nuclei, round and spindle-shaped. The arrangement suggests a resemblance to perineural connective tissue surrounding a nerve bundle in which there has been proliferation of the endoneurium with degeneration of the nerve fibers. Staining with polychrome methyl-blue fails to give the reaction for mastzellen. Unna considers the presence of the latter cells as highly characteristic of neurofibroma.

2. After staining by the Weigert method, careful search has failed to reveal any nerve fibers.

3. Vascular changes: The large arteries (Fig. 4) show nodular arteriosclerosis with thickening of the intima and some degenerative change in the media. More interesting are the changes in some of the medium-sized smaller vessels. By extensive subendothelial proliferation a wide zone of large cells is formed, surrounded by a rim of fibrous connective tissue, mixed in some instances with smooth muscle fibers. (Figs. 6 and 7.)

Examined in cross-section under a low power, the first impression produced is of a nerve bundle surrounded by its perineurium. But close study reveals a central lumen with endothelial lining in all the various areas of this character, showing the vascular nature. If the contention of Lahmann and others that the so-called neurofibroma may sometimes arise from the connective tissues of blood vessels is correct, may it not be possible that the lesions as described above represent an early period in the evolution of the growth?

4. Another histologic factor of interest revealed in the study of the specimen is the presence of non-striped muscular tissue within the fibrous cords.

DIAGNOSIS.

In its clinical aspects the case described seems to be one of plexiform neurofibroma; that is, a new growth arising from the connective tissue of a nerve trunk. Studied pathologically, this is not proved, although it is possible that such complete degeneration of the nerve fibers may have occurred that histologic origin may be difficult to trace. On the other hand, the contention of Lahmann and others that these growths may arise from vascular structures is supported by the following findings in the case: *

- (a) An absence of nerve fibers and of mast cells.
- (b) The arrangement of the strands parallel to and surrounding the arteries.
- (c) Extensive proliferation about the smaller vessels.
- (d) The presence of smooth muscle tissue in the tortuous cords which constitute the chief gross pathologic feature of the neoplasm.

ETIOLOGY AND PREVENTIVE TREATMENT OF SCARLATINAL NEPHRITIS.*

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PHILADELPHIA.

In presenting a paper on the etiology and prevention of scarlatinal nephritis, it is not my purpose to attempt any addition to our knowledge, but rather to emphasize the importance of already-known facts. In striving to control any morbid process, that system of therapeutics should be regarded as best which attempts the destruction of etiologic factors or seeks to mitigate their malign influences on the economy. In dealing with the acute infectious diseases the greatest advances have been made along the line of prevention.

This fact has received special emphasis in those diseases in which the habits of the several specific germs and their means of transmission have been carefully

studied. This has been notably illustrated in tuberculosis, diphtheria, malaria and, more recently, in yellow fever. Many diseases are rightly regarded as specific even in the absence of evidence sufficient to demonstrate any special organism as the active agent. Among diseases of this character scarlet fever stands pre-eminent. These diseases are best prevented by applying to them the same principles of isolation, disinfection and quarantine which are of value in preventing those maladies which are known to be specific. After the inception of such a disease, in the present state of our knowledge, our province is not to attempt to abort or to cure, but to recognize the possible complications and sequelæ in order that we may either prevent them or mitigate their severity. With respect to scarlatina this is especially true. The disease is self-limited and entirely uninfluenced by drugs. The formerly much-vaunted specifics, sodium benzoate, sodium salicylate, belladonna, etc., have been justly discarded as such. The greatest mortality and morbidity of scarlet fever must be accredited to its complications and sequelæ, which are more far-reaching and produce more human wrecks than those of any of the acute infectious exanthemata.

SCARLATINA AND NEPHRITIS.

Not the least interesting of these complications and sequelæ is nephritis. As humanitarians, as well as physicians, it becomes our function to note carefully the etiologic factors concerned in the production of this serious ailment in an attempt to apply such knowledge to its prevention.

The types of this affection are exceedingly variable. From a careful study of the urine it may be learned that, in the beginning, there occurs a form of albuminuria, sometimes associated with a few hyaline casts and epithelial scales, which is more or less common to the initial febrile stage of nearly all the acute infectious diseases. Then there is noted the acutely septic form of kidney disease which occurs as a complication in the very malignant cases which are rapidly fatal. So rapid is the course that suppression of urine and death from uremia occur here often without edema. This type of nephritis is perhaps best described as a part of a universal sepsis, the toxin of which spends its greatest force on the renal tissue. Occurring in varying degrees of severity we have also that well-known form of renal involvement which makes its appearance during the third and fourth week of the disease or after convalescence has been established. This is the so-called post-scarlatinal nephritis, and occurs with a more or less insidious onset, and unless detected early, may lead to serious chronic kidney disease. There is also met what may be designated recurrent intermittent post-scarlatinal albuminuria. This form has received little if any attention at the hands of medical writers, and yet its existence must have been noted by those who have had a greater clinical experience than I. This form of albuminuria occurs in many of those cases which have suffered from even a mild post-scarlatinal nephritis. It is influenced greatly by exercise and diet. Excesses in both these factors act as excitants of an attack, while a reduction in both is universally preventive and curative. The condition, in my limited experience at least, is compatible with apparently robust health. I have noted it at least two years after an attack of scarlet fever. I have not been able to detect tube casts associated with it.

