It is a short step from vagotonia to another subject that increasingly demands our attention; namely, psychopathology. Whatever our preconceived ideas may be toward modern psychoanalysis, it is wise to discard them and to approach the subject with an open mind. Much can be learned as to the causes of the various manifestations of neuroasthenia, including nervous dyspepsia, by the method of approach which we owe to the psychoanalytic school. It is unnecessary at this time to go into further details on this subject. I am hoping, however, that students in medicine will not hear them be ignored without some knowledge of the psychoanalytic method and its language.

1350 Spruce Street.

Erysipelas

VIII. BACTERIAL ALLERGY TO STREPTOCOCCUS ERYSPELATIS IN RECURRENT ERYSPELAS *

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ROCHESTER, N. Y.

The frequency of recurrent attacks of erysipelas, combined with the difference in intensity and duration between the primary attack and the relapses supervening at short intervals, are factors which recently have suggested the existence of a state of bacterial allergy to account for the transitory duration of active immunity in erysipelas. The significance of bacterial allergy in scarlet fever has recently been seriously considered by many investigators who fail to account for the occurrence of the scarlet fever rash and symptoms on any other basis than that of bacterial allergy.

Allergic sensitization early in life to the products of *Streptococcus scarlatinae* is a view greatly strengthened by the convincing experimental data presented by Dochez and Sherman,1 Zinsser and Grinnell,2 Zinsser,3 Bristol,4 Mackie and McLachlan,5 Smith,6 and others who succeeded in inducing sensitization of guinea-pigs and rabbits with whole bacteria or their toxic products. Recently, Dochez and Stevens7 were able to demonstrate that rabbits immunized with filtrates of *Streptococcus erysipelas* showed cutaneous allergy of at least two distinct types: an early phase in which the allergic antigen could be neutralized by erysipelas antiserum and not by scarlet fever antiserum, and a late phase in which the allergic antigen failed to be neutralized by its homologous immune serum. In this article these authors corroborate an earlier expressed suspicion that the "rash in scarlet fever and the Dick reaction are apparently allergic reactions to products of *Streptococcus scarlatinae*." Dochez and Stevens logically infer a possible relationship of allergic reactions in scarlet fever and the toxic substance (Dick toxin) produced by *Streptococcus scarlatinae*. This is accomplished by calling attention to the fact that the Dick test is usually negative early in infancy. According to Cooke,8 negative Dick reactions occur regularly in infants not possessing scarlatinal antitoxin in their blood serum. These observations are in the main analogous with those made by Zinsser and Grinnell9 on the insensitivity of young guinea-pigs to pneumococcus autolyse. These authors found that the serum of such animals failed completely to neutralize the antigens when injected into naturally or experimentally hyperergic animals. Zinsser9 has recently suggested that it is "at least important to consider the possibility that sensitization to an organism (*Streptococcus scarlatinae*) which so frequently invades the human throat may take place and may thereby give rise to an allergic condition to which many of the manifestations of scarlet fever could be attributed."

The constancy with which *Streptococcus erysipelas* is present in the erysipelasous lesion during the acute phases of the disease and the indisputable specificity of this organism in erysipelas are facts which have rendered the problem of the determination of the absence of specific antibodies in recurrent erysipelas comparatively easy of demonstration. During the course of experimental sensitization of guinea-pigs to culture filtrates, autolyses, and living or killed hemolytic streptococci from erysipelas, I was able to corroborate the recent important work on that subject by Dochez and Stevens, previously referred to.7 These results will be published elsewhere. The following observations in erysipelas were accidentally made during the course of active immunization against recurrent attacks of erysipelas.

