houses and Premises.* The most unsanitary condition found in the county is the absence of properly constructed privies. Outside of a part of the city of Spartanburg which is supplied by a water-carriage sewage system, there is no effective provision in the county for the proper disposal of human excreta. A second striking unsanitary condition is the almost complete absence of effective screening of dwellings.

These two conditions present a situation highly favorable to the transmission of disease organisms eliminated in the excreta, both by direct contamination of food and person and by insects. This situation is naturally aggravated in the mill-villages and small towns by the greater congestion of houses. The absence of effective screening for dwellings gives rise to conditions conducive to the possible transfer of diseases transmitted by biting insects.

21. *Dietary.* Observations upon the habitual use of the more common foodstuffs failed to discover any points of difference between pellagrins and non-pellagrins in the county or any facts which would seem to explain the strikingly greater prevalence of pellagra among certain classes of the population.

The most striking defect in the general dietary of the working classes, appears to be the limited use of fresh meats, the animal proteid being supplied largely in the form of cured meats, of which salt pork (especially bacon) is the most important.

Unhygienic preparation of food appears to be a probable important factor in the general health of the population.

Investigation of the kind, quantity, and qualtiy of corn and corn products used in the county failed to bring to light any epidemiological evidence pointing to the agency of corn as an etiological factor in the disease. The presence of two cases in our series giving a definite history of no corn consumption within two years prior to the onset of symptoms, together with several other cases in which corn products were eaten, if at all, only in small quantity and at extremely rare intervals, would seem to argue strongly against any hypothesis that corn products alone are the causative agent of the disease.

III.

AN INTENSIVE STUDY OF INSECTS AS A POSSIBLE ETIOLOGIC FACTOR IN PELLAGRA.[1]

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In 1911, Dr. J. W. Babcock, Superintendent of the State Hospital for the Insane at Columbia, South Carolina, brought to the attention of the State authorities, the desirability of an investigation into the prevalence and etiology of pellagra.

Following this action, through the initiative of Dr. J. A. Hayne, Secretary of the State Board of Health and Representatives A. F. Lever and Joseph T. Johnson of South Carolina, the writers were, early in 1912, assigned by Dr. L. O. Howard, Chief of the Bureau of Entomology, United States Department of Agriculture, under the direction of Mr. W. D. Hunter, of the Bureau, to investigate the possible relation of insects to pellagra and to gather such data as might serve to indicate whether there was ground for the assumption that blood-sucking or other arthropods were involved in the transmission of pellagra in South Carolina.

After several months' work in various parts of the State, we were afforded opportunity to coöperate with the Thompson-McFadden Pellagra Commission of the Department of Tropical Medicine of the New York Post-Graduate School upon its arrival in Spartanburg County. From June 15 until the middle of October, our own studies were carried on in Spartanburg County in collaboration with this Commission, and it is with this portion of our field work that the present preliminary report has to deal.

These studies included the investigation of the premises of pellagrins and of the neighborhoods in which they resided, with special reference to the presence, distribution, and biologies of such insect groups and species as appeared worthy of consideration, after careful study of the conditions.

To this end, we visited the houses of as many as possible of the cases studied by the Commission, and made minute observations

[1] Reprinted from the American Journal of the Medical Sciences, September, 1913, No. 3, vol. cxlvi, p. 411.

of the insect fauna. The patients and their families were questioned in order to obtain such histories as they could give of the attacks or presence of insects and their general experience in regard to the pests with which they were familiar. In many instances the houses were visited more than once, and comparative observations were made under varying conditions. In some instances, the studies were extended to the homes of the non-pellagrous inhabitants of mill villages and elsewhere and the data thus gathered were used to confirm and extend the information obtained from the patients themselves. Sanitary and other conditions which might have a bearing upon the presence or abundance of insects were noted, and the more remote surroundings were inspected and studied in connection with such forms of insect life, occurring in such situations, as might influence the pellagra focus under investigation. When this focus was of considerable importance, with marked incidence of the disease, the neighborhood, as a whole, was investigated comprehensively and all possible facts bearing upon the situation were noted.

As a rule, the persons interviewed were ready to give such information as they possessed regarding the insect pests with which they came in contact. It was fully realized that popular observations of this nature are liable to be highly inaccurate. Great care was therefore exercised in making the inquiries and in sifting the information obtained. Only such reports were recorded as gave evidence of reliability and clearly referred to the insect which was the subject of the inquiry.

The breeding of certain insects was attempted, but owing to the character of the available facilities and the exactions of the active field work, but meagre results were obtained. This phase of the investigation was therefore unavoidably subordinated to that of the entomological side of the general epidemiological study.

Character and Economic Condition of Spartanburg County. The following description of Spartanburg County and its climate is quoted from the preliminary report of the Thompson-McFadden Pellagra Commission:[2]

"Spartanburg County is situated in the northern or Piedmont section of South Carolina. It is forty miles long in a north-south direction, thirty miles from east to west, and contains 762 square miles. Its surface is hilly and broken by a network of small streams and by four rivers which, with their tributaries, flow across the country in a southeasterly direction, one of these rivers forming the county line of the south. The elevation above sea level at Spartanburg, the county seat, is 875 feet. To the northwest, the slope is upward, the northwest corner of the county being situated at the foot of the Blue Mountain range, while to the south and east

[2] Epidemiological Studies, Part I., Amer. Jour. Med. Sci., July, 1913, pp 44–45.

the elevation becomes somewhat lower than at Spartanburg, but with no precipitate fall, the whole county thus resting upon a plateau over 700 feet above sea level."

There are no considerable swamps or marshes, and small areas of boggy ground in the neighborhood of streams, while not uncommon, were generally found to be negligible in connection with the breeding of insects of economic importance.

"The annual mean temperature, as recorded at Spartanburg, is 60° F. While the winters are mild, killing frosts are apt to occur from November to March inclusive, and the normal mean temperature for the months of December, January, and February is about 42° F.

"The total population of the county is 83,465. Spartanburg, with a population of 17,517, is the only city in the county, the remaining population (65,948) being distributed on farms, in cotton-mill villages, and among eleven small towns, only two of which have over 1000 inhabitants. The density of population, as a whole, is 109 per square mile; for the rural population (*i. e.*, outside of Spartanburg City), it is 86.5. While in South Carolina, as a whole, the negroes form 55 per cent. of the total population, in Spartanburg County the whites predominate numerically in the proportion of somewhat over two whites to one negro, there being a white population of 57,055, and 26,410 negroes, the percentage being 68.4 per cent. whites, and 31.6 per cent. negroes."

"The chief industry, and almost the only industry conducted upon a large scale, is that connected with the cotton mills. There are twenty-eight cotton mills in the county, each mill supporting its own village. These mills give employment to approximately 10,000 operatives, representing about 4000 families, and a total mill-village population of about 20,000."

Epidemiology. The epidemiology of pellagra in Spartanburg County presents certain features which have a distinct bearing upon the subject of insect transmission, and may be briefly summarized.

The cases considered in this report are distributed among the population as follows: Mill, 151 cases; rural, 77 cases; and urban, 51 cases.

Divided according to sex, there are: Male cases 71, or 25 per cent., female cases 211, or 75 per cent., or three females to one male.

These are distributed as follows: Mill cases, males, 38; females, 113. Rural, males, 19; females, 58. Urban, males, 11; females, 40.

The racial distribution shows 257 cases among the whites to 25 among the negroes, a ratio of 10 to 1.

The economic condition of the cases may be thus summarized: 85 per cent. were in poor circumstances; 15 per cent. were comfortable; and 2 per cent. were affluent.

The age of the males and females affected is shown as follows: Under five years, 21; five to nine years, 22; ten to nineteen years, 28; twenty to forty-four years, 158; and over forty-four years, 53.

By sex and age, cases appear as follows: Under five years, males, 10; females, 11. Five to nine years, males, 12; females, 12. Ten to nineteen years, males, 7; females, 16. Twenty to forty-four years, males, 16; females, 148. Over forty-four years, males, 25; females, 27.

Sex Incidence. The sex incidence presents striking features. As shown above, the proportion of female to male cases is 3 to 1; and statistics for the entire endemic area in the United States show that this is the approximate ratio throughout.[3] So pronounced an inequality must be based upon some fundamental difference either in environment or physiologic organization of the sexes. It is difficult to account for the inequality upon the ground of great female susceptibility, as such susceptibility is contrary to medical experience and to the well recognized natural law that the female in general is more resistant to adverse influences than the male. Cases of pellagra originating in institutions for the insane have also shown an approximately equal distribution among males and females.[4]

Beall[5] has sought to explain the inequality in sex incidence by associating the immediate cause of pellagra with the dwelling, calling attention to the high rate among females whose time is largely spent about the home, and to the fact that a large proportion of the male cases occurs during the ages when the association with the home is closest, that is, among children and the aged; men during their active years escaping to a great degree.

Of the 282 cases studied, 211, or 75 per cent. were females, of whom 173 were adults; and of these adults, 142, or 82 per cent. were engaged in housework most or all of the time. The adult female population of the mill villages, divided between mill operatives and those who devote themselves mainly or exclusively to household occupations, afforded an opportunity to compare two classes living under seemingly identical conditions with the exception of those of occupation. Of this class, there were 88 female cases, of whom 60 cases, or 68 per cent., gave all or most of their time to housework; the remaining 28 women, or 32 per cent., were engaged in mill work for a portion or all of their time. This disparity, marked as it is, becomes more striking when only those engaged exclusively in house or mill work are compared. Here we find but 12 cases among those who work in the mills, while 46 women, who were occupied exclusively with housework, were

[3] S. A. Roberts, Pellagra, St. Louis, 1912. K. H. Beall, Bull. Texas State Board Health, 1911, v, No. 9. Tennessee State Board Health, Report on 316 Cases of Pellagra, 1911. C. H. Lavinder, Reprint from P. H. Rep. 65, 1911. R. M. Grimm, P. H Rep., 1911, xxvi, No. 38.

[4] H. Douglas Singer, Report Pellagra Commission, State of Illinois, 1911.

[5] K. H. Beall, Loc. cit.

affected, the percentages of these groups being 13.6 and 52 respectively. Thus it is seen that a close correlation appears to exist between pellagrous incidence and the amount of time spent in or about the home, and that this holds, not only when the sexes are compared, but within the sexes, themselves.

A marked characteristic of pellagra in all countries is its rural nature. Although the disease sometimes appears to originate in cities of considerable size, an analysis of conditions in such cities will usually, if not always, show that in certain important aspects, the rural element governing the presence and abundance of insects is predominant.

Isolated sporadic cases of a disease are highly suggestive of an insect carrier, under certain circumstances, especially when exposure of the individual to infection by association with other cases may be excluded. The suggestiveness is strengthened, in the case of pellagra, by the existing evidence against direct contagion and also by the low degree of infectiousness which the disease appears to exhibit.

Another fact which may point to the agency of an insect in pellagra transmission, is the occurrence of several cases in a single family, and this frequently happens. It is obvious that the close association of persons constituting the household would increase the opportunity for transmission by predatory insects. This feature is emphasized by what appears to be a definite chronological connection between such cases.

At the same time, the large number of instances in which but a single member of a household is affected, does not preclude the same possibility. It is conceivable that by reason of habits or constitution, the unaffected members, might, for a time, altogether escape infection. Or, scarcity of the insect carriers, especially if conditions favor their free entrance into and departure from the house, may lessen the chances of transmission within the home.

Attention may be directed to some features of the epidemiology of pellagra which suggest a certain analogy to those of two other diseases, viz., malaria, an insect-borne protozoal disease often of chronic character; and acute anterior poliomyelitis, which, as apparently shown by certain recent experiments, may be transmitted by biting flies, thus strongly indicating at least one of the channels for the communication of that disease.

The seasonal recurrence of pellagra and its period of greatest development during the summer months, the period of greatest insect activity, finds an approximately similar condition in malaria and probably a greater similarity in the case of poliomyelitis. Both of these diseases are largely of rural origin, as is pellagra. Poliomyelitis, moreover, is marked by the occurrence of sporadic cases, not to be explained by contact infection and there is a lack of evidence of direct contagion, two facts which are true of pellagra.

THE INSECTS STUDIED. While the object of our investigation was the study of all insects which may have any part in the transmission of pellagra, it was realized that a careful consideration of conditions and of the insect fauna would inevitably narrow the field to a few genera and species. It became clear that efforts might safely be concentrated upon a few groups of insects, mostly of blood-sucking habits. Keeping in view the conditions which are imposed by the facts of disease transmission by insects, the following groups were given careful attention: Diptera, or two-winged flies; Hemiptera, including the lice and bed-bugs; Siphonaptera, or fleas, and Acarina, or ticks. Some attention was also paid to the roaches, Blattidæ.

ACARINA. The ticks of the family Ixodidæ must be mentioned, although their importance in this connection is negatived by their habits, life history and the infrequency with which the persons who suffer most from pellagra appear to come in contact with these arthropods in Spartanburg County.

It will be remembered that most ticks of the family Ixodidæ (no members of the family Argasidæ occur in Spartanburg County) require three hosts during their period of development, dropping to the ground on the completion of each stage and reattaching themselves to another host, sometimes of a totally different species, when they have advanced to the next stage of their existence. The chances of any tick of this group attaching to successive *human* hosts are remote. It is unusual for these parasites to remain undiscovered on man long enough to complete the stage during which attachment was effected. Almost certainly they are removed and killed and transmission of infection from the first host thereby prevented. The presence of animal reservoirs of infection would therefore seem to offer the only means by which this disease could be transmitted by the group of ticks mentioned and there is no indication that such reservoirs exist. Reports from pellagrins and non-pellagrins of attacks by ticks were rare and in the course of the work only two lots of ticks were collected, one lot from dog and one on the clothing of man. Many dogs and other animals were examined and the indication is that the tick infestation of the country is light. *Amblyomma americanum* and *Dermacentor variabilis* probably occur in the county. The usual hosts of these species are dogs but they are known to attach to man.

It is impossible to explain the sex incidence of pellagra by the incrimination of ticks, men being obviously more exposed to their attack than women. In view of this fact and the lack of evidence that animals are subject to and can serve as reservoirs of pellagrous infection, the almost certain death of all ixodid ticks which bite human beings, together with the equal certainty that not all pellagra sufferers in the region can have been exposed to the bites of ticks, these arthropods can safely be excluded from among the possible factors of pellagra transmission.

Pediculus Vestimenti and Capitis. Head lice (*Pediculus capitis*) were locally said to be far from rare among certain classes of the population, but this statement is not borne out by our observations or by reports received. Only one or two reports of previous experience with the parasite could be obtained, and the writers saw but one case of actual infestation. As reports regarding such insects as bed-bugs and fleas were usually frankly given, it seems hardly probable that reticence could account for the many negative reports in regard to *Pediculus*. We are forced to believe that whatever may be its prevalence, it is far from universal and entirely inadequate as a possible agent in the transmission of the disease. That a wingless insect with the habits and associations of the head louse can be the cause of infection in any but a very limited class of cases, is scarcely to be credited, and such an inference leaves the question of female preponderance and sporadic cases unsatisfactorily answered.

It is well known that head lice will, upon occasion, be transferred from infested to clean persons, but observations indicate that unless the infestation is gross or the association of persons is intimate such transfer of the parasite is not particularly common, and this is borne out by the experience of persons of ordinarily careful habits. We are unable to see that the head louse can be incriminated when we consider its rare occurrence upon persons of fastidious habits, who yet furnish an appreciable number of cases of pellagra.

No reports of *Pediculus vestimenti* were received and no observations of the species were made. The evident rarity of the species as well as its habits exclude it from consideration as definitely as the foregoing.

Cimex Lectularius. The bed-bug (*Cimex lectularius*) was found to be of practically universal occurrence in the houses of the largest class of pellagrins of the region. Of 256 reports received from pellagrins, the actual presence or recent attacks of bed-bugs were admitted in 241 instances. Only 15 persons denied that they had been exposed to this pest, and from their known prevalence in the mill villages and elsewhere some doubt may be entertained as to the accuracy of at least some of the negative reports.

Concerning the incrimination of *Cimex* in pellagra transmission, there is one fact which alone is sufficient to indicate its innocence. This is the sex incidence of the disease. It has never been shown that *Cimex* attacks females more frequently than males, certainly not in the proportion of 3 to 1, or if adults in the prime of life are considered, of 9 to 1. If this is not the case, the explanation of transmission by the insect is unsatisfactory. In the often crowded, badly infested, and none too cleanly homes of a considerable class of pellagra sufferers, indiscriminate attacks of the insect are greatly facilitated and must certainly be made upon the inmates without regard to age or sex.

It is well known that the bed-bug has the power to endure starvation for extended periods, and nothing is more difficult than eradiction of the pest when it has once taken possession of a building. If it were capable of conveying pellagrous infection, these qualities might account for what has been termed the "place infection" of pellagra. At this time, proof is lacking of such a source of infection, but should it be shown to exist, the facts of sex incidence just cited together with the occurrence of but one case in a family in many instances must stand opposed to incrimination of the insect.

While but 2 per cent. of the pellagra cases studied were in affluent circumstances, others of this class have come to our notice in other localities, and it may be asserted that such cases are by no means rare. It cannot be questioned that the habits of life and general associations of such persons greatly minimize the possibility of their infection having been brought about through the agency of the bed-bug.

Specimens of this species were collected in connection with some cases, but no special effort was made to do so in the majority of instances. No systematic search for a causative organism was being prosecuted nor transmission experiments carried on in the field. It was therefore considered that the value of actual collections of bed-bugs, systematically made, hardly justified the time required and the interruption caused to the routine pursued in securing case histories of pellagrins. In addition, the positive reports generally received, supported by occasional collections seemed amply sufficient to establish the almost universal presence of the pest.

BLATTIDÆ. Of roaches, only the common cockroach, *Periplaneta orientalis* and the smaller *Blattella germanica* were encountered. These disagreeable household pests were found to be abundant and generally distributed, but nothing remarkable was noted in their relations to the homes of pellagra cases or of the population in general.

Though armed with strong, biting jaws which enable the insects to commit serious injury to leather and other substances there are few accounts in the literature of attacks upon human beings, and these seem to be confined to nibbling of toenails, eyelashes, etc. Even such as they are, attacks upon man must be considered exceedingly rare, and they cannot be considered a factor in transmission.

The well known habit of roaches of frequenting kitchens and larders, their omnivorous habits, and the inefficient protection of food too frequently practised by the classes who suffer most from pellagra suggest the possibility of its transmission by food contamination. If such means is possible the part played by the insects must be far less important than that of house flies, for the exposure

of food to the latter is unquestionably greater and the carriage of fecal matter far more regular and constant than can be the case with roaches. Certain experiments conducted by one of us (A. H. J.) indicate that roaches will not readily feed upon such material and under normal conditions their opportunities for the contamination of foodstuffs with human excreta are far less than those afforded house flies.

Roaches can, therefore, not be considered an important element in pellagra causation and must be considered in the same category with, but far inferior to, the house fly.

TABANIDÆ. Flies of the family Tabanidæ, which includes the well-known horse-flies, were rare in Spartanburg County during the season of 1912. One or two specimens of *Tabanus atratus* (?) were seen flying about our automobile while in motion, but none were captured. Only two specimens of Tabanidæ were collected in Spartanburg County and these were unfortunately lost before exact determinations were made. The flies of this group are primarily a pest of the larger domestic and also of wild animals in localities where the latter are found, and their habits are such as to exclude them from the possibility of an active role in pellagra transmission. In localities where Tabanidæ are numerous the biting of human beings is by no means uncommon, yet even in such regions bites are scarcely received with the frequency and regularity which are essential to the transmission of human disease in the absence of an animal reservoir of infection.

The comparative scarcity of these flies in Spartanburg County where pellagra is prevalent is the reverse of the conditions of the country near the Atlantic coast where tabanids are exceedingly numerous and pellagra comparatively rare.

SIPHONAPTERA. In our studies, fleas were given particular attention on account of their known role as carriers of certain diseases and the fact that in certain localities they are very abundant and annoying pests.

It must be understood that, except where otherwise stated observations and conclusions regarding fleas refer strictly to conditions in Spartanburg County.

Somewhat to our surprise we found that, in the region studied, fleas, so far as attack on human beings is concerned, seemed to be almost of negligible importance. Reports were obtained from 154 pellagra patients or their families and of these but 10 gave positive accounts of attacks by these insects. Assuming that the reports were reliable, this may seem a remarkable condition, and allowing for a certain percentage of inaccuracy it is still practically certain that these insects are not a universal or constant pest of human beings in the locality.

While persistent attacks of fleas upon man are comparatively infrequent in Spartanburg County, they are much more common

in the low sandy country lying between the Piedmont region and the coast. In the latter section the prevalence of pellagra is slight when compared with the region of which Spartanburg County is a part.

The human flea, *Pulex irritans*, is uncommon even if it exists in Spartanburg County. We failed to find this species upon any of the numerous animals examined, nor did we succeed in collecting it from human beings.

Ctenocephalus canis and *Ctenocephalus felis* were taken on numerous dogs and cats. *Echidnophaga gallinacea*, the chicken flea, is a not uncommon pest of fowls, occurs with some frequency upon cats, dogs, and domestic rabbits, and in one instance, a report of its attack upon human beings was obtained.

In view of the fact that cats and dogs are very commonly kept, and that these animals were found to be practically always heavily infested with their respective fleas, it might be assumed that attacks upon human beings would be of common occurrence. Several reasons for doubting this assumption may be advanced. While the cat and dog fleas are less fastidious in their choice of host and more tolerant of abnormal host species than many other fleas, it is nevertheless quite certain that these species are less frequently a human pest than is usually supposed. Attacks by them upon man are not uncommon, but under ordinary conditions, even in the presence of infested animals, it by no means follows that persons associating with the animals will be infested.

It has been personally noted by one of us, in another locality, that in a house in which cats heavily infested by *Ctenocephalus felis* were kept, the fleas which were a frequent source of annoyance to the human inhabitants were all found to be *Pulex irritans*. Eggs from the flea-infested, long-haired cats must have been freely dropped about the floors, which offered excellent conditions for the development of the insects. It is equally certain that adult fleas were lost from their feline hosts, yet during a period of more than a year, every flea which annoyed the members of the household was carefully sought for and collected. They were all *Pulex irritans* and it is noteworthy that their attacks were usually made at night.