ETIOLOGIC FACTORS.

Scarlatina is a disease peculiarly suited to the occurrence of nephritis. During an attack of this disease,

* Read before the Northern Medical Association, Oct. 27, 1905.

covering a period of from four to eight weeks, perhaps, there is, during the first half of this time, at least, almost complete destruction of skin function. In this manner the disease is not entirely unlike a severe burn of the first degree both in appearance and in its effect on kidney substance. The kidney, already overworked and overirritated, is thus forced to compensate for this loss of skin function.

Other important etiologic factors may be found in the increased toxicity and the increased acidity of the urine. Of the two the former is by far the more important. Whatever the real poison of scarlet fever may be, without doubt it is removed from the economy via the urine, and, unfortunately, it seems to possess a peculiarly irritant effect on the kidney. This statement receives color from the fact that from apparently the mildest attack of scarlet fever may follow the most serious and persistent attack of nephritis. In fact, J. Lewis Smith records a case in which a mother, previously known to be healthy, while nursing her son who was suffering from scarlet fever, complained of symptoms which led to a urinary examination which revealed albumin and casts. Smith regards this as a case in which the nephritis was the only symptom, and cites it as an example of the severely irritating effect of the scarlatinal poison on the kidney. The patient in this instance made a perfect recovery. The frequency and seriousness of kidney irritation has received emphasis from the work of Sørensen, who has demonstrated postmortem renal lesions in patients who exhibited no clinical features of the disease. This statement seems to prove that the irritant is local and produces the morbid changes early. In order to be local it must be in solution in the urine. J. Lewis Smith also cites¹ the cases of four girls in the same family who suffered from desquamative nephritis, after only one of the four had had scarlet fever.

The increased acidity of the urine can be readily determined by analysis. While not such a potent factor, its influence as a producer of kidney irritation can be readily assumed. It is probably the cause of the early albuminuria and, unless permitted to continue, does not cause serious degenerative changes in the renal tissue. The recognition of this fact has an important bearing on our efforts to prevent this affection. The relationship between the concentration of the urine and its acidity is a positive one, and therefore it, too, becomes an important etiologic factor.

Constipation, by preventing the escape of morbid material via the intestinal tract, thereby permits an increase of the toxins in an already overloaded urine. In this manner it may assume the rôle of an important contributory agent. The same may be said of diet. Dietary indiscretion may be nominated as the most important of any one single causal factor. This is especially true when highly organized proteid substances, such as meats, are too early added. These substances act by increasing the toxicity and the acidity of the urine.

The influence of cold can not be entirely disregarded. Its place, however, as a cause of scarlatinal nephritis has not been fully defined. In discussing this point Tyson remarks that "children have been found barefoot in the street with the eruption on them, and yet have escaped Bright's disease." In detailing the prophylaxis of the latter, the same author, however, proceeds thus: "Whatever may be the immediate cause of the renal involvement, it is certain that cold often becomes its exciting cause." Jacobi affirms that "exposure and sudden changes of temperature will always hold their place in

etiology, in the minds of those who do not forget to notice the living case besides the microscopic excrement." My own belief is that it is a factor of much importance in susceptible and anemic cases. The greatest danger lies in a poorly-regulated room temperature, sudden draughts and sudden chilling of the surface by careless bathing. By these means the blood is rapidly driven from the surface capillaries and intense congestion of the internal viscera results.

PREVENTIVE TREATMENT.

The patient should be placed in a well-ventilated room, the temperature of which should be about 68 to 70 degrees, and should be kept uniformly even. If possible, a room of southern exposure is to be selected. Draughts and sudden changes of temperature are to be avoided.

Diet.—A careful regulation of the diet is essential to the prevention of nephritis. The best diet for scarlet-fever patients is milk. It may be given modified to suit the age if the patient be a healthy bottle-fed baby. If a nursing, maternal milk should constitute the sole source of nutriment. The milk is to be secured with a breast pump. Older children may be given whole milk or milk diluted with a cereal water, lime water or Vichy. If digestion be weak the milk is best exhibited peptonized. However given, milk should be practically the sole article of diet for a period covering from four to six weeks or until desquamation is complete. Experience bears out the observation of Jaccoud that an absolute milk diet is of great service in preventing nephritis. Fruit juices serve a useful purpose by rendering the urine alkaline, and they are very refreshing. Toward the end of the period of desquamation freshly cooked tender vegetables, fruits and farinaceous substances may be cautiously added. Proteids may now be carefully given and only in small quantities. These are gradually increased in quantity and quality as tolerance is established. Throughout the course of scarlet fever, from the beginning, and, especially following each change in diet, the urine should be submitted to a careful daily analysis. On the appearance of the least trace of albumin a return to an absolute milk diet must be made at once.