I have already demonstrated10 that during the acute attack of erysipelas the patient's blood serum and urine contain a toxic substance identical with that produced in vitro by *Streptococcus erysipelas*. When this toxic substance is injected intradermally in hypersensitive persons, a skin reaction is elicited which is similar to the Dick test in scarlet fever. This toxic substance is completely neutralized by the erysipelas antitoxin produced in horses by repeated injections of the toxic filtrate of *Streptococcus erysipelas*. I have also demonstrated during the course of erysipelas, circulating toxic substance disappears from the blood stream from six to twelve days after the onset of the disease. Coincidentally with the disappearance of the erysipelas toxin, a rapid concentration of erysipelas antitoxin appeared in the patient's blood serum. This antitoxin, when mixed with proper amounts of erysipelas toxin, completely neutralized the toxic effect of the latter. As long as the erysipelas toxin was demonstrable in the patient's blood serum, the patient's skin remained markedly hypersensitive to the intradermal injection of the erysipelas toxin. Simultaneously with the advent of erysipelas antitoxin in the patient's blood serum during convalescence, the patient's hypersensitiveness to the intradermal injection of the erysipelas toxin completely disappeared. At this time it was likewise difficult to isolate *Streptococcus erysipelas* from the lymph spaces of the resolved erysipelasous lesion. In other words, the toxin had been

*From the Department of Bacteriology, University of Rochester School of Medicine and Dentistry.
removed and in the presence of specific antitoxic substances the attack was brought to an end.

These observations were further corroborated when a careful study of patients suffering from recurrent attacks of erysipelas revealed that the specific antitoxic substances produced by the patient as a result of an attack of erysipelas completely disappeared from the patient's blood serum as soon as six weeks after the last attack. At this time the patient's skin suddenly became hypersensitive to the intradermal injection of the toxic filtrate produced by Streptococcus erysipelas. Although such patients did not experience any symptoms and signs of acute infection at this period, one may reasonably surmise that the cutaneous hypersensitivity reappeared at a time when the antibodies corresponding to the toxic antigen had disappeared. This suspicion was confirmed by a series of toxin-antitoxin titrations in which the patient's blood serum failed completely to neutralize the erysipelas toxin. Thus, when the patient's serum was mixed with definite amounts of the erysipelas toxin and the mixture subsequently injected intradermally in hypersensitive persons, large skin lesions developed as a result of the non-neutralized toxic substance.

The following case histories clearly illustrate on a larger scale the relationship existing between the products of Streptococcus erysipelas and the hypersensitive state obtainable in patients subjected to recurrent attacks of erysipelas.

**REPORT OF CASES**

**Case 1.—B. L.,** a woman, aged 48, had had her first attack of facial erysipelas six years before, at which time the erysipelas lesion began at the root of the nose and rapidly extended across both cheeks, involving almost the entire face, ears and neck. The attack lasted fourteen days. No complications followed. Twelve weeks after this attack, the patient sustained a relapse of erysipelas in the same areas previously affected. The second attack lasted ten days, and its severity was similar to that of the first attack. From this time until January, 1926, the patient had suffered from three to four attacks yearly, the erysipelas lesion always being confined to the face, ears and neck. The lesion was invariably at the root of the nose, and the attack usually lasted from eight to twelve days. The patient gave a definite history of each attack having been initiated by a severe cold in the head and sore throat.

Jan. 25, 1926, the patient was seen during the acute attack of a typical facial erysipelas. The face and forehead were greatly swollen and the edge of the erysipelas lesion had extended to the angle of the jaw below and slightly beyond the hair line above. The temperature was 103.1 F. and the pulse 110. The tonsils were moderately enlarged and deeply injected. On pressure, creamy pus was freely liberated. Before the administration of 10,000 units of erysipelas antitoxin, cultures were made of the erysipelas lesion by injecting sterile saline solution into the margin of the lesion and immediately withdrawing as much of the fluid as possible. This fluid was then mixed with blood-agar, poured into sterile Petri dishes and, after hardening, incubated for twenty-four hours at 37 C. Swab cultures were likewise made of the tonsillar pus, plated into blood-agar and incubated for twenty-four hours. Ten cubic centimeters of blood was also withdrawn from the patient's right basilic vein to determine the circulating toxin. Following the injection of the antitoxin, a critical drop in temperature and pulse rate took place within eighteen hours, and on the fourth day the patient was apparently fully recovered.

The blood taken from the patient on January 25 was free from any micro-organisms. When 0.1 cc. of the blood serum was injected intradermally in persons previously found to be hypersensitive with the toxin of Streptococcus erysipelas, a deeply injected and swollen area appeared about the site of injection, measuring about 3 cm. in diameter. A quantitative toxin determination of the patient's serum showed that 1 cc. contained more than 500 skin test doses of toxin. This toxin was completely neutralized by the erysipelas antitoxin produced in horses. January 28, about seventy hours after the injection of the erysipelas antitoxin, the patient's serum was free from any circulating erysipelas toxin. Simultaneously with the disappearance from the blood serum of the toxic substance, the patient's skin failed to react hyperergically with ten skin test doses of Streptococcus erysipelas toxin.