This extreme instance is cited to indicate that except at times of unusual abundance the fleas of domestic animals are not likely to attack human beings freely. It is true that individual fleas of cats and dogs ordinarily remain on human hosts but a short time, frequently leave him without biting and are probably but rarely transferred directly from man to man, factors which would tend to lessen the probability of their acting as carriers of a purely human disease.

The number of domestic animals kept by pellagrins or their families is of interest in this connection. Of 227 instances in which

notes were made regarding the keeping of the smaller flea-bearing domestic animals, cats or dogs were kept in 120 cases, or 53 per cent., while none were kept in 107, or 47 per cent., of cases. This is significant in connection with the host habits of fleas which have just been discussed. If human beings in Spartanburg County are freely and regularly attacked by fleas derived from cats or dogs, which are usually heavily infested, it seems remarkable that in so few instances were the keepers of these animals able to report their noticeable presence.

Of the 10 cases reporting attacks of fleas, dogs or cats were kept in 9 instances and none were kept by but one family. This is too small a number upon which to base conclusions. There were 149 cases in which data were secured on both the keeping of cats or dogs and the attacks of fleas. Animals were present in the houses of 78 of these cases and absent in 71. Of the former, 9 reported attacks of fleas, while, of those who kept no animals, but 1 gave such a history. The ratio of the number of reported attacks, by families in which cats or dogs were kept, to those by families with none of these animals is therefore 9 to 1 and seems to indicate that when fleas are troublesome, domestic animals are the usual source. In connection with the figures relative to the number of animals kept, it is also indicated that these animals by no means always cause the infestation of their human associates.

Sixty families who kept domestic animals and 70 who kept none, reported no attacks of fleas.

The presence of rats was reported in 38 cases, and of mice in 124. In spite of efforts to secure specimens of rat fleas, it was possible to do so in only one instance so that the degree of infestation of the rats of the region and the species occurring upon them could not be learned. The single rat secured has been determined as a cross between *Mus rattus* and *Mus alexandrinus*. The fleas with which this rat was infested proved to be *Xenopsylla cheopis*, the Indian rat flea. The occurrence of this flea at a point so far inland is interesting as is the species of its host, an animal with which it is intimately associated in the East and in many parts of its littoral range.

The facts opposed to the incrimination of fleas in pellagra transmission are: those of the sex incidence of the disease, its association with the home, the host habits of fleas, the comparative infrequency of their attacks upon human beings in the districts suffering most heavily from the disease and the inverse ratio of their abundance to the occurrence of pellagra.

In consideration of these facts it is impossible to base any satisfactory theory of transmission upon the agency of these insects.

Culicidæ. The abundance of mosquitoes, both of species and individuals, their agency in the transmission of important human diseases, their persistence in seeking blood and, in certain instances,

their close association with man cause these troublesome pests to assume a position of the highest economic importance.

Although present to a greater or less degree in most parts of Spartanburg County, they are few in number in comparison with those present in many less favored localities. The topographical features of the district have much to do with this condition, and owing to the conformation of the land and the character of its drainage, extensive breeding areas do not exist.

When this group is considered in connection with the possibility of pellagra transmission, certain salient facts are to be noted.

The longevity with which some mosquitoes are known to be endowed, their great abundance and the predilection displayed by certain species for man's vicintiy, appear to fully qualify these insects for the role of transmitters of human disease. This is amply shown to be true by the number of diseases which are transmitted by them.

Furthermore, mosquitoes are readily transported in various ways other than by their own flight to places far distant from their original habitat, with the attendent possibility of spreading infection.

Their power of flight renders the carriage of infection from house to house an easy matter, although the distance travelled is probably not great in the case of house mosquitoes and ordinarily the radius of infection conveyed by them would be correspondingly short.

It is unquestionably an argument, though not necessarily a conclusive one, against the incrimination of mosquitoes in pellagra transmission that no one species, occurring in endemic regions, has a range as wide as the geographical distribution of the disease and different species would necessarily (if the group be incriminated) assume the role of transmitters in different parts of the endemic area.

It is possible, were pellagra transmissible by mosquitoes, that several species might have the power to transmit the disease, yet there is often a high degree of specialization in insect vectors. In view of the nice physiologic adjustment between the insect host and its parasite, which is evidently necessary to the function of transmission, the foregoing assumption is not necessarily valid.

The most important fact which is opposed to the agency of these insects is the preponderance of cases among females and especially among home-keeping females. If, as indicated, the disparity is due to the greater exposure of women to infection, a cause must be sought which affects this class only and excludes those classes which show a low pellagrous incidence. In other words, the cause must be active in the day time when housewives, children, and old men are largely at home and which does not operate at night when all ages and sexes of the household are within the home influence. It is illogical to seek the cause in an insect whose activities are confined to the night hours, however well it may otherwise conform to the epidemiological and other facts of the disease.

It is to be noted, as we have said, that while mosquitoes are, comparatively speaking, not abundant in the Piedmont region where pellagra abounds, they are a more serious pest and infinitely more numerous in the low-lying country near the coast where pellagra, though not absent, is by no means abundant.

While a very considerable number of our cases reported attacks of mosquitoes, more than an appreciable percentage of these referred to localities beyond the bounds of our terrritoy, largely to places in the low country below the Piedmont.

The scarcity of mosquitoes was noted by all members of the party and it is highly probable that their number falls short of that required for effective disease transmission. It is admitted that diseases fail of transmission and cease to exist even in the presence of their known carriers when the number of the carriers falls below a definite point.

Certainly, it will hardly be asserted that a group of insects, represented so sparingly as are mosquitoes in this locality, can be the agent of causation of a disease having the activity displayed by pellagra in this region at the present time.

Culex quinquefasciatus and *Culex restuans* are the principal species recorded by us. *C. quinquefasciatus* was taken at a number of points and is, as might be expected, widely distributed in the county. Some water barrels were heavily infested and were producing enough mosquitoes to infest the entire immediate neighborhood. *C. restuans* is rather widely distributed and probably ranks with *C. quinquefasciatus*, as a general nuisance. *Aedes calopus*, the yellow fever mosquito was not taken within the county although quite ample facilities for its propagation exist. It is undoubtedly introduced, probably every year, but appears not to be a constant resident, the winters being usually too severe to admit of its survival. It can have no importance in the present connection in spite of its day biting proclivities and house haunting habits. Its geographical range is not as wide as the distribution of pellagra and it thrives as well in large cities as in small.

Spartanburg County bears the reputation of being almost entirely free from malaria, a reputation sustained by the small number and especially the character of the anopheline mosquitoes recorded by us. *Anopheles crucians*, a host of the estivo-autumnal parasite was encountered but once. The only other species observed was *Anopheles punctipennis* whose incrimination in malaria transmission remains somewhat doubtful. This species was met with chiefly in the vicinity of Spartanburg, a place whose physicians unanimously declare to be free from endemic malaria. Of 240 pellagra patients questioned as to the biting of mosquitoes, 160 gave positive reports while 40 only were negative.

Simuliidæ. Although but recently incriminated in disease transmission, the flies of the genus *Simulium* have long been known in

both Europe and America as a serious pest of man and animals, their visitations assuming in certain regions the proportions of a scourge. Much has been written regarding their blood-thirstiness and the intolerable nature of their onslaughts, the heavy loss occasioned among all kinds of domestic animals and even the death of human beings. Some of the accounts of their depredations seem to bear the stamp of a vivid imagination, but the more conservative and scientific statements, especially those of later years, are sufficient warrant for classing them among the more important and blood-thirsty of predaceous insects.

The attractive theory propounded and defended by Sambon, that these gnats are the active agents in the causation of pellagra has brought them into prominence from a new point of view.

He bases his belief in the agency of the Simuliidæ upon the following: *Simulium* affects the same topographical conditions as pellagra; in its adult state, it seems to present the same seasonal incidence; it is found only in rural districts and, as a rule, does not enter towns, villages, and houses; these flies cause severe epizoötics in Europe and America. The disease, he finds, is limited to agricultural laborers (to be explained satisfactorily only by the incrimination of the gnats); the range of the group seems to cover that of pellagra, although indeed it exceeds it.[6]

Knab has pointed out that close association with man is one of the essential factors in disease transmission by insects, when, as premised by Sambon in the case of pellagra, the disease is of parasitic origin and the organism is present in the blood stream.

Simulium inhabits regions in which pellagra is endemic and in many well-watered localities presents a picture of distribution which completely covers every part of large areas. Its numbers are often great enough to cause annoyance and even injury to all warm-blooded inhabitants, yet in spite of these phenomena it can not be said to show the association with man to which we have referred. The species of *Simulium* are essentially "wild" and there is no evidence, in what is known of their life history and habits, that repeated attacks on human beings with intervening periods of, at least, several days can take place with sufficient frequency to confer upon the insect the character of an effective disease tranmitter. As Knab cogently insists: "It is not sufficient that occasional specimens bite man, as for example, is the case with forest mosquitoes. Although a person may be bitten by a large number of such mosquitoes, the chances that any of these mosquitoes will survive to develop the parasites in question (assuming such development to be possible) and then find opportunity to bite and infect another person are altogether too remote."[7]

[6] L. W. Sambon, Progress Report Investigation Pellagra, Jour. Trop. Med. and Hyg., October 1, 1910, xiii, No. 19.

[7] Frederick Knab, Unconsidered Factors in Disease Transmission by Blood-Sucking Insects, Jour. Econ. Ent., 1912, v, No. 2.

Although Knab cites, as an example, the forest mosquitoes, the principle is of wide application and includes within its scope the species of *Simulium*, which, indeed, he excludes upon this very ground, from consideration as potential transmitters of disease.

It must be borne in mind that the essential factor here, is not the possibility that an occasional individual might sometimes be able to fulfil these conditions, but rather that the group lacks the habits (of close association with man) necessary to the establishment of the biologic relations between the vertebrate host, the invertebrate host, and the parasite of the disease.

Our observations of the group in Spartanburg County are strongly corroborative of the foregoing. We found *Simulium* breeding near or even within the limits of mill villages as well as of towns, but we failed to detect the slightest disposition on their part to seek out and attack man, to come about his dwellings, or to come in contact with him in any but the most casual and incidental manner.

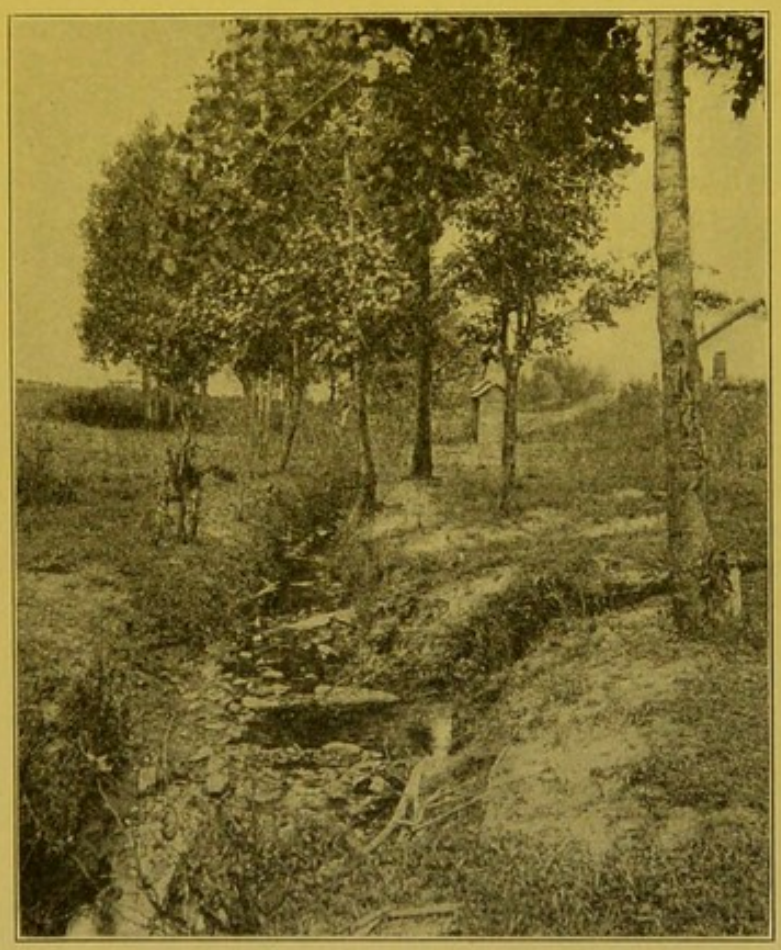

FIG. 1.—Stream at edge of mill village. A breeding place of *Simulium venustum*.

The assertion that these flies cause severe epizoötics is certainly not supported as regards America, at least. The heavy loss of domestic animals which occurs during severe visitations of the gnats can not be attributed to any specific disease which is com-

municated by them. All the evidence indicates that death is caused by the venom injected and by the worry and irritation occasioned by the myriad bites.[8]

Individuals are carried to or through mill villages as well as other communities, upon animals (in the ears of horses and to a less extent on cattle). This might be a limited source of supply for localities removed from the vicinity of the breeding grounds of the fly. However, it is not even known that, after a full engorgement, the female will seek a second blood meal. The extreme degree with which the flies distend themselves with blood, when undisturbed during biting, coupled with the probably short life of the adult insect, suggest that they do not ordinarily bite again.[9]

Species of *Simulium* are unquestionably found in numbers in large areas of country in which pellagra is rampant, but there is evidence to show that, contrary to Sambon's assumption, the disease is found where *Simulium* is not. We have information that pellagra occurs endemically in Barbados and as yet not only has no species of *Simulium* been found in the island, but its physical characteristics entirely preclude the existence there of the fly.[10] There are arid regions in the United States in which the same situation exists but under different conditions and there are still other localities where these gnats are far too rare to satisfactorily account for the cases of pellagra originating in them.

That the extension of the range of *Simulium* beyond the limits of pellagrous endemicity is certainly, as Sambon says, no argument against its incrimination for there are many localities inhabited by insects with known powers of disease transmission, yet which are entirely free from the diseases which these insects may confer. In the absence of the human carrier of infection and the proper conditions, the insect vectors are innocuous.

The seasonal appearance of *Simulium*, which is supposed to correspond with that of pellagra, is probably of less significance than has been assumed. The studies of the Commission have shown that the spring-fall recrudescences of the disease do not occur, with the intensity ascribed, at least in the area under consideration,[11] although the period of greatest abundance and activity of *Simulium* appears to be here, as in Italy, the early spring. Until more light is thrown upon the length of the incubation period of the disease, which seems to be variable, assumptions as to the exact time at which infection is incurred, must be received with reserve.

The disease is of essentially rural distribution but in South Carolina, it occurs in towns of considerable size. As has been

[8] C. V. Riley, The Southern Buffalo Gnat, Report of Comm. Agric., United States Dept. Agric., 1886.

[9] C. V. Riley ibid.

[10] Personal letter from Dr. H. A. Ballou, Imperial Entomologist, Barbados.

[11] J. F. Siler and P. E. Garrison, An Intensive Study of the Epidemiology of Pellagra, loc. cit.

pointed out, in these places the rural element, as regards insect life, is predominant and the conditions do not necessarily preclude the occurrence of rural diseases.

In the classes of the population affected by pellagra, a very marked contrast appears to exist between European and American conditions, if European reports are accurate. The practical confinement of the disease in Italy to agricultural laborers, a class living under conditions of abject poverty, finds no economic or occupational parallel in America. Although, in Spartanburg County, the farming class furnishes a considerable percentage of all cases, the highest incidence of the disease is found among inhabitants of mill villages, whose conditions and habits of life are radically different in most essential features from those of the Italian peasant.

The fact that more than one species of *Simulium* would have to be involved to cover the entire range of pellagra is not a convincing argument against incrimination of the group but it lessens, to a certain degree, the probability of their agency. (See page 92 on mosquitoes.)

It seems to have been assumed that because the many streams of a well-watered country are infested with the larvæ of *Simulium*, the inhabitants of that country, especially those living in close proximity to streams, must be exposed to and incur the bites of the gnats.

Knowledge of the biting habits of the American species is incomplete, but it is clear that some of these species show great irregularity in their practice of seeking blood. The variation in the exercise of this habit seems to have in it a large geographic, or possibly, topographic element, for a species may be a serious pest of man in one part of its range, yet seem to ignore him entirely in another. Thus, *Simulium venustum*, one of the so-called "black flies" while proverbial for its onslaughts in the Maine woods, is only moderately troublesome in the Adirondack Mountains. In the mountains of Henderson County, North Carolina, these flies were found by one of us to be exceedingly abundant but offering no attack to man though this was courted. Sitting or standing quietly with small swarms of the flies "dancing" about the head, no attempt was made to bite. This occurred both in the presence and absence of animals which in the former case were being actively attacked. Persons of intelligence who were questioned, denied that the flies bite people and in only one instance was such a report elicited. In this case the identity of the fly was open to question, although probably a *Simulium*.

Similarly, *Simulium vittatum* is known to bite man in some parts of its habitat, but on excellent authority it is stated that in Idaho it "does not bite people."[12]

[12] Personal Letter from Prof. J. M. Aldrich.

Such variation in biting habits is not without parallel among blood-sucking flies, as *Glossina palpalis* is reported by Steudel to bite man on Victoria Lake but not on Lake Tanganyika.[13]

This variability is of special significance, for it points to the fallibility of deductions based upon the mere presence of *Simulium* larvæ in a given locality without regard to the species represented and the *local* biting habits of that species.

Simulium pictipes, a widely distributed and often abundant species, does not bite man at all.

So numerous are the streams in the county that the homes of 275 pellagrins stood within an average distance of 210 yards from running water, and 215 of these streams were found to be infested with *Simulium*.

FIG. 2.—A typical breeding place of *Simulium pictipes*.

In spite of this fact, but 16 cases reported attacks of flies, the description of which could with any probability of truth, be interpreted as referring to *Simulium*. Great patience was exercised in eliciting these reports and they were carefully weighed before recording.

[13] Steudel, Deutch. Kolonialblatt, 1912, 15 Mai, xxiii, No. 10, and Beihefte zum Archiv f. Schiffs und Tropenhygiene, 1912, Mai, Beiheft 4.

The distance of *Simulium*-infested streams from the homes of 11 cases reporting bites of the fly averaged 236 yards, no data as to infestation of streams being available in 5 cases reporting bites.

The distance of *Simulium*-infested streams from the homes of 125 cases reporting *no* bites of the fly averaged 221 yards.

This difference in average distance is not actually great but it is interesting nevertheless. It is a striking fact that so large a number of persons living a shorter average distance, many within a few yards, from infested streams should not have been bitten and points forcibly, not only to the uncertain biting habits of *Simulium*, but to the lack of significance in the proximity of streams, even when *Simulium*-infested.

We may add that adult *Simulium* were collected in the immediate neighborhood of 46 cases who reported no bites.

The tenor of these reports is amply corroborated by those of many persons, including a considerable number who were especially well qualified through intelligence and experience with the flies in other localities or who had observed their attacks upon animals in this.

It cannot be questioned that as a pest of man in Spartanburg County, the species of *Simulium* are of small importance and that at most their attacks are delivered locally and are few in number. When comparison is made between this condition and that existing in places (including Spartanburg County) infested by stable flies, sand flies, mosquitoes, etc., the contrast is striking. These insects are always well known, even when not abundant, as we have shown in regard to mosquitoes in this locality. It is practically impossible that *Simulium* could be present and bite man in sufficient numbers and with enough persistence to satisfactorily explain the occurrence and spread of pellagra without being a well recognized and familiar pest.

Three species of the genus were encountered by us within the limits of our territory, namely: *Simulium venustum*, *S. vittatum*, and *S. pictipes*.

The former is by far the most numerous and generally distributed of the three. It was taken in its four stages, adults being collected about twelve times, either in the act of attacking animals or of ovipositing.

Simulium vittatum was taken in the larval, pupal, and adult stages, and also probably in the egg. Adults were twice collected while attacking horses or mules.

Simulium pictipes occurs quite locally in large colonies where suitable conditions exist. These consist of a rapid flow of clear water over boulders and sheets of rock in the larger streams. Such conditions are not very frequently met with in this vicinity owing to the turbidity of most of the creeks and rivers of the locality.

There are no records of this species attacking man and it need not be considered in the present connection.

The facts as set forth above do not support the incrimination of *Simulium* in the transmission of pellagra.

House and Blow Flies. So abundant is the current literature regarding the nature, habits, and pernicious activity of the house fly, that a general discussion of this well known and troublesome species seems superfluous. Its familiar role as an active mechanical carrier of bacterial disease, however, renders it of the highest economic importance and necessitates its consideration in the present study. The possibility of the transmission of pellagra by house flies through the contamination of food to which they have access, or by direct mechanical transmission of the virus (if it exists) from man to man, is evident.

Musca domestica was present everywhere and was usually extremely numerous. Sanitary conditions were only too frequently such as to attract, if not actually to breed, the filth-loving species of flies, but in the more or less congested village and town communities there was no strict correlation between the sanitary condition of the individual premises and the number of flies present. Even well-kept homes offered sufficient attraction to insure their infestation by the flies which in every neighborhood were present in large numbers.

In mill villages the principal source of house flies appeared to be the accumulations of manure of horses and cattle at the stables and sheds in which the draught animals of the mill companies and the cows of the operatives were sheltered. In those villages in which milch cows are allowed to be pastured and stabled indiscriminately through the village, breeding occurred almost everywhere in the haunts of the animals.

The type and condition of privies in mill villages are conducive to the presence and breeding of this species as well as to the carrion flies, *Calliphora*, *Lucilia*, and the *Sarcophagidæ*. Upon otherwise cleanly premises, the privy was often a source from which flies emanated and was a standing menace of infection.

Musca domestica was found in and about the homes of practically all of the cases studied as well as those of non-pellagrins. In a very few instances case histories make no mention of the species, but this is unquestionably due to inadvertence.

Until the transmissibility of pellagra is disproved or the nature of its virus and the manner of its communication are known, the house fly must be regarded with suspicion.