Both the smears and the poured blood-agar plates made from the fluid aspirated from the margin of the erysipelas lesion were free from micro-organisms. The cultures made with the pus from the tonsils and the contained erysipelas toxin were sterile. The nasal cultures did not show any hemolytic streptococci. Ten strains of the throat hemolytic streptococci were isolated from the blood-agar plates in pure cultures. Four of these strains agglutinated in high titer (from 1:1,280 to 1:2,560) with antiserums prepared in rabbits with Streptococcus erysipelas. These four strains were found to be strong toxin-producers (1 cc. = from 15,000 to 20,000 skin test doses). The erysipelas antitoxin neutralized all these toxins completely in high dilutions.

After convalescence the patient returned to the laboratory every two weeks for experimental purposes. In the course of these visits it was noted that on April 10 the patient's skin became hyperergic with ten skin test doses of the erysipelas toxin. At this time the patient's blood serum failed completely to neutralize small doses of the erysipelas toxin. The patient requested to be actively immunized with Streptococcus erysipelas toxin-vaccine. This toxin-vaccine contained 20,000 skin test doses of erysipelas toxin per cubic centimeter and about 5 billion killed erysipelas streptococci.

April 11, 0.1 cc. of the erysipelas toxin-vaccine was injected intramuscularly in the right biceps area. No immediate reaction was observed during the following two hours. The patient returned home. In the course of eight hours after the injection, she felt chilly and nauseated and vomited once. She retired feeling feverish and with general malaise. Two hours later she related that 'an intense itching and swelling spread rapidly over the entire face, closing both eyes, worse than in any previous attacks of erysipelas.' The patient was seen sixteen hours after the injection of the toxin-vaccine. She presented a typical case of facial erysipelas, having a definitely raised edge which spread in all directions across the face, forehead, ears and neck. The lesion was invariable at the root of the nose, and the attack usually lasted from eight to twelve days. The patient gave a definite history of each attack having been initiated by a severe cold in the head and sore throat.

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The blood taken from the patient on January 25 was free from any micro-organisms. When 0.1 cc. of the blood serum was injected intradermally in persons previously found to be hypersensitive with the toxin of Streptococcus erysipelas, a deeply injected and swollen area appeared about the site of injection, measuring about 3 cm. in diameter. A quantitative
sustained any recurrent attacks of erysipelas since active immunization was established.

Case 2.—H. M., a man, aged 31, with a definite history of recurrent attacks of erysipelas on the right leg every ten weeks over a period of two years, was seen, Jan. 10, 1926, during an acute attack of erysipelas of the right leg. The lesion extended from the dorsum of the foot to midway on the thigh. No abscess developed in the skin. Perspiring edema was marked throughout the erysipelas lesion. The patient complained of sore throat and nose, which he stated had always preceded each attack of erysipelas. Both tonsils were greatly hyper¬trophied and ragged in appearance. The crypts were very deep, and a thick, whitish yellow pus was expressed on slight pressure. The tonsils and faucial adenoids were both nates, and the tonsils were deeply injected. Intradermal cultures were made of the erysipelas lesion, both along the margin and centrally. These cultures were subsequently found to be sterile. Both tonsillar and nasal cultures contained an abundance of hemolytic streptococci. Eight tonsillar strains and eight nasal strains of hemolytic streptococci were isolated in pure culture. Of the eight tonsillar cultures, six were identified as typical type A erysipelas streptococci both by agglutination with immune erysipelus sera and by toxin production and its subsequent neutralization with the erysipelas antitoxin. Of the eight nasal cultures, five were identified by agglutination and toxin production as being true erysipelas streptococci. The patient’s blood serum was found to contain the antitoxic effect for erysipelas toxin and 1 cc. of the serum was found to contain about 400 skin test doses when tested on susceptible persons. After the usual preliminary bacteriologic and immu¬nologic studies, the patient was given 15,000 units of erysipelas antitoxin intramuscularly. During the following eighteen hours the temperature gradually fell from 103.1 to 99.5 °F, and in forty-eight hours the erysipelas lesion had completely cleared up. January 13, the patient’s blood serum was found to be free from circulating erysipelus toxin and at this time the patient’s skin failed to react positively with ten skin test doses of the erysipelas toxin. Convalescence was uneventful.