Stomoxys Calcitrans Linn. The biting stable fly is an insect of cosmopolitan distribution and great economic importance. In most localities within its habitat it is very abundant, and though it feeds by preference upon domestic animals, man is very frequently attacked. Attacks upon human beings are more common when the

animals upon which it normally feeds are not available and its onslaughts are often severe and persistent.

The injury inflicted upon live stock is often very serious and many deaths are caused during the occasional outbreaks of this fly, which sometimes occur under unusual conditions favoring its inordinate propagation. At all times it is a serious pest of animals and has been incriminated in the transmission of trypanosomal diseases of animals, anthrax in animals and man, and of anterior poliomyelitis in man.

While *Stomoxys* is, as a rule, more abundant in country districts, owing to the greater facilities for propagation which it finds in the rural environment, it is usually common in towns and cities of even the largest size. In the very heart of the great cities and in such neighborhoods as practically preclude the possibility of its breeding, it may be seen in considerable numbers along the main thoroughfares. The vicinity of markets and wharves is especially likely to be heavily infested and this is the case even when scrupulous scavenger work renders its propagation at the spot impossible. The source of supply under such circumstances may be far removed and the fly population maintained by the constant arrival of individuals which accompany animals on their journeyings or which are guided by their sense of smell in independent flights from more or less distant localities.

The stable fly will breed in unmixed manure of horses and cattle, in such materials mingled with particles of straw and in rotting straw alone. While we have repeatedly bred the stable fly in large numbers from naturally infested, unmixed dung of horses and even a few individuals from that of cattle, the observations of Bishopp during a recent severe outbreak of the fly in north Texas, indicate that decaying straw is the material most favorable to its propagation. His careful work shows conclusively that in the order of preference, the substances in which *Stomoxys* will breed are oat, rice, barley, and wheat straw, horse manure, lot manure, and cow manure; that pure horse and cow manure are less attractive to the fly than when mixed with a considerable quantity of straw and that under a combination of conditions of plentiful moisture and abundance of rotting straw, breeding will occur at its maximum intensity.[14]

Similar observations have been made by Lucien Iches in Argentina.[15]

There is a direct relation between the presence and numbers of domestic animals and the abundance and distribution of this fly, which wanders far from its breeding places in search of food and will follow animals for long distances. This, however, is not its

[14] F. C. Bishopp, The Stable-Fly (*Stomoxys calcitrans L.*). Jour. Econ. Ent., 1913, vi, No. 1.

[15] Lucien Iches, *Stomoxys calcitrans L.* et le betail Argentin., Bull. Soc. nation Acclimat., France Ann., 1909.

only means of dispersion, as steamships, passenger trains, and those carrying live stock upon railroads are a common aid to its migration. We have encountered the species under all these conditions and have seen it carried for hours on the under side of an automobile top, in spite of wind and jolting over rough roads. In the latter case, the fly appeared to be full fed and, resting in this way after engorgement, it would be more likely to remain in such a situation and to be carried to a new locality. This is of special significance in connection with disease transmission. It is evident that flies carried in the ways mentioned, if infected or acquiring infection en route would have the power to carry the disease to a new locality remote from endemic foci. Particularly would this be the case if opportunity for feeding during the journey was lacking, as the hungry fly would upon arrival immediately seek a meal of blood, human or animal, and thus transmit the infection. An instance of the persistence of *Stomoxys calcitrans* in seeking blood was observed by us on the coast of South Carolina. The six occupants of a fishing boat were attacked, more than a mile from land, by numerous flies which suddenly appeared and which had evidently not been carried in the boat. It must be borne in mind that the stable fly is not attracted to offensive substances, and the odors from the fish-scented boat can hardly have played a part in drawing the flies so far from land. All the persons in the boat were bitten one or more times and the bare-legged boatmen greatly annoyed. They stated that such an occurrence was very common and that they were frequently attacked when at sea. *Stomoxys calcitrans* is very abundant along this line of seacoast and in the adjacent country. The day was clear and hot with a gentle off-shore breeze.

Although primarily a pest of live-stock, infesting and breeding in situations frequented by domestic animals, this fly often invades dwellings. While indoors it attacks the human inhabitants and we have even seen it more numerous in living rooms of mill dwellings than the ever-present house fly. It must be understood that in such cases the latter species was somewhat less numerous than usual.

Stomoxys has the habit of utilizing several hosts in order to secure a single meal, either from choice or because when dislodged by one host it flies to another.[16] This habit is important in connection with disease transmission. Especially is this the case in the interior of dwellings where all the members of the household would be exposed to the infection, if transmissible, which might be carried by one of its members.

It is, moreover, within the possibilities that a puncture of the

[16] C. T. Brues and P. A. E. Sheppard, The Possible Etiological Relation of Certain Biting Insects to the Spread of Infantile Paralysis, Jour. Econ. Ent., 1912, v, No. 4; Herbert Osborn. Insects Affecting Domestic Animals, Bull. 5, N. S. Bu. Ent. United States Dept. Agric., 1896; H. Maxwell-Lefroy, Biting Flies of India, 1907

skin by an infected fly's proboscis might introduce the infection although no blood is drawn. This has been shown to be experimentally possible in the non-mechanical transmission of trypanosomiasis by *Glossina palpalis*.[17]

As has been pointed out, the members of the household who suffer most from pellagra are those who pass the most time in the home or its vicinity in the day time and it is these members, the females, who are most exposed during daylight hours to the attacks of *Stomoxys*.

As we have stated, *Stomoxys calcitrans* is not attracted by the odors of putrefaction. Hog-pens and privies are not inviting to it, nor is it apparently drawn to the nasal secretions of animals nor presumably to those of man as is the house fly, this discrimination being of importance in connection with the carriage of certain diseases.

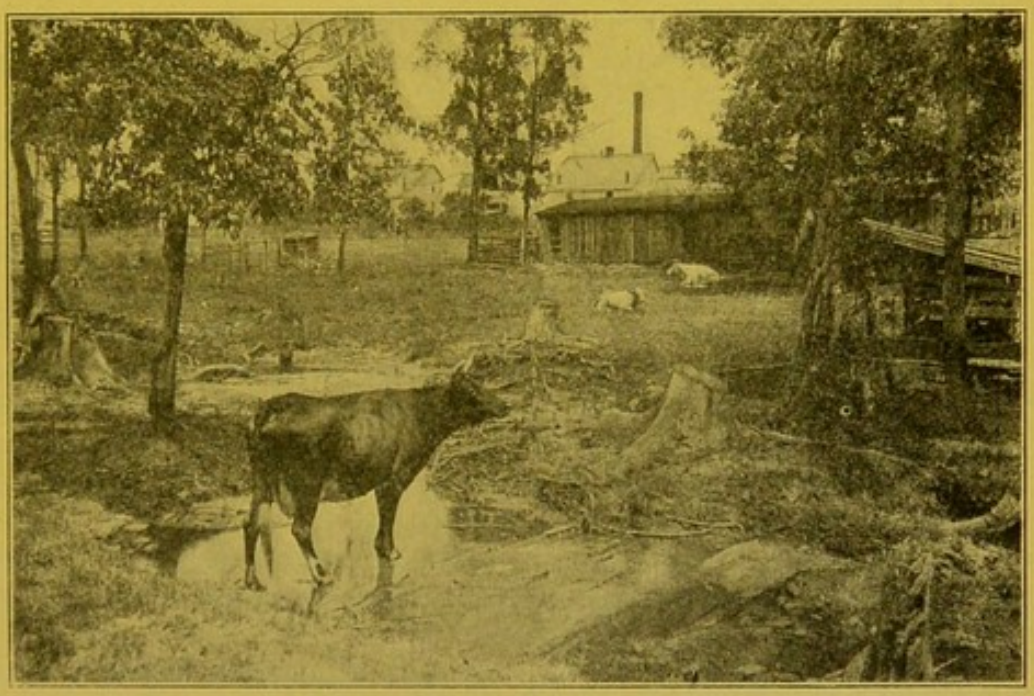

FIG. 3.—A pasture provided by mill authorities for cows, etc. of operatives. Note cow-sheds, hog-pens, and proximity of dwellings. The stream in foreground breeds *Simulium*.

The stable fly is exceedingly abundant and generally distributed in Spartanburg County. In most of its geographical range the species is of importance in its relation to live stock and, our studies indicate, that it is also a pest of man with which it is necessary to reckon. No part of the region is free from this fly and it may be seen in numbers upon the streets of towns and villages, about barnyards, modest dwellings, and pretentious residences. Every

[17] A. D. Fraser and H. L. Duke, Proc. Roy. Soc., August 24, 1912, Ser. B, lxxxv, No. B, 581 Abs. Sleep. Sick. Bull, 1912, 4, No. 40

team upon the roads is followed, and every cow in pasture or barnyard is constantly exposed to its attack during the daylight hours

As a part of the study devoted to this species, statements regarding its biting were obtained from as many persons as it was possible to interview, the questions being put to pellagrins and their families as well as to non-pellagrins. In obtaining reports on the biting habits of the fly, great care was exercised not only to be sure of the identity of the fly of which the individual was speaking, but to suggest nothing which might influence the tenor of the report. All reports were rejected which after careful consideration seemed doubtful, either as to the identity of the insect or the details of the statement.

Reports relative to the biting of *Stomoxys* were obtained from 227 pellagra patients and of these 115, or 50.7 per cent., gave positive histories of attacks and to these should be added 10 from members of families of pellagrins who could not themselves recall having been bitten. In 112 cases, or 49.3 per cent., the patient could remember no bites or was positive that none had been inflicted.

In addition to the above reports, many persons not included among our pellagra sufferers recounted experiences with the persistence of attack and voracity of the fly.

Close attention was given to the presence of the fly in such situations as would facilitate its attack upon the inmates of dwellings of all descriptions, that is, its presence or absence about the yards and premises, especially upon the outside of houses near open, unscreened windows, upon porches, and the interiors of dwellings. The distribution of the fly in the latter situation has some significance, and observations were made to determine its preference for different kinds of rooms.

Stomoxys was present about premises, yards, sides of house, or porch of the homes of 136 pellagrins, being abundant in 94 instances.

An illustration of the universal distribution of the fly was seen in a mill village which was studied with special care. This village contained 113 inhabitated buildings, including the company's store and office. Stable flies were found about 103 of these buildings and inside of several of them. It was found that the distribution varied somewhat, houses seemingly free from the flies at the time of our first visit would be infested at a later time, the reverse also being true. Nevertheless, there were few dwellings about which individuals could not be found at any time and it is to be assumed that they were present at all buildings more or less frequently.

For various reasons, it was quite often impossible to make a careful search of the interiors of pellagrous dwellings and conditions of weather, light, etc., were sometimes unfavorable to the presence of the flies at the time of inspection and made their discovery

difficult. Enough observations of its presence were made to show that invasion of human habitations is of common if not regular occurrence.

Its presence was noted in more than 30 dwellings of pellagrins, in fully half of which it was abundant, and in one instance a partial count showed 30 individuals.

The character of the rooms frequented by the fly has a bearing, not only upon the opportunity for attack, but upon its general habits. Strong preference was shown for the living rooms and in more than half of the houses studied these were the only rooms infested. In about one-fourth, flies were found in both living rooms and kitchen, while in only one instance was the kitchen alone infested and then by only one or two flies. In the houses of mill workers the living room is usually also a bed room. It will be seen that in case of illness or during moments of relaxation, the occupant of a bed in a *Stomoxys*-infested room invites the attack of the fly. It was evident that in addition to the odors of putrefaction, those of cooking are not attractive to this species, which is in strong contrast to habits of the house fly. The difference in domestic habitat of the two species is very striking, kitchens frequently swarming with house flies where living rooms were only moderately infested, the same houses showing infestation of *Stomoxys* in living rooms only.

Management of Live-Stock in Mill Villages, Etc. The relation of domestic animals, especially horses and cattle to the presence and abundance of *Stomoxys* is so important, that a knowledge of the number and management of these animals is essential to a study of the bionomics and distribution of house and stable flies.

Cattle, horses, mules, and hogs are very commonly kept in Spartanburg County especially upon farms, while in the cities, towns, and hamlets, many of the non-farming residents maintain milch cows and driving or draft animals. The inhabitants of the mill villages also keep many cows, one cow to about three families being a fair average.

Upon farms, the stables and sheds in which animals are housed are usually placed about the barnyard at no great distance from the dwelling. Manure is often allowed to accumulate, and the floors of the outbuildings are frequently covered by a deep layer of droppings, the fresher portions heavily infested with fly larvæ. These conditions are by no means invariable and in many instances manure is not allowed to accumulate about the stable or barnyard, but is disposed of more or less promptly.

The definite allotment of land for purposes of pasturage is not invariable and, especially when but a few head of stock are maintained, they are pastured in a more or less indiscriminate fashion upon waste land, in lanes, woods, and such situations as prevent danger to growing crops. As a rule the milch cows are brought

to the barn to be milked, and draught-stock is invariably stabled and fed. Hogs are sometimes pastured but are frequently confined to small yards or pens which, too often, are unsanitary in the extreme and highly attractive to house and blow flies.

In cities and small towns, with the exception of the poorer dwellings, many, if not most, residences are provided with a stable in which a horse or cow, sometimes both, are sheltered. Depending somewhat upon density of population, these animals may be pastured upon vacant lots, road sides, and door yards or they may be confined to small yards adjacent to the stable. The care given the animals and their quarters varies greatly, but ample opportunity for fly propagation occurs. Hogs are usually excluded from the corporate limits of the larger communities.

In most of the mill villages there are no regulations regarding the keeping of domestic animals, including hogs. Cows are pastured indiscriminately about streets and village lots. They are stabled in small shacks upon the house lots of their owners or even under the houses when these stand upon sloping ground and sufficient room for this purpose is afforded. The cows are milked and fed grain, etc., on the premises, and their droppings are a source, sometimes a prolific one, of fly breeding.

In a few of the mill villages a common pasture is provided in which the cows of the mill operatives must be kept. They are not permitted upon the streets or house lots, and rough shed stables are usually provided in which the animals are fed, milked, and sheltered in inclement weather. These sheds are roughly constructed and although the droppings are removed from the stalls at intervals, piles of manure are left for varying periods in the immediate vicinity providing breeding places for great numbers of flies.

The plan of exclusion is an excellent one, but, unfortunately, the benefit is minimized by certain details of its application. Pastures are usually contiguous to the village, the nearest houses often standing within 100 feet of the pasture boundary and cow sheds. In one instance the pasture is almost at the centre of the village and is closely approached on three sides by the dwellings. In another village there are two pastures at opposite sides of the village and a large part of the community is thus exposed to the flies frequenting or produced within them. The rule of exclusion is not always rigorously enforced and exceptions are sometimes permitted; calves are occasionally, either openly or surrepticiously, kept about the owner's house and in one instance which came under our notice a cow was regularly brought for milking to the owner's house in spite of the regulation and an examination of the surroundings showed a large number of stable flies about the house adjoining that of her owner, whose premises were comparatively free from them.

A fact bearing upon the importance of domestic animals in connection with *Stomoxys* in its relation to human beings is that of

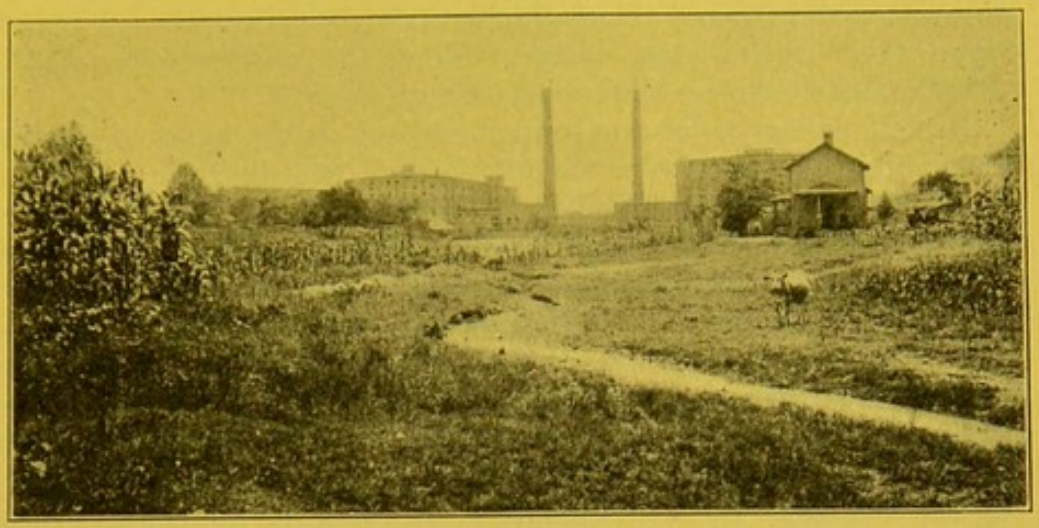

FIG. 4.—Open commons used as cow pasture by mill operatives. The stream in foreground is an active *Simulium* breeding place. Houses of operatives in middle distance.

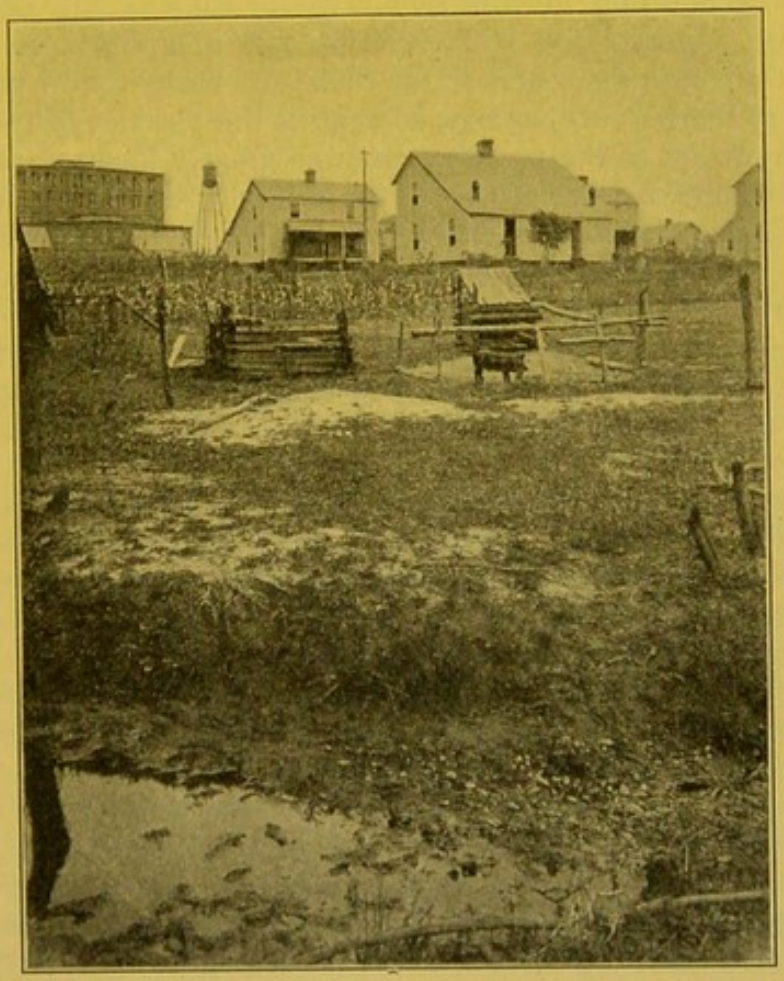

FIG. 5.—Part of a mill pasture with hog-pens and dwellings. Nearest house is about sixty yards from fence.

attack upon milkers. Although in the presence of animals which the fly normally prefers to man, the comparative quiescence of the persons so engaged, renders them peculiarly liable to attack, while those attending to and associating with cattle while actively engaged upon their duties may escape. That the milker is frequently attacked is shown by the reports we received.

But 21 pellagrins of our series had been in the habit of milking cows, and 2 of these were not questioned regarding the fly in this connection. Of the remaining 19, 14 or about 74 per cent., stated that they had been bitten while milking, and a considerable number of non-pellagrins made similar statements.

The comparative distribution of *Stomoxys* in urban, rural, and mill districts is interesting. Infestation of premises—the presence of *Stomoxys* upon the outside of houses, upon porches and in the immediate vicinity—in places from which entrance to the house or attack upon its inmates would be easy, occurred most frequently in mill villages. In these villages 97 per cent. of the homes visited were infested in the way described while of rural and farm homes 67 per cent., and of urban, 50 per cent. were similarly frequented.

The explanation of this seems to be that in the presence of domestic animals, the stable flies in the immediate vicinity will be concentrated upon and about them and many follow them when driven to work or to pasture, so that in the absence of the animals the infestation of the premises may be greatly lessened or the flies be so few as to escape notice. In the mill villages, the flies, separated from passing teams or cattle become generally distributed, seeking shelter and food among the dwellings, and it is significant of the truth of this explanation that in mill villages whose rules do not exclude cows from the village precincts, the number of stable flies present about the houses is more variable although apparently larger in the aggregate than in those villages which practice exclusion.

In comparing the reports of biting by *Stomoxys* received from pellagrins of the three classes, it is interesting to note that 55 per cent. of the reports received from mill cases were positive; 54 per cent. from rural cases were also positive; while but 13.4 per cent. of the urban cases could recall attacks by the fly.

It will be seen that the highest percentage of reports of bites by *Stomoxys* was received from the mill villages which also furnish the greatest number of pellagra cases. The rural districts follow closely in their percentage of positive reports though there is a greater discrepancy between pellagra incidence in the mill villages and that of these districts than is indicated in the reports. This fact might be accounted for by the lack of congestion of population in the rural sections with a lower percentage of possibly infected flies.

These reports evidently indicate that there is a definite correlation

between the abundance of *Stomoxys*, the character of its distribution and its biting of man.[18]

SUMMARY. Our investigation was entered upon with no bias in favor of the infectiousness of pellagra or its transmissibility by insects. In the nature of the case, however, and as a basis for our work, it was necessary to assume that both were among the possibilities.

No preconceptions as to the involvement of any particular insect were indulged, and our conclusions regarding individual species of insects are based upon the epidemiological picture of pellagra, mainly as presented in Spartanburg County, and upon the habits and distribution of the insects as observed by us and as elsewhere recorded.