The patient was anxious to undergo active immunization with the vaccine in the hope of preventing relapses of the disease. January 25, 0.1 cc. of the toxin-vaccine was injected intramuscularly in the left biceps area. No immediate reaction followed within one hour of laboratory observation. About eight hours after the injection, the patient complained bitterly of nausea, perspiration due to fever and the beginning of a red swelling across the lower right leg. The patient was seen eight hours after the injection of the toxin-vaccine. The erysipelas-like lesion had now extended from the ankle to just below the knee. Pitting edema was most marked across the dorsum of the foot. No eruption was noted elsewhere on the body. The patient was perspiring freely, the temperature was 101.3, and the pulse rate 98. An intradermal culture of the lesion was found to be sterile. About ten hours after the toxin-vaccine injection the patient was to all appearance fully recovered, except for a slight residual tender¬ness in the left arm about the site of injection.

February 4, 0.1 cc. of the toxin-vaccine was injected intra¬muscularly in the right biceps area. Again the patient developed an erysipelas-like lesion on the lower right leg along the course previously affected. The pitting edema was very slight. The second attack was attended by a mild generalized malaise, which gradually came on about eight hours after the toxin-vaccine injection. The temperature was elevated to 100.5 and the patient perspired freely. Within sixteen hours the lesion had completely disappeared. Following the third dose of 0.2 cc. of toxin-vaccine, only small patches of redness developed over the lower right leg about ten hours after the injection. These eruptions were attended by a marked pruritus. Within a few hours the scattered lesions coalesced and then rapidly faded away without leaving any residual discomfort.

During the subsequent injections of from 0.3 to 3 cc., nothing untoward. April 5, five days after the last injection consisting of 3 cc. of the toxin-vaccine, the patient’s blood serum agglutinated with Streptococcus erysipelas in 1:640 dilution, and 1 cc. of the serum neutralized about 800 skin test doses of erysipelas toxin. The patient has been under observation for the last two years. During this time there has not been any return of the skin hypersensitiveness to the ery¬sipelas toxin and no recurrent attacks of the disease have developed.

Case 3.—S. T., a woman, aged 36, with a definite history of repeated sore throat and recurrent attacks of facial ery¬sipelas every fourth month for a period of three years, each attack being moderately severe and lasting about eight days, was seen, Jan. 26, 1926, during a moderately severe attack of facial ery¬sipelas. In most of the face, forehead, right cheek, right and right parietal portion of the scalp. One of the intradermal cultures of the erysipelas lesion showed Staphylococcus albus, but, since two other cultures taken at the same time remained sterile, the first culture was considered a contamina¬tion. Both tonsils were extremely swollen and injected and tonsillar cultures yielded a typical beta type A streptococci. Both ears showed no erysipelatous appearance. Eight strains of these streptococci were isolated in pure cultures and six of these were identified as Streptococcus erysipelas by agglutination, absorption and toxin-antitoxin neutralization. During the height of the erysipelas infection, January 27, 1 cc. of the patient’s blood serum was found to contain more than 500 skin test doses of erysipelas toxin. The patient responded favorably with 15,000 units of erysipelas antitoxin and within thirty-six hours the erysipelas had completely cleared away.

The course of active immunization was begun, February 8, with the injection of 0.1 cc. of the erysipelas toxin-vaccine. No untoward or sensitive effects were observed and 1 cc. of both sera was given. February 17, 0.3 cc. of the toxin-vaccine was injected intramuscularly. Eight hours after the injection the patient complained of having chills, followed by fever and frontal headache. She was compelled to take to her bed. Two hours later an erysipelatous-like eruption suddenly broke out over the entire face and the swelling increased rapidly, until in the course of an hour it was impossible for the patient to open the right eye. The course of the eruption was that observed during the previous attack, except that the lesion stopped abruptly at the hair line on the right parietal side. No eruption was observed elsewhere on the body. The temperature was 101.2 °F, and the pulse rate 108. Except for the hypertrophy of the tonsils, no redness or swelling was observed in the fauces. The skin overlying the area on the right biceps into which the toxin¬vaccine was injected was very tender, hot and flushed. The swelling gradually abated and, thirty hours after the onset of symptoms, the erysipelatous-like eruption had completely disappeared and the patient felt comfortable.