Ticks, lice, bed bugs, cock roaches, horse flies, fleas, mosquitoes, buffalo gnats (*Simulium*), house flies, and stable flies (*Stomoxys*) were under consideration. Of these, horse flies have nothing and cock roaches little to support them.

Ticks and fleas are excluded on account of their scarcity and the nature of their biting habits. In view of these characteristics, it is doubtful if even the existence of an animal reservoir of infection would bring the groups into prominence.

Lice and bed bugs do not account for the sex or age incidence or the rural nature of the disease; the scarcity of the former is an additional reason for its exclusion.

The rarity of mosquitoes here and the lack of coincidence between their distribution and that of pellagra for the State in general, together with the night-biting habits of the local species, which fail to account for the sex incidence, seem sufficient cause for their elimination.

House flies (*Musca domestica*) should be active if the malady is an intestinal infection in which the germ is passed with the feces, with contaminated food acting as the vehicle of infection.

The buffalo gnats (*Simulium*) should be eliminated, principally by the facts of their biting habits and lack of those of intimate association with man, also possibly by their comparatively moderate abundance (in our territory). We find that in Spartanburg County they are hardly known as a pest of man and when they do attack him, it is very locally and largely confined to field workers. Had Sambon's theory not been advanced, these flies could hardly have attracted suspicion of any connection with pellagra in this country.

The stable fly (*Stomoxys calcitrans*) displays certain salient characteristics which seem to qualify it for the role of a transmitter of pellagra.

The range of this one species covers and exceeds that of pellagra;

[18] Allan H. Jennings and W. V. King, One of the Possible Factors in the Causation of Pellagra. Jour. Amer. Med. Assoc., January 25, 1913, lx.

its seasonal activity, likewise, is coincident with that of the disease and, although its period of greatest abundance is somwehat later than the maximum intensity of pellagra, its appearance in spring precedes that of most of the spring recurrences and new cases, at which time it is already abundant; it is an abundant species, its abundance being most manifest in rural districts thus corresponding with the rural nature of pellagra, its numbers amply fulfilling our conception of those necessary to effective disease transmission; it bites by day only, thereby offering an explanation of the phenomenon of sex incidence and the related one of age distribution; it is intimately associated with man and habitually infests his vicinity and enters his dwellings; it bites man frequently and persistently; its longivity seems sufficient for the development of a hypothetical causative organism; it is readily and frequently carried long distances and might thus account for the occurrence of sporadic cases of the disease.

IV.

METABOLISM IN PELLAGRA.[1]

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Introduction. A study of the metabolism in pellagra would appear to be of interest from a number of different viewpoints—namely, as an aid to the interpretation of the gastro-intestinal symptoms generally observed; in connection with the maize theory of the etiology of the disease; and, further, because of the resemblance in certain particulars to beriberi,[2] in which the etiologic factor appears to be an inadequate dietary. Despite the reasons which would seem to make a knowledge of the metabolism in this disease desirable no extended study has been carried out in this connection, with the exception of the work of Camurri,[3] in Italy. However, certain points of interest have been noted—namely, the frequent occurrence of gastric anacidity by Johnson,[4] by Cecconi,[5] and by Niles,[6] and the presence of indicanuria by a number of observers, most recently by Ormsby and Singer.[7]

The experiments conducted by Camurri were fairly comprehensive, though directed in particular toward the study of the mineral metabolism. His work included a general study of the

[1] Reprinted from the American Journal of the Medical Sciences, May, 1913, No. 5, vol. cxlv, p. 705.

This paper forms a part of the preliminary report of work performed under the auspices of the Thompson-McFadden Pellagra Commission of the Division of Tropical Medicine, Department of Laboratories, New York Post-Graduate Medical School and Hospital. The results of this work were reported at the Second Triennial Meeting of the National Association for the Study of Pellagra, Columbia, S. C., October 3, 1912, and at a meeting of the Section on Medicine of the New York Academy of Medicine, February 18, 1913. The analytical work was carried out with the assistance of Messrs. G. O. Volovic, W. I. Sivitz, Dr. E. Kister, and Mr. A. Bernhard; and the ward work with the assistance of Mrs. J. H. Brinkerhoff and the Misses H. A. Macarow and H. F. McDowell.

[2] For discussion of literature on beriberi, see Strong and Crowell, Philippine Jour. Sci., 1912, B, vii, 271.

[3] Atti del Quarto Congresso Pellagrologico Italiano, Udine, 1910, p. 67.

[4] South. Med. Jour., 1911, iv, 478.

[5] Gazzetta Degli Ospedali e delle Cliniche, 1911, xxxii, 77.

[6] Pellagra, 1912, p. 77.

[7] Report of the Pellagra Commission of the State of Illinois, 1911, p. 23; also Arch. Int. Med., 1912, x, 123 and 219.

composition of the diet, urine, and feces of pellagrins subsisting upon mixed diets and upon diets composed largely of corn. Balances were given for nitrogen, fat, and salt in comparison with those of normal individuals upon similar diets. The points of interest will be discussed in connection with our own work.

Johnson found the free hydrochloric acid of the gastric juice to be absent in 14 out of 20 cases, while rennin was absent in 7 cases. Diarrhea was observed in the 14 cases with absence of free hydrochloric acid, but only in one of the other 6 cases, and here attributed to another cause. Cecconi found free hydrochloric acid absent in all of his 12 cases, while Niles in an examination of 64 cases of undoubted pellagra found free hydrochloric acid absent in 18, deficient in 31, excessive in 12, and normal in 3. He noted that the gastric secretions were diminished or absent in most cases of long standing, while in the few instances where those juices were increased the cases were acute.

In a study of 55 cases of pellagra, Tucker[8] reported an increase in indican in 3 cases. In the report of the Illinois Pellagra Commission, however, Ormsby and Singer noted a marked reaction for indican in all the cases examined.

The experiments here reported were made upon the patients sent to the Post-Graduate Hospital by the Thompson-McFadden Pellagra Commission. We have endeavored to make a fairly extensive study of the metabolism in pellagra, because a thorough knowledge of the fundamental processes of metabolism appeared particularly desirable in this disease; and, further, because it was believed that points of attack might be disclosed which would offer opportunities for more intensive study.

Methods Employed. The general procedures employed in this metabolism study were to secure gastric contents (after the Ewald-Boas meal) as soon as practical after the admission of the patient to the hospital. Subsequently the patient was placed upon a weighed diet, and the urine and feces collected daily for a period varying usually from seven to ten days. Following this period, gastric contents were again secured in certain of the cases, while in two instances a second metabolism experiment was conducted.

The examination of the gastric contents has been directed particularly to determining the acidities and ascertaining the peptic activity. The customary titration methods were employed for the acidities and Rose's method for pepsin, as conducted in this laboratory.[9]

During the period of the metabolism study a lacto-vegetarian and practically purin-free diet was employed for experimental reasons. The general type of the diet may best be illustrated by a sample day (August 8) taken from Case 8 (M. T.).

[8] Jour. Amer. Med Assoc., 1911, lvi, 246.

[9] Post-Graduate, 1912, xxvii, 506.

	Grams or c.c.
Breakfast:	
Corn-flakes	25
Banana	89
Bread	63
Egg	48
10.30 A.M.	
Water	150
Apple	105
Dinner:	
Apples	125
Water	50
Bread	127
Egg	43
Potato	140
3.00 P.M.	
Graham crackers	26
Supper:	
Cream of wheat	25
Water	300
Bread	101
Egg	46
Orange	148
Water	200
10.00 P.M.	
Banana	97
Distributed between the various meals as desired:	
Cane sugar	63
Milk	800
Butter (salt free)	23
Salt (pure NaCl)	6

This would furnish 91 grams protein (14.6 N × 6.25), 71 grams fat, 460 grams carbohydrate and would yield approximately 2800 calories, which is not far from the average found for the period in this case.

As insufficient time prevented our making a complete analysis of the food intake, the figures for protein, carbohydrate, and fat were for the most part calculated from the data given by Atwater and Bryant[10] for American food materials, while the figures for the mineral constituents were taken from results compiled by Sherman.[11] Many of the figures for nitrogen, however, were from our own analyses, and we believe that the results which we have given for the nitrogen intake are reliable. The protein intake has been calculated from the nitrogen figures by employing the factor 6.25, and the calorific intake obtained by multiplying the grams of protein and carbohydrate by 4 and the grams of fat by 9 and adding these results.

[10] United States Dept. Agri., Office of Exper. Sta., Bulletin 28, Revised, 1906.

[11] Chemistry of Food and Nutrition, 1911, p. 332.

Previous to beginning the metabolism study the patients were placed for several days upon the diet they were to receive during the period of actual examination. The end of the twenty-four-hour urine period was taken as 7.30 A.M. After the excretion of the last sample of urine for the day the patients were weighed and then given their breakfast. The urine specimens were collected in three-liter glass-stoppered bottles and preserved with a liberal supply of toluene. The urines were taken to the laboratory at 9 A.M., made up to some definite volume (1000 c.c. where possible), and the nitrogenous constituents, the ammonia in particular, determined in most cases the same day. At this time the qualitative and microscopic examinations were made. The urines were then refrigerated at 0° C. for future use. The feces were collected in weighed tin pails, the weight of the feces ascertained by difference, and then kept in a common receptacle in the refrigerator at —4° C. until the end of the period. In most of the experiments the feces of the experimental period were marked off with charcoal, though in some of the later experiments carmin was employed. When the feces for the whole period had been assembled, they were thoroughly mixed and a weighed portion, generally one-half, dried over the water-bath with the addition of alcohol acidified with dilute sulphuric acid, and subsequently ground to a fine powder. All determinations with the exception of the indol and skatol were made upon the air-dried feces.

The examination of the urine included the usual qualitative tests—namely, tests for albumin, sugar, acetone, diacetic acid, and a microscopic examination of the centrifugalized sediment, and, in addition, quantitative estimations of the total nitrogen, urea, ammonia, uric acid, creatinin, creatin, chlorides, phosphates, inorganic and ethereal sulphates, neutral sulphur, total acidity, and indican on the individual specimens, and determinations of sodium, potassium, calcium, and magnesium on composite samples. The methods employed were: For total nitrogen, Kjeldahl; for urea, the Benedict (S. R.) method;[12] for ammonia, uric acid and creatinin, the Folin methods;[13] for creatin, the Benedict (F. G.)-Myers' modification of the Folin method;[14] for chlorides, the Volhard-Arnold method; for phosphates, uranium nitrate; for inorganic and ethereal sulphates, the Folin methods;[15] for neutral (total) sulphur, Benedict's (S. R.) method;[16] for total acidity, Folin's method; indican as described by Myers and Fine;[17] the sodium and potassium in part as directed by Folin,[18] the potassium

[12] Jour. Biol. Chem., 1910, viii, 405.
[13] Amer. Jour. Phys., 1905, xiii, 45.
[14] Ibid., 1907, xviii, 397.
[15] Jour. Biol. Chem., 1905-6, i, 131.
[16] Ibid., 1909, vi, 363.
[17] Post-Graduate, 1912, xxvii, 1144.
[18] Handbuch der Biochemichen Arbeitsmethoden, 1911, v, Pt. I, 292.

being estimated by the Drushel cobaltinitrite[19] method, and calcium and magnesium as described by McCrudden,[20] the calcium being estimated volumetrically.

The examination of the feces included certain of the simple routine tests and, in addition, estimation of moisture, nitrogen, fat, carbohydrate, mineral constituents, and the putrefactive products, indol and skatol. The moisture was obtained from the difference in the weight of the moist and air-dried feces. The nitrogen in the air-dried feces was estimated by the Kjeldahl method, the fat on the thoroughly dried feces by the Soxhlet method with anhydrous ether, and the carbohydrate with the Allihn method after hydrolysis of the feces as described by Mendel and Fine.[21] The mineral constituents were estimated in a similar manner to that described for urine. The indol and skatol were determined upon samples of the moist feces, with the aid of Ehrlich's aldehyde.[22] The feces slightly acidified with sulphuric acid were subjected to steam distillation until they failed to give a reaction with this reagent. A portion of the distillate was treated with the reagent to the maximum color, extracted with chloroform, and matched up in a Duboscq colorimeter with a similar extract prepared from mixtures of pure indol and skatol, showing the same color as the specimen under examination. It is believed that in this way an approximation of the amounts of both indol and skatol present was obtained.

Case Histories. A brief history of the cases upon which this study was made follows. A more detailed consideration of the case histories will be taken up in a subsequent paper of this series.

Case 1.—J. A. (Pellagra Commission, No. 1, Union County). Fairly well nourished man, aged sixty years; lesions rather slight; some scaling on hands; no evidence of diarrhea.

Case 2.—M. F. (Pellagra Commission, No. 1, Spartanburg County). Thin, pale, rather poorly nourished girl, aged seventeen years; no marked lesions; had had ovariotomy; no evidence of diarrhea.

Case 3.—M. McH. (Pellagra Commission, No. 2, Spartanburg County). Fairly well nourished woman, aged thirty-seven years; marked erythema on backs of hands and wrists; some erythema on face and mouth; developed acute mania while in hospital; *Strongyloides intestinalis* observed; moderate diarrhea.

Case 4.—C. T. (Pellagra Commission, No. 12, Spartanburg County). Well-nourished woman, aged forty years; very slight scaling on hands; not sufficiently definite for diagnosis; showed marked improvement.

[19] Amer. Jour. Sci., 1908, xxvi, 555; also Myers, Jour. Biol. Chem., 1909, vi, 115.
[20] Jour. Biol. Chem., 1909–10, vii, 83; 1911–12, x, 187.
[21] Ibid., 1911, x, 339.
[22] Herter and Foster, Jour. Biol. Chem., 1906, ii, 267.

CASE 5.—R. N. (Pellagra Commission, No. 9, Spartanburg County). Moderately well-nourished woman, aged thirty-two years; some scaling on forearms; had had erythema before coming to hospital; recovered while in hospital.

CASE 6.—M. L. (Pellagra Commission, No. 68, Spartanburg County). Tall, thin, poorly nourished woman, aged thirty-six years; said to have had tuberculosis, but no evidence of this could be found while patient was in hospital; some erythema and desquamation on back of hands; condition cleared up quickly.

CASE 7.—E. C. (Pellagra Commission, No. 113, Spartanburg County). Well-nourished girl, aged twenty-years; marked thickening of palms of hands; extensive desquamation on back of hands, forearms, elbows, dorsal surfaces of feet, on and around knees; irregular girdle of desquamation about waist; erythema not evident; case recovered very quickly.

CASE 8.—M. T. (Pellagra Commission, No. 114, Spartanburg County). Fairly well-nourished girl, aged about eighteen years; little erythema and desquamation on backs of hands and forearms; recovered quickly.

CASE 9.—L. G. (Pellagra Commission, No. 115, Spartanburg County). Tall, thin, poorly nourished woman, aged twenty-eight years; scaling on forearms and backs of hands, also slightly in front of neck; dull mentally, although said to have been bright previous to attack.

CASE 10.—M. S. (Pellagra Commission, No. 21, Spartanburg County). Rather tall, thin, poorly nourished woman, aged twenty-eight years; extensive lesions on backs of hands, forearms, arms, shoulders; girdle of erythema around neck; had ovarian cyst.

CASE 11.—B. B. (Pellagra Commission, No. 158, Spartanburg County). Fairly well nourished woman, aged thirty-three years; slight erythema, desquamation and pigmentation on backs of wrists; lesions did not cover great area; had pulmonary tuberculosis as demonstrated by an examination of sputum.

CASE 12.—A. N. (Pellagra Commission, No. 206, Spartanburg County). Fairly well-nourished woman, aged forty-three years; erythema, pigmentation, and desquamation up to middle of back of forearms.

CASE 13.—C. McC. (Pellagra Commission, No. 170, Spartanburg County). Poorly nourished woman, aged thirty-five years; extensive desquamation and discoloration of skin on backs of hands, forearms, arms, shoulders, and around neck; palms of hands much thickened, also deep fissures at points of fingers; marked diarrhea; mentality evidently low; delusions and hallucinations; recovered.

CASE 14.—W. L. (Pellagra Commission. No. 166, Spartanburg County). Fairly well nourished woman, aged thirty-five years;

mild desquamation on forearms. In this case no complete metabolism study was conducted, though an analysis of a twenty-four hour urine, gastric contents, and a qualitative examination of feces were made.

Gastric Analyses. The gastric analyses have shown very interesting results, especially when considered in connection with the indican estimations of the urine. In 8 of the 14 cases free hydrochloric acid was absent. The total acidities were low, and pepsin was generally absent, or present only in small quantity. Though considerable amounts of indican were observed in all cases, the quantity was excessive in those with anacidity, reaching in one case nearly a quarter of a gram a day. To emphasize this relationship the data given in Table I have been arranged in order of the amounts of the average daily indican elimination. This association of high indican elimination, with diminished acidity, is indicative of the strong inhibitory influence of the normally acid gastric juice upon putrefaction in the alimentary canal, or at least a certain type of putrefaction. As may be observed, some of the cases with low indicanuria and with free hydrochloric acid present in the gastric juice have a fairly high elimination of ethereal sulphates, but, in general, the total ethereal sulphates as well as the indoxyl-potassium-sulphate are increased in anacidity. Still another factor which may play a part is the activity of the pepsin, especially in the cases where hydrochloric acid is present. Case 12 (A. N.), with only a slightly subnormal acidity, but with a low peptic activity, showed an elimination of indican next in amount to the cases with anachlorhydria. In this series of cases, anacidity was found in about the same percentage of cases as reported by Johnson. Cecconi in the 12 cases which he examined made qualitative tests for indican. Though all of his cases showed an absence of free hydrochloric acid, no uniform relation appeared to exist between the anacidity and the indican, if we are to accept the qualitative tests for indican as representative of the quantitative elimination.

Food Intakes. In general the food intakes may be viewed as indicating the general condition of the patients, since they were allowed considerable liberty in the choice of food, and further provided with all they desired. The food intakes, as shown in Table III, amounted in all cases to from 75 to 110 grams of protein (12 to 18 grams of nitrogen) and 2300 to 3000 calories per day, with the exception of Case 2 (M. F.), during the first period of observation, and Case 3 (M. McH.) during both periods of observation. With the same exceptions all the cases showed a decided plus nitrogen balance during the period of observation, the degree of nitrogen retention being in proportion in general to the gain in weight as shown in the tabulated results. Case 2 (M. F.) during

the first period of nine days, with an intake of 8.9 grams of nitrogen, showed a slight plus daily balance of 0.6 gram, though a decided plus balance was observed with the gain in weight during the second period. Case 3 (M. McH.), with a nitrogen intake of 5.0 grams during the first period, showed a minus daily balance of 1.4 grams, with a decided loss in weight. During the second period, with a nitrogen intake of 7.2 grams, she gained slightly in weight and showed a plus daily balance of 1 gram nitrogen. Corn in the form of corn-flakes was consumed in all the experiments, while Case 2 (M. F.) ate considerable quantities of corn-bread during the second period of observation. During this period of seven days she gained four pounds in weight, showed an average daily nitrogen balance of plus 4.1 grams, and otherwise showed general improvement.

TABLE I.—Gastric Analyses in Comparison with Certain Data of Urine and Feces. Tabulated in Order of Indican Elimination.

Patient.	Gastric analyses.					Urine.			Feces.	
	Volume of contents.	Free HCl.	Total acidity.	Lactic acid.	Peptic content[23] (Rose.)	Indican. Daily average.	Ethereal sulphates as SO_3 Daily average.	Ratio ethereal to inorganic SO_3.	Indol. Daily average.	Skatol. Daily average.
	C.c.					Mg.	Mg.		Mg.	Mg.
13—C. McC.	270	0	5	+	0.5	240	181	1 to 8	—	—
4—C. T.	90	0	8	+	0	208	194	1 to 7	5	10
	180	0	7	+	0					
	50	0	6	+	0					
1—J. A.	94	0	4	+	0	151	207	1 to 6	0	28
	130	0	4	++						
2—M. F.	135	0	14	+	0	128	126	1 to 8	0	2
	60	0	12	+	0	48	98	1 to 11	3	3
9—L. G.	70	0	12	++	0	95	203	1 to 6	11	34
	200	0	4		1					
3—M. McH.	188	0	7	+	2	69	97	1 to 7	2	9
	3	0	—		—	91	122	1 to 5	7	7
	140	0	20	++	7					
8—M. T.	140	0	8	++	0	88	161	1 to 11	3	12
11—B. B.	300	0	4	+	2	71	126	1 to 11	21	51
12—A. N.	65	18	43	..	0.5	65	124	1 to 17	Tr.	Tr.
	20	36	60	..	0.5					
14—W. L.	90	40	64	..	7	57	..	..	—	—
6—M. L.	135	15	32	+	7	45	149	1 to 11	0	1
5—R. N.	35	22	42	..	5	43	59	1 to 20	14	0
	270	14	38	..	10					
	45	26	54	+	7					
10—M. S.	170	8	26	..	16	23	117	1 to 11	2	19
	57	2	20	+	2					
7—E. C.	340	17	34	+	2	21	147	1 to 8	0	16

As the tabulated data show, the food intake, with the few exceptions mentioned, was generally up to the standard set by Atwater, and thus far above the minimum figures given by Chittenden. Both the protein and the calorific intake appear to have been

[23] Normally the peptic activity of the gastric juice after the Ewald meal is 8 to 11 by the Rose method.

ample as judged by these standards, though perhaps the proportion of fat to carbohydrate is a little higher than ordinarily found.

These data hardly allow of comparison with the results observed by Wussow and Grindley[24] at the Peoria State Hospital, for the reason that, with one exception, they were all women and, further, were below the normal average weight. At Peoria they found the general diet supplied per man per day: Protein, 73.5 grams; carbohydrate, 444 grams; fat, 56 grams; energy, 2568 calories; mineral matter, 23.23 grams, of which 1.07 grams were phosphorus; while the corn diet gave protein, 87.2 grams; carbohydrate, 463 grams; fat, 79 grams; energy, 2898 calories; total mineral matter, 27.91 grams, of which 1.64 grams were phosphorus. In general the diet of our patients appeared to furnish a somewhat larger amount of protein and fat, but a smaller amount of carbohydrate. The diets employed by Camurri are likewise of interest in this connection. His mixed diet contained 131 grams protein, 430 grams carbohydrate, 66 grams fat, 24.85 grams mineral matter, and had an energy equivalent of 2600 calories, while his corn diet contained 96 grams protein, 617 grams carbohydrate, 64 grams fat, 26.45 grams mineral matter, and furnished 3450 calories. Camurri calls attention to the small relative amounts of sodium and calcium furnished by certain dietaries. The figures which we have calculated for the salt intake would appear to indicate that in this particular our diet was adequate and well balanced.

Composition of the Urine. The discussion of the urine can best be prefaced by the general statement that the chemical composition of the urine in pellagra does not markedly differ from what one might observe in other individuals of a similar physical condition, except in one particular, the increase in the quantity of the bodies derived from intestinal putrefaction—namely, the ethereal sulphates, and especially the indican. It is perhaps of some significance that a few hyalin casts were observed in 6 out of the 14 cases, while in 2, traces of albumin were detected.

The volume of urine eliminated and the specific gravity gave figures such as one might have anticipated with the fluid and food intake, the average volumes varying between 300 and 1800 c.c., with specific gravities of 1.029 to 1.013. As shown in Table II, the figures for total acidity, chlorides, phosphates, inorganic sulphates, neutral sulphur, for the mineral elements, calcium, magnesium, sodium, and potassium (figures for sodium and potassium not included in table) are such as one might expect under the given dietary conditions, and the same may be said in regard to the various nitrogenous constituents.

[24] Report of the Pellagra Commission of the State of Illinois, 1911, p. 197.

TABLE II.—Summary Table. Average Daily Composition of the Urine.[25]

Patient.	Severity of condition.	Sex.	Age.	Wt. at beginn'g of exper't.	Weight at end of experi'nt.	Average weight	Length of experiment.	Date, 1912.	Volume of urine.	Specific gravity.	Qualitative and Microscopic examination of urine.	Total N.	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Undetermined N.	Creatinin coefficient.
			Yrs.	Lbs.	Lbs.	Kgms.			C.c.			Gms.	Gms.	Gm.	Gm.	Gm.	Gm.	Gms.	
1—J. A.	Moderately severe: chronic	M.	60	143	145	65.3	9	June 14 to 23	912	1.019	Occasional granular casts, occasional leukocytes.	9.40	7.68	.51	.08	.36	.02	0.75	5.5
2—M. F.	Moderately severe; chronic	F.	17	76	75	34.2	9	June 9 to 18	676	1.023	Faint trace of albumin on several occasions, moderate number of pus cells.	7.74	6.75	.25	.06	.20	0	0.48	5.8
2—M. F. Period 2	Moderately severe; chronic	F.	17	78	82	36.3	7	June 29 to July 6	877	1.020	Negative.	7.25	6.07	.30	.05	.22	0	0.61	6.1
3—M. McH.	Severe; acute	F.	37	88	85	39.0	10	June 9 to 19	304	1.028	Moderate number pus cells.	5.89	4.73	.33	.06	.21	.04	0.52	5.4
3—M. McH. Period 2	Severe; acute	F.	37	85	86	38.1	7	June 29 to July 6	318	1.029	Moderate number pus cells.	4.87	3.85	.21	.07	.22	.01	0.51	5.8
4—C. T.	Mild; chronic	F.	40	121	122	54.9	9	July 7 to 16	1439	1.018	Negative.	9.47	7.75	.50	.08	.35	.02	0.77	6.4
5—R. N.	Moderately severe; chronic	F.	32	87	88	39.7	9	July 7 to 16	1198	1.019	Occasional hyaline cast on one day.	8.05	6.09	.41	.08	.23	.09	1.15	5.8
6—M. L.	Moderately severe; chronic	F.	36	94	100	43.8	9	July 21 to 30	1256	1.019	Negative.	10.71	8.94	.56	.09	.30	0	0.82	6.9
7—E. C.	Moderately severe; acute	F.	20	145	150	66.9	7	August 5 to 12	1496	1.014	Occasional hyaline casts on two days.	8.08	6.50	.41	.13	.33	.01	0.70	4.9
8—M. T.	Mild; acute	F.	18	116	118	53.1	7	August 5 to 12	1444	1.017	Occasional hyaline casts on one day.	10.62	9.08	.49	.13	.36	0	0.56	6.8
9—L. G.	Moderately severe; chronic	F.	28	114	118	52.0	8	August 17 to 25	1393	1.015	Trace of albumin on first three days and occasional hyaline casts on first five days.	9.12	7.55	.48	.11	.26	.03	0.69	5.0
10—M. S.	Severe; chronic	F.	28	89	91	41.3	10	August 17 to 27	839	1.023	Negative.	8.64	7.24	.47	.11	.23	0	0.59	5.6
11—B. B.	Mild; chronic	F.	33	90	94	41.7	7	August 23 to 30	987	1.017	Moderate number pus and red blood cells observed on several days and an occasional hyaline cast on one day.	8.80	7.59	.41	.05	.21	.02	0.52	5.0
12—A. N.	Mild; acute	F.	43	91	95	42.2	7	September 12 to 19	1833	1.013	Negative.	12.88	10.92	.35	.05	.25	0	1.31	5.9
13—C. McC.	Severe; chronic	F.	35	70	72	32.0	2	September 18 to 20	646	1.019	Many pus cells.	9.45	7.66	.67	...	.14	.11	...	4.4

[25] The tables of the individual metabolism studies from which these average figures have been computed will be found at the end of the paper.

TABLE II (CONCLUDED).—Average Daily Composition of the Urine.

Patient.	In percentage of total nitrogen.						Urea.	Ammonia.	Uric acid.	Creatinin.	Creatin.	Total acidity terms n/10 acid.	Calcium as CaO.	Magnesium as MgO.	Chlorides as NaCl.	Phosphates as P_2O_5.	Inorganic sulphates as SO_3.	Ratio ethereal: Inorganic SO_3.	Ethereal sulphates as SO_3.	Neutral sulphur as SO_3.	Indican (indoxyl-potassium-sulphate).
	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Undetermined N.															
							Gms.	Gm.	Gm.	Gm.	Gm.	C.c.	Gm.	Gm.	Gms.	Gms.	Gms.		Gm.	Gm.	Mgms.
1	81.7	5.4	0.9	3.8	0.2	8.0	16.5	.61	.24	.97	.06	429	.18	.13	6.08	2.01	1.352	1 to 6	.207	.213	151
2	87.2	3.2	.8	2.6	...	6.2	14.5	.30	.18	.54	0	303	.16	.08	5.14	1.85	1.067	1 to 8	.126	.203	97
2	83.7	4.1	.7	3.0	...	8.5	13.0	.36	.15	.59	0	332	.20	.07	7.88	2.04	1.064	1 to 11	.098	.263	48
3	80.3	5.6	1.0	3.6	.7	8.8	10.1	.40	.18	.57	.12	262	.14	.08	1.73	1.35	.705	1 to 7	.097	.122	69
3	79.1	4.3	1.4	4.5	.2	10.5	8.3	.26	.21	.59	.03	195	.09	.05	3.21	1.32	.577	1 to 5	.122	.154	91
4	81.8	5.3	.8	3.7	.2	8.2	16.6	.61	.24	.94	.06	300	.27	.18	14.05	2.09	1.332	1 to 7	.194	.193	208
5	75.7	5.1	1.0	2.9	1.1	14.2	13.1	.50	.24	.62	.28	315	.15	.12	14.07	2.16	1.150	1 to 20	.059	.168	43
6	83.5	5.2	.8	2.8	...	7.7	19.2	.68	.27	.81	0	257	.16	.07	12.90	1.88	1.635	1 to 11	.149	.203	45
7	80.4	5.1	1.6	4.1	.1	8.7	13.9	.50	.39	.87	.03	353	.39	.25	8.98	2.17	1.189	1 to 8	.147	.250	21
8	85.5	4.6	1.2	3.4	...	5.3	19.5	.60	.39	.97	0	339	.26	.23	9.83	2.56	1.727	1 to 11	.161	.280	88
9	82.8	5.3	1.2	2.9	.3	7.5	16.2	.58	.33	.70	.09	348	.15	.18	9.40	1.92	1.275	1 to 6	.203	.233	95
10	83.8	5.4	1.3	2.7	...	6.8	15.5	.57	.33	.62	0	264	.33	.09	9.46	2.12	1.274	1 to 11	.117	.279	23
11	86.2	4.7	.6	2.4	.2	6.9	16.3	.50	.15	.57	.06	413	.22	.12	6.94	2.21	1.370	1 to 11	.126	.270	71
12	84.8	2.7	.4	2.0	...	10.1	22.7	.43	.15	.67	0	461	.30	.30	8.71	3.36	2.156	1 to 17	.124	.446	65
13	81.0	7.1	...	1.5	1.2	....	16.4	.81	...	.37	.35	367	.25	.09	4.50	2.17	1.462	1 to 8	.181	.208	240

ABLE III.—Average Daily Food Intake, with Nitrogen Balance.

Patient.	Protein.	Fat.	Carbohydrates.	Calories.	Calcium as CaO.	Magnesium as MgO.	Sodium as Na_2O.	Potassium as K_2O.	Phosphates as P_2O_5.	Chlorides as Cl.	Food N.	Urinary plus fecal. N.	N balance.	Approximate daily change in weight.
	Grams.	Grams.	Grams.		Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Kilogram.
1—J. A.	79	126	260	2490	2.0	0.4	3.3	3.0	3.4	4.3	12.6	10.4	+2.2	+.10
2—M. F.	56	89	174	1720	1.8	0.3	2.7	2.6	2.7	3.6	8.9	8.3	+0.6	—.05
2—M. F.	78	103	315	2500	2.1	0.5	4.0	3.5	3.9	5.2	12.5	8.4	+4.1	+.26
Period 2														
3—M. McH.	31	36	122	940	1.2	0.1	0.8	0.1	1.7	1.4	5.0	6.4	—1.4	—.14
3—M. McH.	45	70	182	1540	1.3	0.2	2.1	2.1	2.0	2.9	7.2	6.2	+1.0	+.06
Period 2														
4—C. T.	79	98	278	2310	2.4	0.4	6.5	3.4	3.7	8.2	12.7	11.0	+1.7	+.05
5—R. N.	81	125	285	2590	2.4	0.4	7.1	3.3	3.9	8.9	12.9	10.4	+2.5	+.05
6—M. L.	91	134	281	2700	2.5	0.4	7.3	3.8	4.0	9.0	14.5	11.5	+3.0	+.30
7—E. C.	83	153	328	3020	2.3	0.5	4.6	4.0	3.8	6.8	13.3	9.9	+3.4	+.32
8—M. T.	88	77	372	2530	2.0	0.5	3.7	4.0	3.7	5.0	14.0	12.1	+1.9	+.13
9—L. G.	87	117	288	2550	2.3	0.4	4.4	4.0	3.8	6.5	13.9	10.6	+3.3	+.23
10—M. S.	76	109	261	2330	1.9	0.4	4.9	3.6	3.4	6.3	12.1	9.7	+2.4	+.09
11—B. B.	101	124	280	2640	2.6	0.5	4.2	4.3	4.4	5.3	16.1	11.1	+5.0	+.26
12—A. N.	113	131	339	3000	2.9	0.5	5.0	4.6	5.0	6.3	18.0	14.3	+3.7	+.26
13—C. McC.	106	125	190	2310	3.2	0.4	4.1	3.9	5.1	5.1	16.9	12.2	+4.7	+.45

TABLE IV.—Average Daily Composition of the Feces.

Patient.	Moist feces.	Air dry feces.	Moisture.	Nitrogen.	Nitrogen.	Protein utilization.	Ether extract.	Ether extract.	Fat utilization.	Carbohydrate as glucose.	Carbohydrate as glucose.	Carbohydrate utilization.	Ash.	Ash.	Calcium as CaO.	Magnesium as MgO.	Phosphates as P_2O_5.	Chlorides as Cl.	Indol.	Skatol.
	Gms.	Gms.	Per cent.	Gms.	Per cent.	Per cent.	Gms.	Per cent.	Per cent.	Gms.	Per cent.	Per cent.	Gms.	Per cent.	Gms.	Gm.	Gms.	Gms.	Mgms.	Mgms.
1—J. A.	103	21.6	79	1.01	4.67	92	6.9	31.9	94	.6	2.57	99.8	4.49	20.8	1.40	.25	1.08	.23	0	28
2—M. F.	56	13.7	76	.51	3.71	94	3.2	23.2	96	.4	2.77	99.8	3.06	22.3	1.26	.18	.71	.06	0	2
2—M. F. Period 2	90	23.6	74	1.13	4.81	91	2.7	11.4	98	.9	3.62	99.7	4.95	21.0	2.00	.31	1.01	.11	3	3
3—M. McH.	59	9.7	84	.54	5.53	90	2.1	21.7	94	.2	2.57	99.8	2.16	22.3	.80	.12	.62	.15	2	9
3—M. McH. Period 2	182	22.0	88	1.36	6.27	81	3.2	14.6	95	1.7	7.57	99.0	3.96	18.0	1.08	.26	.76	.42	7	7
4—C. T.	113	24.4	78	1.49	6.10	88	4.5	18.3	95	.6	2.53	99.8	5.05	20.7	1.94	.33	1.39	.38	5	10
5—R. N.	233	36.4	84	2.35	6.45	81	2.9	8.0	98	3.3	9.00	99.0	5.68	15.6	2.17	.35	1.17	.85	14	0
6—M. L.	73	19.0	74	.75	3.97	94	4.5	23.7	97	.8	4.14	99.7	4.52	23.8	1.75	.34	1.44	.14	0	1
7—E. C.	148	28.6	79	1.84	6.43	87	6.4	22.2	96	1.1	4.05	99.6	4.49	15.7	1.70	.20	1.16	.43	0	16
8—M. T.	129	23.1	82	1.49	6.46	89	4.4	19.2	94	.9	4.00	99.8	3.74	16.2	1.49	.25	.97	.33	3	12
9—L. G.	200	31.0	85	1.47	4.75	89	10.9	35.2	91	1.2	3.90	99.6	5.86	18.9	1.99	.33	1.49	.26	11	34
10—M. S.	195	22.8	88	1.10	5.98	91	3.3	14.3	97	1.3	5.67	99.5	4.33	19.0	1.44	.30	.88	.40	2	19
11—B. B.	367	41.1	89	2.28	5.55	86	10.5	25.5	92	1.4	3.36	99.5	7.15	17.4	2.40	.40	1.60	.67	21	51
12—A. N.	147	27.4	81	1.41	5.13	92	5.3	19.4	96	1.2	4.53	99.6	5.84	21.3	2.65	.43	1.03	.41	Faint	Reaction
13—C. McC.	772	42.0	95	2.70	6.44	79	11.1	26.3	89	Trace	Trace	100.0	11.47	27.3	2.47	.36	2.44	2.19	0	0

The elimination of total nitrogen, urea, ammonia, uric acid, and creatinin is perhaps slightly below the so-called normal, though the constituents dependent upon exogenous factors, namely, the urea and ammonia, are in accord with the diet, and those of endogenous origin, namely, the uric acid and creatinin, are such as might be observed in other individuals of similar physical condition. Since Folin[26] first considered the distribution of the nitrogenous constituents in normal urine a large amount of work has been done on this subject. The large amount of data collected in the publications of the Referee Board[27] is unusually good confirmation of the statements of Folin in this particular. Although our data for the percentage of ammonia and undetermined nitrogen are slightly above the so-called normal figures and the other constituents slightly below, these differences are readily interpreted as due to the diet and the physical condition of the patients. As Folin has so well shown, with a reduction of the nitrogen-intake the urinary constituents of exogenous origin necessarily form a smaller percentage of the total nitrogen, and our figures for urea nitrogen, generally 83 per cent., are in accord with the nitrogen of the food. As the endogenous metabolism of the body was at a low state of activity, due to the rather poor physical condition of the individuals, we would hardly expect the uric acid (purin-free diet) and creatinin nitrogen to form an increased percentage of the total nitrogen. On the contrary the percentage of nitrogen in this form is rather below the normal.

An examination of the absolute amounts of the various nitrogenous constituents eliminated by the different individuals shows that in general the urea varied between 10 and 20 grams, the ammonia between 0.3 and 0.8 gram, the uric acid between 0.15 and 0.39 gram, and the creatinin between 0.4 and 1 gram. The absolute amount of the undetermined nitrogen in general falls within normal limits, though, as mentioned above, it forms a rather high percentage of the total nitrogen. In Cases 2 and 12, however, the figures are considerably higher than those found in other cases of the series.

The creatinin elimination is below normal in all cases, this fact being particularly well shown by the creatinin coefficients. Normally, coefficients of 7 to 11 are found, while here the figures vary between 5 and 7. As recently discussed by one of us[28] (Myers), the creatinin elimination is lowered in conditions associated with decreased body efficiency. This general inefficiency is further brought out by the fact that 10 out of the 14 cases eliminated creatin, though in only 2 cases was it present in large amount.

The elimination of the mineral constituents hardly requires

[26] Amer. Jour. Phys., 1905, xiii, 66.

[27] United States Dept. of Agric., Report No. 88, 1909, and No. 94, 1911.

[28] Amer. Jour. Med. Sci., 1910, cxxxix, 256.

further comment, except for that part containing an organic radicle, namely, the ethereal sulphates. Certain of the facts in this connection are best brought out in Table I, in which the data are arranged in order of the amounts of indican eliminated. The absolute amounts of the ethereal sulphates appear to be increased in a few instances, in which case there exists a low ratio to the ethereal sulphates. This is especially pronounced in the cases of anacidity, in which very large amounts of indican were eliminated. Here the indican appears to parallel the total ethereal sulphates, but apparently for the reason that the indican forms a considerable part of the total ethereal sulphates. The low ratio of inorganic to ethereal sulphates was observed in the cases reported by Camurri.

Composition of the Feces. The examination of the feces as shown in Table IV revealed widely varying conditions as to volume and consistency—watery stools, soft stools, well-formed stools, and hard stools—the average daily elimination amounting to from 60 to 700 grams of moist feces and 20 to 40 grams of air-dried feces, the moisture varying between 75 and 95 per cent. The microscopic examination of the feces has not yielded data of special significance, though in certain cases evidence of digestive inefficiency has been observed, and in some cases considerable mucus, probably in part due to the diarrhea. In several instances strongly positive fermentation tests with Schmidt tubes have been observed, notably in Case 3 (M. McH.), period 2, though the estimation of the carbohydrate content of the feces ought to be a more adequate criterion. The daily fecal nitrogen was found as low as 0.5 gram where the nitrogen intake was low, and as high as 2.7 grams in the reverse condition, accompanied by severe diarrhea. These figures fall within the normal limits, however, and the percentage of nitrogen in the air-dried feces cannot be said to be excessive, though perhaps slightly above the normal average in a few cases. In 3 cases (Case 3, period 2, Case 5, and Case 13) the so-called protein utilization was below the other figures observed, but probably in part due to the diarrhea. The daily fat eliminated varied from 2 to 11 grams, with percentages of the air-dried feces ranging between 8 and 35 per cent. The fat utilization was good in all cases, though the figures for Cases 9, 11, and 13 were slightly below that observed in other cases. The figures for the carbohydrate were from direct estimation, and are therefore much more reliable than the results generally reported as determined by difference. The tabulated data show that the utilization was 99.5 to 99.8 per cent. in all but 2 cases (Case 3, period 2, and Case 5), where the utilization was 99 per cent. and the percentage content in the feces 7.6 and 9 per cent. These results show quite conclusively that the ability of the pellagrins to absorb their food is only slightly if at all impaired and that this is in part due to the diarrhea. The data on the feces

reported by Camurri bring out similar points, though he has only five sets of average figures with which to make comparison.

The examination of the feces has included quantitative determinations of calcium, magnesium, phosphates, chlorides, as shown in Table IV, and also of sodium and potassium. These data have not revealed any apparent derangement of mineral metabolism, though certain interesting relationships have been brought to light, which will be presented in a subsequent paper.

The feces of pellagrous individuals have a most characteristic aromatic odor, and the estimations of the indol and skatol would indicate that this odor was due to the large amounts of these aromatic bodies found to be present. Normally only traces of these bodies are present, and from the investigation of Herter[29] and also of one of us[30] (Myers) with Fisher and Diefendorf, the amounts detected, especially of skatol, may be regarded as decidedly abnormal and indicative of peculiar bacterial conditions in the intestine. When these results are compared with the acidity determinations in the gastric juice, some relation between the amount of skatol formation and anacidity is apparent.

Summary. The ability of individuals suffering from pellagra to utilize the various foodstuffs as indicated by our series of fifteen experiments appears to be only slightly if at all below the normal.

The elimination of mineral and nitrogenous constituents in the urine is such as would be anticipated under the dietary and physical conditions of the individuals. A lowered physiologic efficiency is indicated by the low creatinin coefficients and the elimination of small amounts of creatin in the urine. The presence of a few hyalin casts in about 45 per cent. of the cases points to some possible irritation of the kidney.

Anacidity is a condition common in pellagra, found in eight of our fourteen cases. It is generally associated with an entire absence of pepsin, or with pepsin in only very minute quantities.

Individuals suffering from pellagra show a marked indicanuria, which is excessive in the cases with gastric inefficiency. Though the ethereal sulphate hardly parallels the indoxyl-potassium sulphate, the quantities eliminated are much higher where anacidity exists and they furthermore hold a higher ratio to the inorganic sulphates.

The feces contain decidedly abnormal amounts of indol and skatol, especially the latter.

The presence of excessive amounts of indican in the urine, associated with a high elimination of ethereal sulphates, when considered in connection with the abnormal amounts of indol and skatol in the feces, points to some unusual bacterial conditions in the intestine. From the data at hand this putrefaction would appear to take place rather high up in the intestine.

[29] Bacterial Infections of the Digestive Tract. 1907, p. 239.

[30] Zentralbl. f. Stoffwechsel, 1908, ix, 849; Amer. Jour. Insanity, 1909, lxv, 607.