The mild and localized erysipelas-like eruptions continued to appear on the face, forehead and right ear following the injection of 0.2 and 0.3 cc. During the subsequent injections of 0.5, 0.8, 1.2 and 3 cc., nothing unusual developed except the slight local tenderness at the site of the toxin-vaccine injections. May 8, the patient’s blood serum agglutinated with Strepto¬coccus erysipelas in 1:40 dilution. The serum neutralized about 800 skin test doses of erysipelas toxin. The patient has been under observation for two years and has repeatedly shown negative skin hypersensitiveness to the ery¬sipelas toxin. She has not had any recurrent attacks of erysipelas.

Comment

During the last three years, sixty-eight patients with recurrent erysipelas have been actively immunized by means of gradually increasing doses of Streptococcus erysipelas toxin along with a mixture of the toxin and the killed streptococci. Although many of these patients have experienced the usual discomforts attending a course of immunization with bacterial antigens, in only six cases have I observed erysipelas-like eruptions along the routes previously affected by the relapsing attacks of erysipelas. Three of these cases have been studied carefully both bacteriologically and immunologically. The outstanding features have been: first, the recurrence of erysipelas in the identical anatomic positions previously affected or sensitized; second, the conspicuous absence of Streptococcus erysipelas from the lymph spaces within the erysipelatous lesion, where this organism is present in almost every case during the acute
stages of the disease; third, the isolation of *Streptococcus erysipelas* from distant foci of infection, such as the tonsillar crypts or the nasal recesses and the demonstration in the blood stream of erysipelas toxin produced from distant foci into the blood stream, and fourth, the development of antigenic substances following the injection of the erysipelas toxin-vaccine which subsequently immunize against recurrent attacks of the disease.

These instances of induced recurrent attacks of erysipelas naturally call to mind the Arthus phenomenon, or the "secondary reaction" described by Andrews, Derick and Swift. In the former phenomenon, Arthus observed that the subcutaneous tissues of the rabbit, by means of repeated injections of horse serum, can be sensitized and thus made to react so as to cause their destruction, the rest of the body meanwhile not showing any increase in sensitiveness. In the latter reaction, Andrews, Derick and Swift observed that rabbits injected intradermally with certain strains of green streptococci present well marked lesions which, after reaching a maximum size in from twenty-four to forty-eight hours, begin to regress, only to reappear in more than 50 per cent of these animals as a secondary reaction in the same areas about eight or nine days after the original inoculation.

However, the slow development of premonitory febrile symptoms and the subsequent eruption of erysipelas-like lesions from eight to thirty hours after injection of the erysipelas toxin-vaccine is unlike the immediate nonspecific protein shock reactions described by many workers in typhoid, rheumatic fever, and other diseases following the injection of a variety of such substances.

The recurrence of the strictly localized erysipelas-like eruptions within previously sensitized areas are decidedly unlike urticarial patches in their slow development from eight to twenty-four hours after the onset of febrile premonitory symptoms. These peculiar manifestations hold a closer relationship to the study of Dochez and Stevens or to the bacterial allergy to nonmethemoglobin-forming streptococci in rheumatic fever as recently described by me and confirmed by Kaiser, and further elaborated by Derick and Swift, and by Swift, Derick and Hitchcock.

On the other hand, one must consider seriously Durham's theory of relapses in erysipelas in relation to the cases presented in this paper. Durham holds that in erysipelas a particular strain of micro-organism predominates during the primary attack. Although effective antibodies may be produced to this variety of micro-organism and in that fashion bring the acute attack to an end, few or perhaps no antibodies may be produced to less abundant strains. Durham logically supposes that, for some unexplainable reason, micro-organisms of one or more of the several strains which previously remained latent in various foci during the primary attack, and to which little or no antibody response occurred during the primary attack, may now suddenly become active during convalescence from the first attack. By the sudden liberation of toxic substances during the active phase of growth of the secondary invaders, a relapse takes place. Durham holds that this process may repeat itself indefinitely with a great variety of micro-organisms and thus provide a possible explanation of multiple relapses in erysipelas.