Analyses of Daily Urines Including Daily Nitrogen Balance.

Case I.—Mr. J. A. (Pellagra Commission No. 1, Union County).

Date.	Day.	Volume of urine.	Specific gravity.	Total acidity terms n/10 acid.	Chlorides as NaCl.	Phosphates as P_2O_5.	Inorganic sulphates as SO_3.	Ethereal sulphates as SO_3.	Neutral sulphur as SO_3.	Indican.	Total N.	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Fecal N.	Urinary plus fecal N.	Food N.	N Balance.
1912.		C.c.		C.c.	Gms.	Gms.	Gms.	Gm.	Gm.	Mgms.	Gms.	Gms.	Gm.	Gm.	Gm.	Gm.	Gms.	Gms.	Gms.	Gms.
June 14 to 15	6	1185	1.020	425	9.78	2.02	1.445	.283	.242	102	11.31	9.39	.51	.11	.38	.05	1.01	12.34	11.8	— .5
June 15 to 16	7	1200	1.015	301	6.00	1.76	1.131	.227	.161	144	8.94	7.08	.43	.08	.34	.02	1.01	9.95	12.7	+2.7
June 16 to 17	8	630	1.020	393	3.40	2.14	1.158	.107	.210	120	7.42	5.74	.55	.07	.38	0	1.01	8.43	12.3	+3.9
June 17 to 18	9	1085	1.015	393	4.80	2.02	1.393	.125	.190	212	8.68	6.97	.53	.05	.34	0	1.01	9.69	11.3	+1.6
June 18 to 19	10	675	1.021	403	4.50	2.06	1.407	.172	.153	195	8.39	6.75	.55	.06	.34	.05	1.01	9.40	14.8	+5.4
June 19 to 20	11	855	1.020	538	5.00	2.07	1.574	.174	.258	147	10.10	8.56	.30	.08	.34	.05	1.01	11.11	12.4	+1.3
June 20 to 21	12	960	1.016	481	6.10	1.94	1.331	.275	.204	100	9.42	7.72	.60	.10	.34	.04	1.01	10.43	14.6	+4.2
June 21 to 22	13	860	1.022	525	8.06	2.07	1.720	.247	.234	189	10.43	8.52	.61	.09	.41	0	1.01	11.44	12.4	+1.0
June 22 to 23	14	762	1.018	405	7.10	2.02	1.407	.235	.189	150	9.91	8.36	.49	.07	.40	0	1.01	10.92	12.6	+1.7
Average . .	6 to 14	912	1.019	429	6.08	2.01	1.352	.207	.213	151	9.40	7.68	.51	.08	.36	.02	1.01	10.41	12.6	+2.2

Urine acid in reaction to litmus on all days tabulated. No albumin or sugar detected on any day. Microscopic examination of urinary sediment showed occasional granular casts and leukocytes on all days except the twelfth.

Case II.—Miss M. F. (Pellagra Commission No. 1, Spartanburg County).

Date.	Day.	Volume of urine.	Specific gravity.	Total acidity terms n/10 acid.	Chlorides as NaCl.	Phosphates as P_2O_5.	Inorganic sulphates as SO_3.	Ethereal sulphates as SO_3.	Neutral sulphur as SO_3.	Indican.	Total N.	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Fecal N.	Urinary plus fecal N.	Food N.	N Balance.
1912.		C.c.		C.c.	Gms.	Gms.	Gms.	Gm.	Gm.	Mgms.	Gms.	Gms.	Gm.	Gm.	Gm.	Gm.	Gms.	Gms.	Gms.	Gms.
June 9 to 10	1	545	1.024	303	5.30	1.40	.798	.121	.230	81	6.08	5.07	.37	.06	.19	0	.51	5.58	9.5	+3.9
June 10 to 11	2	730	1.020	308	4.70	1.96	.993	.129	.243	29	7.38	6.22	.25	.06	.21	0	.51	7.89	10.2	+2.3
June 11 to 12	3	710	1.021	373	4.80	2.14	1.303	.139	.266	32	8.72	8.01	.30	.07	.20	0	.51	9.23	8.8	— .4
June 12 to 13	4	413	1.030	373	4.40	2.11	.999	.140	.212	162	8.09	7.03	.20	.07	.21	0	.51	8.60	8 5	— .1
June 13 to 14	5	765	1.023	273	6.00	1.88	1.166	.145	.187	139	9.18	8.06	.20	.07	.20	0	.51	9.69	10.8	+1.1
June 14 to 15	6	885	1.020	325	6.20	2.11	1.132	.149	.176	139	8.40	7.30	.24	.06	.20	0	.51	8.91	8.8	— .1
June 15 to 16	7	1020	1.016	186	8.04	1.63	.912	.123	.163	106	7.25	6.21	.28	.05	.18	0	.51	7.76	8.6	+ .8
June 16 to 17	8	560	1.017	217	2.80	1.40	.761	.089	.188	65	5.50	4.63	.20	.05	.18	0	.51	6.01	5.0	—1.0
June 17 to 18	9	460	1.034	370	4.00	1.98	1.540	.097	.167	121	9.09	8.17	.22	.07	.21	0	.51	9.60	9.7	+ .1
Average . .	1 to 9	676	1.023	303	5.14	1.85	1.067	.126	.203	97	7.74	6.75	.25	.06	.20	0	.51	8.25	8.9	+0.6

Urine acid in reaction to litmus on all days. Faint trace of albumin detected on third, fifth, and seventh day of observation. Microscopic examination of urine revealed a moderate number of pus and many epithelial cells on all days.

Case II.—Miss M. F. (Period 2.)

June 29 to 30	1	440	1.030	308	5.80	1.65	.885	.052	.156	68	5.44	4.43	.28	.06	.22	0	1.13	6.57	16.5	+9.9
June 30 to July 1	2	990	1.015	353	7.80	1.81	.896	.106	.172	44	6.84	5.47	.44	.05	.22	0	1.13	7.97	10.0	+2.0
July 1 to 2	3	1320	1.014	332	11.10	2.49	1.079	.114	.397	63	7.89	6.59	.29	.06	.22	0	1.13	9.02	8.8	— 2
July 2 to 3	4	778	1.020	303	5.80	2.11	1.014	.092	.284	44	7.09	5.66	.15	.04	.22	0	1.13	8.22	12.0	+3.8
July 3 to 4	5	1155	1.020	315	8.60	1.99	1.243	.099	.321	33	8.37	7.08	.36	.03	.23	0	1.13	9.50	13.9	+4.4
July 4 to 5	6	605	1.022	363	7.35	2.17	1.249	.116	.254	39	7.78	6.62	.31	.07	.21	0	1.13	8.91	13.9	+5.0
July 5 to 6	7	850	1.020	350	8.70	2.07	1.079	.105	.255	44	7.36	6.63	.24	.04	.22	0	1.13	8.49	12.8	+4.3
Average . .	1 to 7	877	1.020	332	7.88	2.04	1.064	.098	.263	48	7.25	6.07	.30	.05	.22	0	1.13	8.38	12.5	+4.1

Urine acid in reaction to litmus on all days. No albumin or sugar detected. The microscopic examination generally showed a moderate number of epithelial cells and a few leukocytes.

Case III.—Mrs. M. McH. (Pellagra Commission No. 2, Spartanburg County).

Date.	Day.	Volume of urine.	Specific gravity.	Total acidity terms n/10 acid.	Chlorides as NaCl.	Phosphates as P_2O_5.	Inorganic sulphates as SO_3.	Ethereal sulphates as SO_3.	Neutral sulphur as SO_3.	Indican.	Total N.	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Fecal N.	Urinary plus fecal N.	Food N.	N Balance.
1912.		C.c.		C.c.	Gms.	Gms.	Gms.	Gm.	Gm.	Mgms.	Gms.	Gms.	Gm.	Gm.	Gm.	Gm.	Gms.	Gms.	Gms.	Gms.
June 9 to 10	1	505	1.022	456	3.46	2.01	1.243	.104	.203	98	8.30	6.65	.46	.07	.27	0	.54	8.84	8.4	— .4
June 10 to 11	2	267	1.029	328	1.90	1.46	.527	.093	.179	55	4.89	4.14	.21	.07	.22	0	.54	5.43	4.6	— .8
June 11 to 12	3	205	1.033	213	1.30	1.22	.731	.089	.127	93	4.93	3.99	.27	.05	.20	.01	.54	5.47	5.2	— .3
June 12 to 13	4	293	...	373	0.86	2.02	.952	.125	.133	102	7.37	6.00	.40	.04	.25	.05	.54	7.91	4.5	—3.4
June 13 to 14	5	285	1.030	208	0.96	1.16	.798	.132	.093	81	7.33	5.82	.32	.12	.20	.05	.54	7.87	6.2	—1.7
June 14 to 15	6	190	1.032	170	0.80	0.95	.547	.099	.067	65	4.38	3.89	.21	.06	.19	0	.54	4.92	7.2	+2.3
June 15 to 16	7	325	1.027	223	1.30	1.30	.547	.063	.138	49	5.46	4.26	.36	.03	.20	.05	.54	6.00	5.2	— .8
June 16 to 17	8	285	1.025	199	0.90	1.07	.608	.072	.085	32	5.16	4.06	.29	.03	.15	.04	.54	5.70	5.2	— .5
June 17 to 18	9	365	1.028	256	2.90	1.32	.861	.094	.093	75	6.20	4.98	.36	.05	.19	.11	.54	6.74	3.1	—3.6
June 18 to 19	10	315	1.030	198	2.90	1.03	.433	.095	.151	40	4.80	3.48	.41	.04	.19	.05	.54	5.34	0.8	—4.5
Average . .	1 to 10	304	1.028	262	1.73	1.35	.705	.097	.122	69	5.89	4.73	.33	.06	.21	.04	.54	6.43	5.0	—1.4

Urine acid in reaction on all days. No albumin or sugar present. The microscopic examination of the urinary sediment generally showed a moderate number of pus and epithelial cells.

Case III.—Mrs. M. McH. (Period 2.)

June 29 to 30	1	540	1.022	250	5.87	1.68	.911	.125	.186	108	7.15	5.91	.11	.10	.27	.03	1.36	8.51	9.4	+ .9
June 30 to July 1	2	290	1.030	183	2.10	1.04	.468	.099	.149	108	3.50	2.77	.21	.03	.17	.02	1.36	4.86	5.0	+ .1
July 1 to 2	3	267	1.031	216	2.40	1.29	.536	.134	.171	113	5.00	3.82	.25	.07	.22	0	1.36	6.36	6.2	— .2
July 2 to 3	4	350	1.029	103	4.20	1.18	.534	.128	.146	95	4.89	3.82	.17	.04	.21	.03	1.36	6.25	6.4	+ .1
July 3 to 4	5	270	1.031	..	2.20	1.68	.656	.100	.160	63	5.75	3.95	.95	.11	.27	0	1.36	7.11	9.0	+1.9
July 4 to 5	6	200	1.032	..	2.60	1.07	.351	.074	.131	63	3.10	1.49	1.06	.10	.18	0	1.36	4.46	4.6	+ .1
July 5 to 6	7	308	1.027	223	3.10	1.30	.582	.123	.135	84	4.72	3.59	.30	.05	.23	0	1.36	6.08	9.4	+3.3
Average . .	1 to 7	318	1.029	195*	3.21	1.32	.577	.122	.154	91	4.87	3.85*	.21*	.07	.22	.01	1.36	6.23	7.2	+1.0

Urine alkaline on fifth and sixth day, acid on other days. No albumin or sugar present. Urinary sediment showed uniformly a moderate number of leukocytes.
* Average data for acidity, urea, and ammonia do not include urines of fifth and sixth day.

Case IV.—Mrs. C. T. (Pellagra Commission No. 12, Spartanburg County).

Date.	Day.	Volume of urine.	Specific gravity.	Total acidity terms n/10 acid.	Chlorides as NaCl.	Phosphates as P_2O_5.	Inorganic sulphates as SO_3.	Ethereal sulphates as SO_3.	Neutral sulphur as SO_3.	Indican.	Total N.	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Fecal N.	Urinary plus fecal N.	Food N.	N Balance.
1912.		C.c.		C.c.	Gms.	Gms.	Gms.	Gm.	Gm.	Mgms.	Gms.	Gms.	Gm.	Gm.	Gm.	Gm.	Gms.	Gms.	Gms.	Gms.
July 7 to 8	1	1340	1.013	255	10.65	1.50	1.148	.194	.175	284	7.89	6.32	.48	.07	.32	0	1.49	9.38	11.5	+2.1
July 8 to 9	2	710	1.025	225	8.30	1.63	1.196	.195	.156	228	7.96	6.51	.36	.09	.28	0	1.49	9.45	10.9	+1.4
July 9 to 10	3	1135	1.018	252	10.74	2.04	1.259	.197	.207	187	9.05	7.37	.46	.08	.31	.03	1.49	10.54	12.9	+2.4
July 10 to 11	4	805	1.025	245	11.00	2.05	1.254	.170	.181	189	8.50	7.16	.41	.08	.30	0	1.49	9.99	12.9	+1.9
July 11 to 12	5	1780	1.015	284	15.78	2.45	1.491	.183	.264	176	10.89	8.84	.63	.06	.47	0	1.49	12.38	11.7	− .7
July 12 to 13	6	1720	1.020	281	19.44	2.55	1.498	.250	.122	227	10.45	8.74	.45	.09	.47	0	1.49	11.94	14.4	+2.5
July 13 to 14	7	1960	1.015	390	17.34	2.16	1.405	.175	.184	160	10.58	8.59	.47	.06	.33	.03	1.49	12.07	14.5	+2.4
July 14 to 15	8	1660	1.015	329	14.76	2.04	1.184	.190	.234	199	9.25	7.91	.57	.08	.31	.05	1.49	10.74	13.7	+3.0
July 15 to 16	9	1845	1.015	440	18.40	2.37	1.556	.192	.213	221	10.64	8.30	.64	.07	.36	.05	1.49	12.13	12.4	+ .3
Average . .	1 to 9	1439	1.018	300	14.05	2.09	1.332	.194	.193	208	9.47	7.75	.50	.08	.35	.02	1.49	10.96	12.7	+1.7

Urine acid in reaction to litmus on all days. Tests for albumin and sugar negative. Microscopic examination showed the presence of a few leukocytes and a moderate number of epithelial cells on the various days.

Case V.—Mrs. R. N. (Pellagra Commission No. 9, Spartanburg County).

July 7 to 8	1	820	1.020	235	9.90	1.67	.862	.016	.188	27	5.84	4.55	.34	.07	.20	.07	2.35	8.19	10.9	+2.8
July 8 to 9	2	530	1.027	363	6.95	1.96	1.053	.060	.128	48	6.75	4.93	.33	.10	.22	.11	2.35	9.10	10.6	+1.5
July 9 to 10	3	800	1.023	278	9.95	2.25	1.047	.064	.192	23	7.78	5.99	.30	.11	.23	.11	2.35	10.13	11.9	+1.8
July 10 to 11	4	980	1.018	330	11.00	2.30	1.084	.033	.142	33	7.11	5.61	.44	.09	.22	.08	2.35	9.46	13.2	+3.7
July 11 to 12	5	1575	1.017	279	18.72	2.41	1.200	.090	.232	59	9.21	7.00	.55	.07	.25	.09	2.35	11.56	11.6	0
July 12 to 13	6	1335	1.017	240	17.25	2.12	1.303	.053	.270	54	9.54	6.51	.37	.08	.23	.08	2.35	11.89	14.7	+2.8
July 13 to 14	7	1545	1.017	356	17.60	2.25	1.273	.059	.095	37	9.24	6.15	.46	.09	.23	.11	2.35	11.59	14.1	+2.5
July 14 to 15	8	1760	1.015	378	17.64	2.21	1.210	.050	.126	43	8.54	7.05	.45	.08	.24	.10	2.35	10.89	12.5	+1.6
July 15 to 16	9	1440	1.018	379	17.62	2.24	1.325	.107	.143	60	8.39	6.99	.49	.07	.24	.08	2.35	10.74	15.3	+4.6
Average . .	1 to 9	1198	1.019	315	14.07	2.16	1.150	.059	.168	43	8.05	6.09	.41	.08	.23	.09	2.35	10.40	12.9	+2.5

Urine acid in reaction to litmus on all days. Tests for albumin and sugar negative. The microscopic examination showed an occasional hyaline cast on the fifth day, and a few leukocytes and epithelial cells on all days.

Case VI.—Mrs. M. L. (Pellagra Commission No. 68, Spartanburg County).

Date.	Day.	Volume of urine.	Specific gravity.	Total acidity terms n/10 acid.	Chlorides as NaCl.	Phosphates as P_2O_5.	Inorganic sulphates as SO_3.	Ethereal sulphates as SO_3.	Neutral sulphur as SO_3.	Indican.	Total N.	Urea N.	Ammonia N	Uric acid N.	Creatinin N.	Creatin N.	Fecal N.	Urinary plus fecal N.	Food N.	N Balance.
1912.		C.c.		C.c.	Gms.	Gms.	Gms.	Gm.	Gm.	Mgms.	Gms.	Gms.	Gm.	Gm.	Gm.	Gm.	Gms.	Gms.	Gms.	Gms.
July 21 to 22	1	700	1.020	194	7.70	1.30	1.067	.110	.205	37	7.97	6.50	.40	.10	.30	0	.75	8.72	8.7	0
July 22 to 23	2	590	1.018	265	7.60	1.68	1.318	.125	.213	44	8.09	6.50	.40	.09	.28	0	.75	8.84	12.0	+3.2
July 23 to 24	3	1100	1.017	250	9.68	1.51	1.219	.127	.182	42	8.39	7.10	.49	.07	.26	0	.75	9.14	11.7	+2.6
July 24 to 25	4	1338	1.020	259	14.10	1.93	1.695	.192	.181	59	11.67	9.95	.63	.08	.31	0	.75	12.42	16.9	+4.5
July 25 to 26	5	1410	1.018	278	11.25	1.91	1.706	.218	.206	51	11.85	10.08	.50	.10	.29	0	.75	12.60	17.4	+4.8
July 26 to 27	6	1560	1.018	...	17.04	2 02	1.811	.164	.231	44	11.00	8.83	1.63	.09	.30	0	.75	11.75	17.8	+6.0
July 27 to 28	7	1440	1.017	...	14.60	2 03	1.551	.147	.189	37	10.26	6.81	1.66	.09	.29	0	.75	11.01	11.7	+ .7
July 28 to 29	8	1280	1.019	182	9.36	1.68	1.961	.125	.223	44	11.78	9.30	.90	.10	.34	0	.75	12.53	13.9	+1.4
July 29 to 30	9	1885	1.020	371	24.70	2.85	2.390	.135	.195	49	15.37	13.19	.62	.13	.36	0	.75	16.12	20.6	+4.5
Average . .	1 to 9	1256	1.019	257*	12.90	1.88	1.635	.149	.203	45	10.71	8.94*	.56*	.09	.30	0	.75	11.46	14.5	+3.0

Urine acid in reaction to litmus on all days, except the sixth and seventh Albumin and sugar absent. The microscopic examination of the urinary sediment showed a few epithelial cells and a moderate number of leukocytes.

* Average data for acidity, urea. and ammonia do not include urines of the sixth and seventh day.

Case VII.—Miss E. C. (Pellagra Commission No. 113, Spartanburg County).

August 5 to 6	1	1200	1.015	288	6.80	1.78	1 128	.162	.154	7	7.70	6.16	.44	.13	.31	.02	1.84	9.54	13.4	+3.9
August 6 to 7	2	1325	1.014	413	9.10	2.30	1 102	.127	.269	11	7.66	5.96	.55	.13	.31	.03	1.84	9.50	13.2	+3.7
August 7 to 8	3	1675	1.012	344	14.41	2.21	1 213	.153	.267	21	8.27	6.60	.43	.13	.33	.04	1.84	10.11	12.8	+2.7
August 8 to 9	4	710	1.020	215	7.00	1.33	782	.088	.272	18	5.41	4.34	.22	.11	.23	0	1.84	7.25	13.2	+5.9
August 9 to 10	5	1600	1.013	426	9.12	2.24	1 198	.152	.269	35	8.37	6.67	.43	.13	.37	0	1.84	10.21	13.3	+3.1
August 10 to 11	6	2560	1.010	416	10.92	2.63	1 420	.162	.293	32	9.64	7.83	.47	.12	.39	0	1.84	11.48	14.6	+3.1
August 11 to 12	7	1400	1.017	371	7.42	2.68	1 580	.183	.225	26	9.49	7.94	.32	.13	.35	0	1.84	11.33	13.2	+1.9
Average . .	1 to 7	1496	1.014	353	8.98	2 17	1.189	.147	.250	21	8.08	6.50	.41	.13	.33	.01	1.84	9.92	13.4	+3.5

Urine acid in reaction to litmus on all days No albumin or sugar detected. The microscopic examination showed the presence of an occasional hyaline cast on the first and seventh day and a few leukocytes and epithelial cells on all days.

Case VIII.—Miss M. T. (Pellagra Commission No. 114, Spartanburg County).

Date.	Day.	Volume of urine.	Specific gravity.	Total acidity terms n/10 acid.	Chlorides as NaCl.	Phosphates as P_2O_5.	Inorganic sulphates as SO_3.	Ethereal sulphates as SO_3.	Neutral sulphur as SO_3.	Indican.	Total N.	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Fecal N.	Urinary plus fecal N.	Food N.	N Balance.
1912.		C.c.		C.c.	Gms.	Gms.	Gms.	Gm.	Gm.	Mgms.	Gms.	Gms.	Gm.	Gm.	Gm.	Gm.	Gms.	Gms.	Gms.	Gms.
August 5 to 6	1	1220	1.018	319	11.44	2.23	1.670	.195	.257	88	11.50	9.24	.54	.13	.36	0	1.49	13.99	14.4	+ .4
August 6 to 7	2	1900	1.013	342	16.34	2.56	1.668	.172	.336	88	10.23	9.14	.56	.12	.38	0	1.49	11.72	15.5	+3.8
August 7 to 8	3	1445	1.017	356	13.50	2.53	1.815	.185	.402	165	11.04	9.52	.51	.13	.38	0	1.49	13.53	12.6	+1.1
August 8 to 9	4	2400	1.011	444	7.20	3.30	1.794	.156	.254	71	12.26	10.02	.62	.13	.45	0	1.49	13.75	12.6	+ .8
August 9 to 10	5	1430	1.016	307	9.30	2.57	1.908	.158	.264	60	11.50	10.00	.40	.18	.40	0	1.49	12.99	14.6	+1.6
August 10 to 11	6	1130	1.016	324	6.00	2.22	1.771	.135	.210	62	10.62	9.02	.47	.13	.33	0	1.49	12.11	11.6	− .5
August 11 to 12	7	580	1.027	283	5.00	2.54	1.464	.130	.237	77	8.18	6.65	.34	.11	.22	0	1.49	9.67	17.2	+7.5
Average . .	1 to 7	1444	1.017	339	9.83	2.56	1.727	.161	.280	88	10.62	9.08	.49	.13	.36	0	1.49	12.11	14.0	+1.9

Urine acid to litmus on all days. No albumin or sugar present. An occasional hyaline cast observed in the urinary sediment of the first day and a few leukocytes and epithelial cells on all days.

Case IX.—Miss L. G. (Pellagra Commission No. 115, Spartanburg County).

August 17 to 18	1	1320	1.012	330	5.40	1.44	1.042	.188	.215	94	7.66	6.13	.48	.09	.25	.02	1.47	9.13	10.7	+1.6
August 18 to 19	2	1017	1.016	255	6.00	1.74	.988	.196	.216	88	7.55	6.04	.27	.12	.26	.04	1.47	9.02	9.9	+ .9
August 19 to 20	3	780	1.020	303	6.60	1.65	1.125	.231	.187	110	8.33	7.05	.43	.12	.25	.03	1.47	9.80	12.1	+2.3
August 20 to 21	4	1260	1.015	419	9.90	1.98	1.362	.204	.217	82	10.04	8.24	.57	.13	.26	.03	1.47	11.51	15.4	+3.9
August 21 to 22	5	1860	1.014	365	13.00	2.50	1.435	.203	.214	104	9.91	8.47	.47	.11	.29	.03	1.47	11.38	13.6	+2.2
August 22 to 23	6	1360	1.016	349	10.00	1.85	1.309	.216	.183	88	9.21	7.62	.41	.12	.25	.05	1.47	10.68	15.7	+5.0
August 23 to 24	7	1910	1.015	380	12.80	2.18	1.558	.228	.334	98	10.52	8.71	.65	.12	.30	.02	1.47	11.99	16.6	+4.6
August 24 to 25	8	1640	1.012	385	11.60	2.00	1.383	.159	.296	93	9.73	8.14	.55	.09	.25	.03	1.47	11.20	16.8	+5.6
Average . .	1 to 8	1393	1.015	348	9.40	1.92	1.275	.203	.233	95	9.12	7.55	.48	.11	.26	.03	1.47	10.60	13.9	+3.3

Urine acid to litmus on all days. Trace of albumin detected on the first three days of period but not on days following. No sugar present. The microscopic examination showed occasional hyaline casts on the first five days and a few leukocytes and epithelial cells on all days.

Case X.—Mrs. M. S. (Pellagra Commission No. 21, Spartanburg County).

Date.	Day.	Volume of urine.	Specific gravity.	Total acidity terms n/10 acid.	Chlorides as NaCl.	Phosphates as P_2O_5.	Inorganic sulphates as SO_3.	Ethereal sulphates as SO_3.	Neutral sulphur as SO_3.	Indican.	Total N.	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Fecal N.	Urinary plus fecal N.	Food N.	N Balance.
1912.		C.c.		C.c.	Gms.	Gms.	Gms.	Gm.	Gm.	Mgms.	Gms.	Gms.	Gm.	Gm.	Gm.	Gm.	Gms.	Gms.	Gms.	Gms.
August 17 to 18	1	1640	1.011	173	10.03	2.17	1.112	.110	.492	25	10.90	9.16	.50	.11	.24	0	1.10	12.00	9.9	—2.1
August 18 to 19	2	675	1.020	172	8.55	1.76	1.001	.099	.402	18	6.44	5.10	.40	.10	.22	0	1.10	7.54	10.1	+2.6
August 19 to 20	3	525	1.025	162	6.45	1.51	.912	.118	.218	17	5.69	4.48	.38	.08	.19	0	1.10	6.79	9.0	+2.2
August 20 to 21	4	750	1.025	205	9.00	2.00	1.206	.130	.214	22	8.36	7.30	.35	.12	.23	0	1.10	9.46	12.0	+2.5
August 21 to 22	5	985	1.021	285	11.30	2.22	1.308	.132	.237	31	8.91	7.45	.55	.11	.23	0	1.10	10.01	12.6	+2.6
August 22 to 23	6	766	1.027	320	10.85	2.24	1.360	.118	.288	19	8.21	6.84	.55	.11	.23	0	1.10	9.31	13.8	+4.5
August 23 to 24	7	650	1.028	358	8.15	2.12	1.382	.098	.228	18	8.70	7.30	.48	.10	.22	0	1.10	9.80	13.0	+3.2
August 24 to 25	8	850	1.026	350	10.75	2.45	1.513	.133	.290	29	10.16	8.60	.46	.10	.25	0	1.10	11.26	14.0	+2.7
August 25 to 26	9	705	1.025	265	9.50	2.19	1.305	.109	.184	19	8.57	7.18	.49	.10	.22	0	1.10	9.67	12.0	+2.3
August 26 to 27	10	840	1.018	353	10.05	2.55	1.643	.139	.234	29	10.43	9.02	.51	.13	.24	0	1.10	11.53	14.6	+3.1
Average . .	1 to 10	839	1.023	264	9.46	2.12	1.274	.117	.279	23	8.64	7.24	.47	.11	.23	0	1.10	9.74	12.1	+2.4

Urine acid to litmus on all days. No albumin or sugar present. The microscopic examination showed uniformly a few leukocytes and many epithelial cells in the sediment.

Case XI.—Mrs. B. B. (Pellagra Commission No. 158, Spartanburg County).

August 23 to 24	1	1200	1.011	380	6.00	2.17	1.223	.137	.310	81	9.01	7.78	.32	.04	.20	.03	2.28	11.29	15.9	+4.6
August 24 to 25	2	800	1.016	377	5.10	2.12	1.292	.091	.218	31	8.07	7.02	.40	.06	.21	.01	2.28	10.35	14.6	+4.2
August 25 to 26	3	700	1.018	456	6.70	2.10	1.195	.100	.200	40	8.06	6 65	.46	.07	.22	.07	2.28	10.34	14.1	+3.7
August 26 to 27	4	840	1 018	368	6.20	1.94	1.303	.147	.240	84	8.36	7.10	.38	.04	.20	.02	2.28	10.64	15.4	+4.8
August 27 to 28	5	970	1.016	425	6.80	2.34	1.321	.085	.271	48	8.51	7.67	.44	.04	.21	0	2.28	10.79	16.7	+5.9
August 28 to 29	6	1200	1.019	450	8.90	2.37	1.465	.150	.340	110	9.78	8.51	.46	.04	.22	.01	2.28	12.06	18.7	+6.6
August 29 to 30	7	1200	1.020	438	8.90	2.43	1.442	.170	.310	101	9.71	8.43	.40	.04	.23	.01	2.28	11.99	17.1	+5.1
Average . .	1 to 7	987	1.017	413	6.94	2.21	1.370	.126	.270	71	8.80	7.59	.41	.05	.21	.02	2.28	11.08	16.1	+5.0

Urine acid to litmus on all days. Tests for albumin and sugar negative. Microscopic examination showed the presence of a considerable number of red blood cells and leukocytes on the first three days, and in addition an occasional hyaline cast on the fourth day, moderate number of leukocytes, epithelial cells, and uric acid crystals on remaining days.

Case XII.—Mrs. A. N. (Pellagra Commission No. 206, Spartanburg County).

Date.	Day.	Volume of urine.	Specific gravity.	Total acidity terms n/10 acid.	Chlorides as NaCl.	Phosphates as P_2O_5.	Inorganic sulphates as SO_3.	Ethereal sulphates as SO_3.	Neutral sulphur as SO_3.	Indican.	Total N.	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Fecal N.	Urinary plus fecal N.	Food N.	N Balance.
1912.		C.c.		C.c.	Gms.	Gms.	Gms.	Gm.	Gm.	Mgms.	Gms.	Gms.	Gm.	Gm.	Gm.	Gm.	Gms.	Gms.	Gms.	Gms.
September 12 to 13	1	2130	1.010	484	7.57	3.23	2.191	.124	.461	67	13.44	11.65	.40	.05	.26	0	1.41	14.85	18.2	+3.3
September 13 to 14	2	1613	1.014	429	7.82	3.04	2.061	.114	.559	83	12.45	10.33	.47	.05	.26	0	1.41	13.86	18.2	+4.3
September 14 to 15	3	2060	1.013	462	11.55	3.20	2.215	.130	.695	71	13.91	11.29	.40	.06	.24	0	1.41	15.32	16.4	+1.1
September 15 to 16	4	1625	1.014	442	8.50	4.01	2.022	.088	.385	0	11.68	10.05	.18	.06	.22	0	1.41	13.09	20.1	+7.0
September 16 to 17	5	1550	1.014	476	7.36	3.38	2.035	.116	.340	61	11.68	9.92	.40	.03	.24	0	1.41	13.09	15.4	+2.3
September 17 to 18	6	1825	1.014	418	8.55	3.07	2.230	.126	.329	67	13.15	11.08	.26	.05	.26	0	1.41	14.56	20.3	+5.7
September 18 to 19	7	2025	1.012	514	9.66	3.60	2.336	.170	.354	109	13.85	12.12	.38	.05	.28	0	1.41	15.26	16.8	+1.5
Average . . .	1 to 7	1833	1.013	461	8.71	3.36	2.156	.124	.446	65	12.88	10.92	.35	.05	.25	0	1.41	14.29	17.9	+3.6

Urine acid in reaction to litmus on all days. No albumin or sugar present. Microscopic examination of sediment showed a moderate number of leukocytes and epithelial cells on all days.

Case XIII.—Mrs. C. McC. (Pellagra Commission No. 170, Spartanburg County).

September 18 to 19	1	753	1.016	367	4.70	2.00	1.680	.170	.240	190	10.67	8.68	.74	...	.14	.13	2.70	13.37	16.7	+3.3
September 19 to 20	2	539*	1.021	...	4.20	2.33	1.245	.192	.175	291	8.23	6.64	.63	...	.13	.09	2.70	10.93	17.1	+6.2
Average . . .	1 to 2	646	1.019	367	4.50	2.17	1.462	.181	.208	240	9.45	7.66	.67	...	.14	.11	2.70	12.15	16.9	+4.7

Urine acid in reaction to litmus on both days. No albumin or sugar present. Microscopic examination of urinary sediment showed a rather large number of pus cells and a few epithelial cells.

* A small amount of urine was lost on this day, though a correction was made. As the samples following were incomplete they are not included.

Case XIV.—Mrs. W. L. (Pellagra Commission No. 166, Spartanburg County).

August 30 to 31	1	1810	1.014	...	13.58	....	....	....	....	57	13.15	10.70	.64	...	.30	.06				

Urine acid in reaction to litmus. No sugar or albumin present. Microscopic examination showed a few leukocytes and a moderately large number of epithelial cells.

V.

SOME HEMATOLOGICAL FINDINGS IN PELLAGRA.[1]

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Introduction. The material upon which the following report is based was obtained from cases of pellagra which were sent from the field headquarters of the Commission at Spartanburg, South Carolina, together with slide specimens of pellagrous blood taken from cases in South Carolina and forwarded for study to the New York Post-Graduate Medical School and Hospital during the summer and early fall months of 1912. In spite of the fact that the number of cases under consideration at that time was not large, nevertheless, it seemed advisable to record briefly the most important points in connection with the work that had already been done.

The blood was examined with a view of determining the hemoglobin content, the number of red and white cells per cubic millimeter, the differential leukocyte count, and at the same time the general morphologic characteristics of the blood in stained preparations. A few observations were also made on the coagulation time.

A review of the literature on this particular phase of the hematology of pellagra reveals an agreement of opinion in regard to the presence of a mild degree of secondary anemia of the chlorotic type without any marked structural or tinctorial alterations in the red corpuscles unless the anemia is pronounced. The majority of investigators state that the total leukocyte count varies, and that occasionally a leukocytosis exists which in most instances cannot be accounted for by the presence of a definite complication. The differential leukocyte count has apparently proved to be the most interesting and variable feature, and, judging from the available data, a fairly constant departure from the normal seems to be found in a large number of cases. Lavinder, in 1909, found "a relative large mononuclear increase with an absence of eosinophilia,

[1] Reprinted from the American Journal of the Medical Sciences, April, 1913, No. 4, vol. cxlv, p. 507.

except in cases with such complications as roundworms or hookworms." Sambon, working in Italy, also noticed a relative increase of the large mononuclear leukocytes. Contrary to these findings, Buhlig at the Peoria State Hospital, failed to demonstrate any increase in the large mononuclears. Bardin, quoted by Niles, found in uncomplicated cases of pellagra a lymphocytosis, with a corresponding reduction in polynuclears and a marked reduction in eosinophiles. Lavinder states that Fiorini, Gavini, and Masini in Italy found a decided eosinophilia. In the recent work of the Illinois Pellagra Commission no significant changes were observed in the differential leukocyte count.

Technique Employed. The blood was taken for examination in the midforenoon or midafternoon. The percentage of hemoglobin was estimated with the Sahli hemoglobinometer, two "readings" being made and the results averaged; this method was found quite satisfactory. The erythrocytes were counted with a Thoma-Zeiss apparatus, using a dilution of 1 to 200 and counting the corpuscles on the four corner "blocks" of twenty-five small squares in two drops. The average was then taken and the number of cells per cubic millimeter computed on this basis. In estimating the number of leukocytes a Zappert-Ewing chamber was used, thus affording an opportunity of counting 9 square millimeters in one drop. Two such determinations were made from a dilution of 1 to 20 in a "Rieder" pipet and the average taken; the usual calculation was then made. A difference of not more than twenty cells per field (high power) in the red count and eight cells per field (1 square millimeter, low power) in the white count was permissible. If a greater discrepancy existed a third drop was usually sufficient to rectify it, in either count.

For differential leukocyte counting films were made on clean, new slides, and a preparation selected in every case, on which the distribution of the corpuscles was moderately thin. Five hundred cells were counted over the midportion of each slide, care being taken not to encroach too closely on the ends, where frequently there is a relative increase in the more bulky leukocytes. The blood was stained with Wright's modification of Leishman's polychrome eosin-methylene blue mixture. The following classification was adopted: Polynuclear neutrophiles, small lymphocytes, large lymphocytes, large mononuclears, transitionals, eosinophiles, and mast cells. Differentiation between the small and large lymphocytes was to a certain extent unsatisfactory, inasmuch as intermediate gradations in size were occasionally encountered. Mononuclear cells measuring 12 to 15 microns in diameter, and having a comparatively wide zone of protoplasm, were classified as large lymphocytes; these were generally found to contain round nuclei staining not quite so intensely as the nucleus of the small lympho-

cyte. The large mononuclear leukocyte was recognized by its size, being two to three times that of a red blood corpuscle and containing a pale oval nucleus, frequently eccentric in position; the protoplasm was usually abundant, and feebly basic. It was realized that distinction between these two cells is a matter of no little difficulty, and depends to a large extent upon the personal equation, which forms an important factor in this much-debated question in the cytology of the blood. The reason for attempting to classify these types separately arose from the desire to ascertain whether the so-called large mononuclear leukocyte exhibited any relative or absolute variation from normal limits.

The patients examined were divided into two groups, A and B. Under Group A were included those cases that were under observation in the hospital at the time the examinations were made. These patients received no medicine, and were allowed a liberal diet. In Group A the hemoglobin percentages were determined, the red and white cells counted, and differential leukocyte counts made; this series of investigations is designated as "complete blood counts." As will be seen in Table I, several such complete counts were made on most of the cases. Under Group B (Table II) are included those cases in which only differential leukocyte counts were done, it not being convenient to make a more detailed examination at the time.

Analysis of Findings. In Table I the hemoglobin percentages show considerable variability, ranging from 58 to 107 per cent., with an average of 83 per cent. The erythrocytes are not markedly decreased, the lowest number being 3,920,000 per c. mm. As will be observed, several counts are 5,000,000 and over, the highest figures being 5,440,000. This occurred in the only male patient of the group, and was associated with a moderate reduction of the hemoglobin (65 per cent.). The patient was a poorly nourished individual, who was suffering from a mild attack of pellagra of about one year's duration. The majority of the members of this group appeared decidedly pale and anemic, according to general clinical criteria, and it was a matter of surprise to note the comparatively slight reduction in erythrocytes and hemoglobin that existed. The average red-cell count was 4,758,000 per c.mm. The color index was 1 or 1 plus in twelve determinations, the highest index being 1.3. In twenty instances it was under 1, the lowest being 0.6; the average index was 0.8. A careful examination of the stained blood films exhibited practically no changes in size, shape, or coloring of the red cells; nucleated corpuscles were never seen nor were there any staining variations from the normal, such as polychromatophilia and basophilic granulation. The average leukocyte count was 10,403 per c.mm., a trifle above the maximum normal.

TABLE I (GROUP A).—COMPLETE BLOOD COUNTS

No.	Date.	Sex.	Age.	Hemoglobin. Per cent.	Erythrocytes. Per c.mm.	Color index.	Leukocytes. Per c.mm.	Differential leukocyte counts. Polynuclears. Per cent.	Polynuclears. No.	Small lymphocytes. Per cent.	Small lymphocytes. No	Large lymphocytes. Per cent.	Large lymphocytes. No.	Large mononuclears Per cent.	Large mononuclears No.	Transitionals. Per cent.	Transitionals. No.	Eosinophiles. Per cent.	Eosinophiles. No.	Mast cells. Per cent.	Mast cells. No.	Stage of disease and clinical remarks.
	1912																					
1	June 4	F.	36	70	5,290,000	0.6	6,300	49.60	3125	40.00	2520	3.00	189	3.40	214	0.60	38	3.00	189	0.40	25	First attack, severe; duration, three weeks; watery diarrhea; strongyloides intestinalis numerous in stool.
	June 15			85	5,430,000	0.7	7,000	52.80	3696	27.20	1904	6.20	434	2.60	182	1.60	112	8.00	560	1.60	112	
	June 24			85	5,200,000	0.8	7,400	43.60	3227	40.00	2960	10.00	740	1.20	89	1.40	103	3.40	251	0.40	30	
	July 1			83	5,140,000	0.8	9,000	59.30	5337	24.60	2214	8.70	783	2.00	180	0.70	63	3.70	333	1.00	90	
	July 23			88	5,060,000	0.8	9,100	47.40	4313	42.00	3822	2.80	255	2.80	255	2.00	182	2.40	218	0.60	55	
2	June 4	F.	17	60	4,620,000	0.7	8,300	71.00	5893	18.00	1494	2.20	183	3.00	249	2.20	182	3.00	249	0.60	50	Recurrent attack, severe;[2] duration, three weeks.
	June 14			84	4,640,000	0.9	8,800	50.40	4435	33.40	2940	5.80	510	1.80	158	4.20	370	4.00	353	0.40	35	
	July 1			87	4,700,000	1.0	8,200	63.40	5199	21.20	1738	5.40	443	3.60	295	1.40	115	4.40	361	0.60	49	
3	June 4	M.	60	65	5,440,000	0.6	6,500	66.60	4329	24.00	1560	1.40	91	4.20	273	2.00	130	1.40	91	0.40	26	First attack, mild; duration, one year.
	June 12			98	5,040,000	1.0	7,100	55.80	3962	35.00	2485	1.60	114	4.40	312	1.40	99	1.60	114	0.20	14	
	June 19			95	5,000,000	0.9	8,000	55.00	4400	31.00	2480	6.75	540	2.00	160	1.00	80	3.75	300	0.50	40	
	June 25			93	4,900,000	0.9	7,200	62.00	4464	27.40	1972	4.80	346	2.00	144	0.80	58	2.60	187	0.40	29	
4	July 6	F.	40	105	4,000,000	1.3	8,000	41.15	3295	37.00	2960	13.35	1068	4.35	348	2.25	180	1.90	153	....	..	Recurrent attack, mild; duration, two and one-half months.
	July 16			100	4,560,000	1.0	7,200	55.00	3960	33.00	2376	2.20	159	4.20	303	1.60	115	3.60	259	0.40	29	
	July 27			102	5,100,000	1.0	10,000	45.50	4550	39.00	3900	8.20	820	5.50	550	1.30	130	....	...	0.50	50[3]	
5	July 6	F.	32	98	4,200,000	1.1	10,000	41.60	4160	42.30	4230	9.70	970	2.70	270	2.20	220	1.40	140	0.10	10	Recurrent attack, severe; duration, two months.
	July 16			102	4,250,000	1.2	8,000	50.20	4016	36.40	2912	5.40	432	3.20	256	0.40	32	4.40	352			
	July 27			107	4,400,000	1.2	11,000	56.50	6215	28.00	3080	6.50	715	5.00	550	1.00	110	3.00	330			
6	July 31	F.	18	88	4,800,000	0.9	9,000	69.00	6210	21.60	1944	4.40	396	1.80	162	1.40	126	1.80	162	....	..	First attack, mild; duration one month; no intestinal parasites found in stools.
	Aug. 8			86	5,000,000	0.8	14,000	60.20	8420	21.40	2996	5.60	784	3.40	476	1.40	196	7.80	1092	0.20	28	
7	July 31	F.	20	91	4,800,000	0.9	13,000	56.60	7358	37.20	4836	2.80	364	2.00	260	0.20	26	1.20	156			First attack, mild; duration, two weeks.
	Aug. 8			81	4,800,000	0.8	9,000	58.80	5292	32.00	2880	2.40	216	0.60	54	0.60	54	5.40	486	0.20	18	
8	July 17	F.	36	100	4,500,000	1.1	12,000	71.20	8544	15.00	1700	5.40	648	5.60	672	1.40	168	1.00	120	0.40	48	Recurrent attack, mild; duration, 3 weeks.
	Aug. 8			90	5,000,000	0.9	16,800	76.40	12835	16.20	2721	1.20	202	3.00	504	1.20	202	2.00	336			
9	Aug. 8	F.	28	78	4,800,000	0.8	10,000	60.00	6000	32.00	3200	3.00	300	1.00	100	1.00	100	3.00	300	....	..	Recurrent attack, severe; duration, 3 mos.
10	Aug. 4	F.	38	67	5,000,000	0.6	14,400	78.60	11318	17.20	2477	1.80	259	0.80	115	....	...	1.20	173	0.40	58	First attack, mild; duration, one month; chronic pulmonary tuberculosis.
	Aug. 17			70	4,320,000	0.8	11,000	66.25	7288	22.50	2475	2.50	275	1.00	110	4.50	495	2.50	275	0.75	82	
11	Sept. 7	F.	43	58	4,410,000	0.6	10,800	68.60	7409	26.60	2872	1.80	194	0.20	22	0.20	22	2.00	216	0.60	65	Recurrent attack, mild; duration, five months.
	Sept. 17			85	3,920,000	1.0	16,000	61.80	10358	32.00	5312	2.80	465	1.60	267	1.40	232	0.40	66			
12	Sept. 12	F.	34	65	5,400,000	0.6	18,000	72.60	13068	18.60	3348	3.20	576	1.00	180	2.40	432	2.20	396	....	..	Recurrent attack, mild; duration, four months.
	Sept. 24			100	4,380,000	1.1	9,100	61.30	5578	31.50	2866	3.50	319	1.30	118	1.50	109	0.90	73			
	Sept. 28			97	4,140,000	1.1	12,700	64.20	8143	26.40	3353	4.00	508	2.00	254	1.20	152	1.80	229	0.40	61	
	Average		33	83	4,758,000	0.8	10,403	59.13	4887	29.36	2828	4.63	446	2.59	252	1.50	144	2.73	263	0.34	31	

[2] The term "severe" implies the presence of gastro-intestinal symptoms, nervous manifestations, and extensive skin lesions.
[3] Two hundred and twenty leukocytes counted.