Durham's ingenious theory of relapses in erysipelas seems precluded from consideration in the pathogenesis of the cases reported in this paper for the following reasons: the absence of *Streptococcus erysipelas* and of any other micro-organism in the erysipelas lesions; the repeated induction of erysipelas-like eruptions by injection of the bacterial products of *Streptococcus erysipelas*; the identity of the toxin circulating in the patient's blood stream during the height of the attack of erysipelas with the toxin produced in vitro by *Streptococcus erysipelas*; the ease with which repeated attacks of erysipelas were induced in previously hypersensitive persons with the products of the erysipelas streptococci, and, finally, the fact that repeated injections of the erysipelas toxin-vaccine developed sufficient antibodies to change the patient's hypersensitive state to an immune phase in which relapses of the disease also disappeared.

Although the observations reported in this paper conform perfectly well with the old conception of antigen-antibody reactions, certain phases of the ready production of recurrent attacks of erysipelas in previously sensitized anatomic positions distant from the site of injection of the bacterial products, and the absence within the erysipelas-like lesion of erysipelas streptococci, are facts which strongly suggest some form of bacterial allergy. Experimental studies by the Dicks, by Dochez and Stevens, and by Zinsser and Grinnell have clearly demonstrated that in the Dick toxin we possess a heat stable bacterial product which is both an excellent sensitizing antigen and a substance neutralizable by immune serum. These investigators have shown that animals subjected to repeated injections with the bacterial substance can be removed from the allergic state and rendered immune to the same bacterial product.

In view of the clinical data presented in the three cases of recurrent erysipelas here reported, it seems logical to me to believe that a state of bacterial allergy may possibly play an important rôle in certain cases of recurrent attacks of erysipelas.

**SUMMARY**

1. During the course of active immunization against recurrent attacks of erysipelas by means of gradually increasing doses of *Streptococcus erysipelas* toxin-vaccine, erysipelas-like eruptions developed in six persons in the identical anatomic location of previous attacks of erysipelas.

2. The erysipelas-like eruption developed slowly from eight to twelve hours after the intramuscular injection of the bacterial products, and the febrile state cleared up completely within from twenty-four to thirty hours of the onset of the symptoms.

3. Persistent immunization of such persons with *Streptococcus erysipelas* toxin-vaccine resulted in the development of immune substances which neutralized the erysipelas toxin and apparently immunized the person against recurrent attacks of erysipelas.
4. An unusual absence of *Streptococcus erythraeae* in the erysipelatos lesions of six persons with a history of recurrent attacks of erysipelas was observed, and the organism was subsequently isolated from nasal or tonsillar foci of infection.

5. The existence of a state of bacterial allergy to *Streptococcus erythraeae* products is suggested as a possible explanation of recurrent attacks of erysipelas strictly within previously sensitized anatomic areas.

**Crittenden Boulevard.**

**CHRONIC GLYCOPENIA**

A CLINICAL PICTURE, AN ANALYSIS OF ITS CAUSES AND SUGGESTIONS FOR ITS THERAPY*

**ERNST PRIBRAM, M.D.**

Professor of Pathology, University of Vienna and University of Chicago

CHICAGO

The knowledge of the clinical picture which is caused by the fall in the blood sugar level is of recent date. The administration of overdoses of insulin produces weakness, pallor, flushing and tremulousness, if the sugar content of the blood falls to 80 and 70 mg. per hundred cubic centimeters; when it falls to 60 or 55 mg. the patient becomes faint, anxious, excited and emotionally unstable; vertigo may be complained of; profuse sweating is common, and diplopia and incoordination may develop. With blood sugar levels between 50 and 40 mg. per hundred cubic centimeters the symptoms are accentuated, and sensory and motor aphasia, delirium, disorientation, delusions, confusion and bradycardia may occur. When the blood sugar drops to 35 mg. the patient becomes unconscious.1

The clinical picture presented by the chronic depression of the blood sugar standard is given little attention as yet and its causes are rarely understood. Cammidge 2 recently discussed the chronic hypoglycemia in a general treatise on this subject, without giving exact data and without referring to any literature. I too could not find any other literature as yet on the subject.