TABLE II (GROUP B).—DIFFERENTIAL LEUKOCYTE COUNTS ONLY.

No.	Sex.	Age.	Polynuclears.	Small lymphocytes.	Large lymphocytes.	Large mononuclears.	Transitionals.	Eosinophiles.	Mast cells.	Stage of disease and clinical remarks.
1	M.	23	52.80	34.40	1.20	1.60	1.00	9.00	....	Recurrent attack, severe; duration, one month; stools not examined.
2	F.	34	59.20	32.00	2.40	2.40	2.00	2.00	....	First attack, severe; duration, one month.
3	F.	30	56.00	32.00	3.40	1.00	0.40	7.20	....	Recurrent attack, mild; duration, two months; stools not examined.
4	F.	19	56.00	33.40	1.80	2.00	1.80	5.00	....	First attack, mild; duration, one month; no intestinal parasites found in stools.
5	F.	40	66.00	28.00	4.00	1.00	....	1.00	....	First attack, mild; duration, two months.
6	F.	35	69.80	23.60	2.20	2.40	0.60	1.20	0.20	First attack, mild; duration, one month.
7	F.	26	49.20	39.00	4.00	1.40	1.60	3.40	1.40	Recurrent attack, mild; duration, two months.
8	F.	21	50.00	40.20	4.20	2.60	1.20	1.60	0.20	First attack, severe; duration, one month.
9	F.	30	60.60	32.80	2.80	2.60	0.40	0.80	....	First attack, severe; duration, two months.
10	F.	38	58.40	31.60	4.00	1.60	2.00	2.40	....	Recurrent attack, mild; duration, two months.
11	F.	38	56.80	31.60	2.40	2.80	2.00	4.00	0.40	Recurrent attack, mild; duration, four months.
12	F.	30	51.20	36.40	4.40	2.40	2.40	3.20	....	First attack, mild; duration, two months.
13	F.	35	61.00	30.60	4.40	2.40	1.00	0.60	....	First attack, mild; duration, two months.
14	F.	36	56.40	35.00	4.20	1.40	1.20	1.80	....	Recurrent attack, mild; duration, two months.
15	F.	27	34.80	50.40	5.20	4.80	0.40	2.80	1.60	Recurrent attack, mild; duration, five months; recovering.[4]
16	F.	44	37.80	40.40	10.00	4.80	0.40	5.60	1.00	Recurrent attack, mild; duration, one month.
17	F.	32	47.60	40.40	5.20	1.20	2.00	2.60	1.00	First attack, mild; duration, three months; recovering.
18	F.	36	62.60	26.00	3.00	0.20	0.40	7.80	....	Recurrent attack, mild; duration, four months; recovering; no intestinal parasites found in stools.
19	F.	28	68.00	21.80	3.40	2.00	1.00	3.80	....	Recurrent attack, severe; duration, five months.
20	M.	25	62.00	27.00	6.00	....	1.00	3.00	1.00	Recurrent attack, mild; duration, three months; recovering.
21	M.	36	57.00	31.00	5.00	0.50	1.50	5.00	....	Recurrent attack, mild; duration, six months.
22	F.	34	50.00	33.00	8.00	5.00	1.00	2.00	1.00	First attack, mild; duration, one month.
23	F.	19	55.00	38.00	4.00	1.00	0.20	1.00	0.80	Recurrent attack, mild; duration, three months; recovering.
24	M.	35	50.00	41.00	5.00	3.00	1.00	....	....	First attack, severe; duration, two months; recovering.
25	F.	32	64.00	23.00	7.00	1.00	....	4.00	1.00	First attack, mild; duration, four months.
26	F.	26	56.00	32.00	8.00	0.80	0.80	2.00	0.40	Recurrent attack, mild; duration, two months.
27	F.	40	60.00	30.00	7.00	2.00	....	1.00	....	First attack, mild; duration, three months.
28	M.	22	54.00	38.00	6.00	1.00	....	1.00	....	First attack, severe; duration, two months.
29	F.	48	63.00	25.00	8.00	....	1.00	3.00	....	Recurrent attack, severe; duration, three months
30	M.	39	54.60	32.40	5.20	1.20	0.60	6.00	....	First attack, mild; duration, five months; stools not examined.
31	F.	40	58.00	30.00	6.00	3.00	....	3.00	....	Recurrent attack, mild; duration, four months; recovering.
32	F.	34	60.00	27.00	8.00	3.00	....	2.00	....	First attack, mild; duration, two months.
33	F.	17	37.50	44.00	10.00	4.50	0.50	3.00	0.50	First attack, mild; duration, two months.
34	F.	38	73.60	20.00	3.20	1.00	1.00	1.20	....	First attack, severe; duration, four months.
35	F.	22	58.20	28.60	7.20	2.00	1.00	3.00	....	First attack, severe; duration, one month.
36	M.	58	60.20	26.20	9.40	2.00	....	2.20	....	First attack, severe; duration, five months.
37	M.	8	54.40	32.00	9.60	2.00	1.00	0.60	0.40	First attack, severe; duration, three months; recovering.
Average		29	56.00	32.37	5.28	1.98	0.87	2.94	0.26	

[4] The term "recovering" means that the patient had no active signs or symptoms of pellagra when the blood was examined.

A slight or moderate leukocytosis existed in several cases at some time during their residence in the hospital. No complications could be discovered in these patients. One patient with chronic pulmonary tuberculosis and much emaciation had a leukocytosis of 11,000 to 14,000; she had an irregular temperature, not exceeding 100.2° F. All the other cases were afebrile, and frequently had subnormal temperatures.

The differential leukocyte count revealed an absolute polynucleosis in those cases associated with a leukocytosis of over 10,000, except in one instance. Three of these cases, however, showed a slight relative decrease in the polynuclears. Out of thirty-two differential counts in this group, twenty-four gave a relative and, in addition, an absolute lymphocytosis, including under this term both small and large forms of lymphocytes. The average total lymphocytosis of the series was 33.99 per cent. The average large mononuclear count was 2.59 per cent. The highest percentage recorded was 5.5 per cent. The transitional forms averaged 1.5 per cent. These last two types taken together (Ehrlich's classification) form 1 to 6 per cent. of the leukocytes in normal blood; therefore, from the above figures it cannot be said that they show any constant alteration from the normal. The average eosinophile count of 2.73 per cent. is within normal limits. A few cases showed slight eosinophilia, the highest being 8 per cent. in which patient *Strongyloides intestinalis* was found in the stools.

The coagulation time was determined in the first three cases with a Brodie-Russell coagulometer and was found to be six minutes and twenty seconds, four minutes and eight seconds, four minutes and twenty-five seconds, respectively, all of which readings are within the normal range for this instrument.

Table II. The differential leukocyte count on a series of slides taken from 37 cases at their homes in South Carolina was carefully determined without discovering any essential variation from the average results obtained in Group A. The average lymphocytosis of 37.65 per cent. is a little higher than in the previous group.

Summary. From a consideration of the above data it is evident that there occasionally exists in pellagra a variable degree of chloranemia, which, however, is not a prominent feature of the attack. The disease, apparently, may be present for some time without leading to any anemic changes. Whether the anemia is due to the actual existence of pellagra, or is the result of an indefinite train of antecedent conditions extending over a period of time before the inception of the disease, is difficult to say. On the other hand, many cases are perfectly well up to the onset of the attack.

One of the most noteworthy features in connection with the leukocytes is the not infrequent presence of a leukocytosis, which appears to be inexplicable in the light of our present knowledge of the disease. This might suggest the possibility of an infectious

etiology of obscure origin, or may be due to complicating disturbances. The lymphocytosis is interesting and is probably in accordance with the general cachectic condition of most pellagrins who are also often the subjects of gastro-intestinal disorders.

This investigation would seem to indicate that there are no characteristic or constant variations in the large mononuclear leukocytes and eosinophiles.

The writer wishes to thank Drs. P. S. Barrett, R. M. Brown, S. S. Irwin, and E. Kister, of the resident hospital staff, for assistance in making the blood examinations.

VI.

OBSERVATIONS ON THE INTESTINAL BACTERIA IN PELLAGRA.[1]

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A general survey of the fecal bacteria in pellagra was undertaken in 1910 and 1911 by the Illinois State Pellagra Commission. A brief summary of that work has been published[2] and the detailed record of the work has also recently appeared.[3] In general it was ascertained that the fecal bacteria in pellagra, when examined directly with the microscope, are different from the normal in their quantitative relationships, and that unusual kinds of bacteria, more or less heterogeneous in nature, are present. The cultural tests also brought to development unusual quantities of certain normal types, *Bacillus bifidus*, *Bacillus welchii*, and micrococci, in some cases, as well as a considerable variety of bacterial forms not ordinarily found in the feces of healthy men. None of these changes appeared to be constant. During the acute attack accompanied by diarrhea the Gram-positive cocci were nearly always abnormally numerous, and the Gram-negative bacilli were less numerous than normal in these cases. These changes were also observed in the subacute cases and even persisted to a slight degree after recovery from the skin lesions. The percentage of these cocci and bacilli are indicated in Chart I, along with data of similar observations on healthy men[4] for comparison. These changes, which were nearly constant, were such as might be expected as a natural result of the digestive derangement. There was no indication of a substitution of the normal intestinal bacteria by

[1] Reprinted from the American Journal of the Medical Sciences, June, 1913, No. 6, vol. cxlv, p. 801.

[2] Pellagra in Illinois, Arch. Int. Med., August and September, 1912, x, 123 to 168, 219 to 249

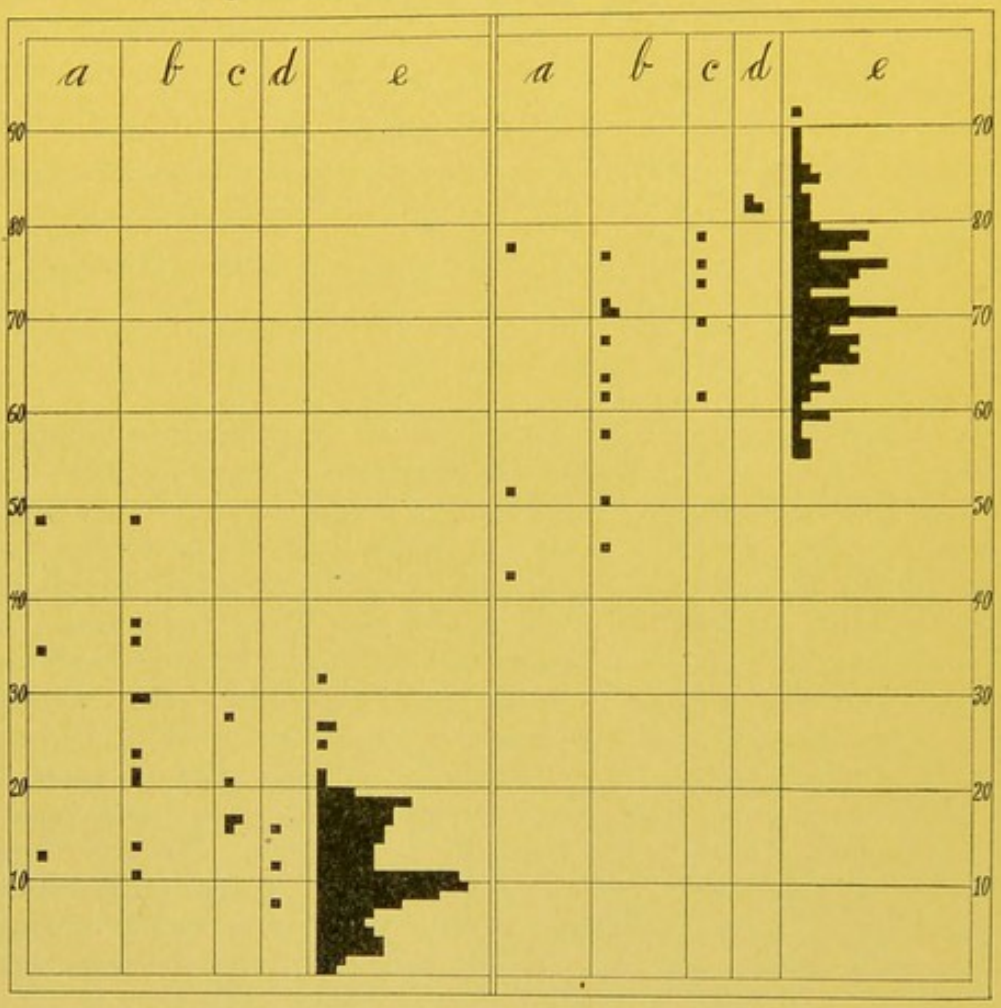
[3] Report of the Pellagra Commission of the State of Illinois, Springfield, Illinois, 1912.

[4] Jour. Infect. Dis., April, 1909, vi, 123 to 169.

an abnormal invader. The abnormal types were various in nature and in no case dominant in numbers.

During the course of the primary examinations subcultures were made from a number of colonies and preserved for subsequent study. One hundred of these bacterial strains were subjected to

CHART I.—Percentage of gram-positive cocci and of Gram-negative bacilli in the feces.



Percentage of Gram-positive micrococci and of Gram-negative bacilli in the feces: (*a*) three examinations in acute pellagra; (*b*) ten examinations in subacute pellagra; (*c*) four examinations after recent recovery from pellagra; (*d*) three examinations in insane individuals not pellagrins; (*e*) one hundred and thirty-seven examinations in healthy men. The data for *a*, *b*, *c*, and *d* are taken from MacNeal, Allison, and York, Report of the Pellagra Commission of the State of Illinois, Springfield, 1912, pp. 55 to 160, and the data for *e* from MacNeal, Latzer, and Kerr, the Fecal Bacteria of Healthy Men, Jour. Infect. Dis., 1909, vi, 123 to 169.

agglutination tests, using the blood serum from cases of pellagra and from normal individuals. Three of the one hundred strains reacted in a somewhat suggestive manner. These were strains Nos. 14, 35, and 67. All were derived from cases of pellagra at Peoria, Illinois. They were agglutinated by sera of pellagrins at Peoria, at Kankakee, and at Chicago. The suggestion of a specific

relationship to the disease was considerably weakened by the fact that these bacteria were also agglutinated by the sera of insane patients, not pellagrins, at Peoria and at Kankakee, and by the sera of apparently normal persons at Kankakee, Chicago, and Urbana, Illinois. Two of these bacterial strains, Nos. 14 and 67, appear to be identical in nature. The organism is a short rod about 4.0 μ long by 1.4 μ thick on the average. The size is variable, however, variations in length from 2.4 to 6.2 μ, and in thickness from 1.0 to 1.6 μ being observed in young vigorous cultures. Gelatin is not liquefied. In litmus milk the organism grows without producing an acid reaction. There is slight coagulation after four days and a slow digestion of the casein. No gas is produced in broth containing dextrose, levulose, lactose, saccharose, or maltose. Fresh cultures on agar are colorless, but later assume an orange color, and this production of pigment seems to become more pronounced with continued artificial culture. Strains Nos. 14 and 67 agree in all these characters, and strain No. 35 in all except the pigment production. It has remained colorless. Inoculation of animals (guinea-pigs, rabbits, and monkeys) has been followed by loss of weight, but has not resulted in the death of any animal.

Further study along these lines has been undertaken by the Thompson-McFadden Pellagra Commission at the New York Post-Graduate Medical School during the summer of 1912. The opportunity was here presented to test this culture against the sera of pellagrins from a different part of the country, South Carolina. These recent cases have been divided into four series: First, 66 pellagrins showing lesions on the skin at the time the blood was taken; second, 43 pellagrins who did not show an eruption at the time but in whom a reliable history of the disease was obtained; third, 22 individuals living in the pellagrous district, Spartanburg County, South Carolina, but free from any sign or definite history of the disease; fourth, 27 individuals in New York, including clinic patients and some physicians who kindly furnished their own blood for this work. The agglutination tests were performed by the macroscopic method, a suspension of the bacteria in salt solution being mixed with an equal volume of a 20 per cent. solution of the serum in a small tube for each test, the final dilution of the serum being one part in ten. It was incubated for an hour and the progress of events recorded at intervals of fifteen minutes. Complete clumping and precipitation of the bacteria to the bottom of the tube was recorded as a complete reaction. Grades of almost complete, marked, slight, and negative were also distinguished. The results are shown graphically in Chart II.

Of the 66 sera in the first series, from pellagrins with the skin eruption, 51 gave complete agglutination, 5 almost complete, 3 slight, and 4 negative reactions. The 43 sera of the second series

gave reactions distributed as follows: complete 30, almost complete 6, marked none, slight none, negative 7. Of the whole 109 different sera from pellagrins, 74.3 per cent. gave complete agglutination, 10.1 per cent. almost complete, 2.7 per cent. marked, 2.8 per cent. slight, and 10.1 per cent. negative reactions. The

CHART II.—Results of agglutination tests.

Results of the agglutination tests. Complete reactions (1) in solid black at the left in each series; then in order (2) almost complete, (3) marked, (4) slight, and (5) negative reactions.

22 sera of the third series, non-pellagrins of South Carolina, gave 5 complete agglutinations, 1 almost complete, 3 marked, 6 slight, and 7 negative reactions. The 27 New York controls gave 6 complete agglutinations, 3 almost complete, 10 marked, 1 slight, and 7 negative reactions. Of the total 49 controls, 22.5 per cent. gave complete agglutination, 8.2 per cent. almost complete, 26.5 per

cent. marked, 14.3 per cent. slight, and 28.5 per cent. negative results. These findings are obviously not sufficiently clear-cut to warrant the assumption of a specific agglutination reaction of this bacterium with the serum of pellagrins, and yet they are such as to stimulate further work along this line.

The conservatism of this statement is not due to the fact that we have employed serum dilutions of one in ten instead of higher dilutions, for many of these positive sera have been tested in higher dilutions, up to one in four hundred, and have produced definite agglutination in such strength. The suggestion of specificity is, however, seriously opposed by the fact that sera from apparently normal individuals give precisely parallel results in some instances.

We have attempted to employ the complement-fixation test on a number of sera, using an antigen prepared from a culture of strain No. 67. Positive results have been obtained in a few cases, but it has not been possible to try it in a sufficient number of cases to determine the value of the test. We are also attempting to perfect a precipitin test. We hope that it may be possible, by employing these in conjunction with the agglutination test, to obtain more decisive results during the coming pellagra season.

A few cutaneous and intracutaneous tests on patients were performed during the year of 1912, using a vaccine made from a culture of strain No. 67. Of the 9 patients to whom the cutaneous test was applied, 1 gave a moderate reaction, 3 a slight reaction, and 5 were negative. The intracutaneous test on the same 9 patients gave a marked reaction in 1; a marked and a moderate reaction in another case in 2 tests; a slight reaction in 3 cases; a slight reaction and a negative reaction in another case in 2 tests; and a negative reaction in the 3 remaining cases; 2 controls gave negative results, one of them in two tests. The behavior of the cases, especially those on whom the test was repeated, seemed to suggest a difference in the reaction according to the stage of the disease, but the cases tested are still too few to bear analysis along this line.

While these various experiments with this culture were in progress we have undertaken to isolate further bacterial strains from the intestinal contents of pellagrins brought to New York for study. These cultures have been isolated by the methods previously employed, more especially by plating on blood-agar and ascitic-fluid-agar, from the feces, and also from the intestinal juice obtained through the Einhorn duodenal tube; 693 new bacterial strains were isolated in this way during 1912, and these have been tested against sera of pellagrins and others in approximately 2000 agglutination tests. This work is not yet completed, but it seems certain that we have failed to isolate any germ similar to strain No. 67 from the feces of these new cases. From the duodenal fluid, however, a few strains have been obtained which

have given positive agglutination tests with the serum of cases of pellagra, and which seem to agree in their biologic characters, so far as they have been tested, with strain No. 67.

It is evident that this phase of the investigation is in an unfinished condition, and we do not wish to draw any definite conclusions at this time. This report will give an idea of one of the avenues along which we have approached the possible bacteriologic phase of the problem of pellagra, and indicates one of the lines we hope to follow during the present year.