This paper deals with those cases only in which the level of the blood sugar is constantly low, not really subnormal (hypoglycemia), but around 80 to 90 mg. per hundred cubic centimeters. The name which I suggest for this last condition, which probably is more common than is supposed, is “glycopenia.” I have observed three cases within less than half a year and I am convinced that, in view of the clinical symptoms, it will be easy for any physician to find many more such cases in his private practice. The abbreviated records of these three patients follow:

**REPORT OF CASES**

**CASE 1.—Sister P.,** aged 36, had weighed 118 pounds (53.5 Kg.) eleven years before, but had lost weight gradually. She could not determine the time of the beginning of this loss, and could not allege any cause for her condition. Chronic constipation, occasional vomiting, general weakness and headaches were the clinical symptoms. When she first came into the hospital the weight was around 80 pounds (36.3 Kg.); the height was 5 feet (152.4 cm.). On account of her emaciation a tuberculin treatment was ordered and carried out, although no positive clinical symptoms could be elicited. Starting with 0.00005 cc. of old tuberculin, the dosage was gradually increased until she finally received 0.1 cc. after three months (December, 1927). No reactions other than a slight increase of the body temperature could be observed; occasionally headaches were complained of. She left the hospital about the middle of December and returned in the beginning of January. The body weight was then 78 pounds (35.4 Kg.). There was general weakness, inability to work or to even walk, vomiting, but regular menstruation. A thorough examination, like the first one, was without result. The attempt to get a metabolism test failed at that time. The patient, though very quiet, started to cry after a few minutes, and the test evidently resulted in too high figures. Later, the metabolism test on March 17 was minus 14 per cent. The blood sugar was 80 mg. per hundred cubic centimeters; the blood calcium, 13 mg.

**CASE 2.—Miss Mac B.,** aged 26, always a weak girl, never seriously sick but pale and tired, had been feeling weaker for a few years, in the morning more so than in the evening, and had suffered from chronic constipation, headaches and occasionally vomiting. Menstruation was irregular, at times occurring every third week, sometimes ceasing for months. The basal metabolism was plus 7.5 per cent; the blood sugar, January 8, was 90 mg.; February 29, 82 mg.; March 17, 79 mg., and March 31, after therapy, 100 mg.

**CASE 3.—Miss K.,** a resident nurse of the hospital, after a goiter operation three weeks before showed signs of hypoparathyroidism, such as tetany and vomiting. She improved with the administration of calcium and parathyroid gland. The clinical observations at present are enlarged thyroid gland, a slow pulse and general weakness, with sometimes vomiting. The basal metabolism is minus 7 per cent; the blood sugar, 80 mg., and the blood calcium, 12 mg.

**Diet Prescribed for Underweight**

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<td>2 slices buttered toast</td>
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<td>1 egg</td>
<td>75</td>
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<td>1 coffee</td>
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*The grand total of this diet is approximately 3,000 calories, which does not include anything the patient receives between meals or the sugar added from the tray. In addition to this, she drinks 100 Gm. of saccharose every morning. Later on, instead of saccharose, dextrose was given. The patient, who is very anxious to increase her weight, eats almost all her meals completely.

It was observed, therefore, that three patients with similar symptoms had a low blood sugar. The clinical symptoms of weakness, chronic constipation, vomiting and headaches were found in all cases. The body weight and the general development of the patients were different. Patient 1 was underdeveloped, 60 inches (152.4 cm.) high, with a subnormal body weight (80 pounds, or 36.3 Kg.) and a low basal metabolism (minus 14 per cent); patient 2 was normally developed, 63 inches (160 cm.) high, weighing 110 pounds (50 Kg.), with a slight hyperthyroidism, disturbances in menstruation, but a normal basal metabolism; patient 3 was a well built and well developed girl, 64 inches (162.6 cm.) in height and 133 pounds (60.3 Kg.) in weight, with a distinct hypoparathyroidism.

A sugar tolerance test was made in the first case: 100 Gm. of dextrose was given to the patient. After

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1 From Rush Medical College (University of Chicago) and St. Elizabeth Hospital.