Hydrotherapy.—Asked to designate any one single remedy which is of the greatest service in preventing scarlatinal nephritis, I should unhesitatingly name water. Its free and continuous use is indicated for the reason that, by increasing the amount of urine, it dilutes toxins and diminishes the acidity, thereby lessening kidney irritation. By stimulating catharsis and diaphoresis the elimination of toxins is facilitated. Water can be employed with advantage in three different ways: by mouth, balneotherapy and by enteroclysis, a combination of all these methods being productive of the best results. It is my practice to order a definite amount of water to be given with as much regularity as the food. It is best given between feedings. If plain water can not be readily taken use may be made of the various mineral waters as Poland or Celistin's Vichy, or, better yet, it may be exhibited as lemonade or orangeade. To a pint of either of the last two may be added, with advantage, a teaspoonful of cream of tartar.

A daily bath, given with friction, is a valuable adjunct. Aside from being the only means to be employed to reduce temperature, it increases the capillary circulation of the skin and thus relieves internal congestion. The bath must be given carefully, otherwise serious chilling of the surface will ensue and the purpose for which it was employed will be defeated. For this reason the full

1. From the *British Medical Journal* Nov. 29, 1879.

tub bath is best, the child enveloped in a blanket being completely immersed. A dry blanket is warmed and held ready to receive the patient when the bath is completed. This is followed by free diaphoresis. If the full tub bath can not be used, it may be replaced by sponging, care being taken to sponge only one part of the body at a time, while the rest of the surface is kept covered. The temperature of the water is regulated by the temperature of the patient. It should never be more than five or ten degrees lower. For young children and infants the warm bath is always desirable. Its effect on temperature is often amazing and the diaphoretic effect is always beneficial.

Enteroclysis is a valuable prophylactic agent. From one to eight ounces of normal saline solution should be thrown into the rectum to be retained once or twice a day. It lessens thirst, reduces fever, prevents constipation, lessens toxemia and allays renal irritation.

Medicinal.—The only drugs which are of any value in preventing renal complications are alkalis and laxatives. Urinary antiseptics possess little if any controlling influence. The administration of urotropin is useless and expensive. The salts of the organic acids as the citrate or acetate of potassium are changed to alkaline carbonates in the blood and are eliminated as such in the urine. They thus overcome the acidity of the urine, thereby destroying an etiologic factor of some importance. They are given in the dose of five to ten grains. From the beginning of the attack and throughout the course of the disease minute doses of calomel should be given at intervals of every three or four days. These are best followed by broken doses of magnesium sulphate conveniently dispensed as follows:

R. Magnesii sulphatis.....	gr. v-x	3-6
Ac. acetici diluti.....	m. v	3
Syr. zingiberis.....	m. xx	12
Aquæ dest. q. s. ad.....	℥i	30

M. Sig.: A teaspoonful every two or three hours in water.

Antitoxin.—As noted before, the specific organism of scarlet fever has not been determined. Of all the organisms found the streptococcus seems to be the one most often present. It is nearly always present in the discharge from an otitis media, and has been recovered from the renal tissue. For these reasons it is regarded by some authors as the primal cause of the complications. This view is accepted by Charlton, who, however, regards the presence of the streptococcus as the result of a secondary infection. For this reason he employs Moser's antistreptococcic serum early in the treatment of scarlet fever. Escherich and E. von Leyden comment favorably on the use of this serum for the control of the general symptoms, but assert that it does not influence the occurrence of complications. Moser himself believes that his serum has a beneficial influence on the grave forms of scarlatina, but that it does not prevent nephritis.

Pernicious Anemia.—Menetrier, Aubertin and Bloch report a case of essential pernicious anemia in which by feeding with red marrow and attention to general nutrition the number of red corpuscles increased from 680,000 to 3,000,000 in a short time. They conclude that in every case of grave cryptogenetic anemia, when there is a myeloid reaction, however feeble, it is advisable to try medullary opotherapy. In certain rare cases where the myeloid reaction is marked this treatment by reinforcing and regulating the efforts of the organism itself may cause an increase of the blood globules and at least a temporary cure. Where there is total absence of myeloid reaction this treatment is absolutely without effect.

Special Article

THE PHARMACOPEIA AND THE PHYSICIAN.*

SALINE CATHARTICS.

CHAPTER VIII.

A salt may be defined as a substance resulting from the chemie union of an acid with a base. For the present purpose we shall exclude from this classification salts of alkaloids and of other organic bases, and confine our definition to the popular conception of salts, or purgative salts.

The purgative salts, in contrast to the antiquity of many of the vegetable cathartics, are of but comparatively modern use, many of the inorganic salts being introduced into Europe by the Moors, but not coming into general use until after the time of Paracelsus.

Most of the purgative salts have a disagreeable, bitter taste, but when taken in an effervescing draught this bitterness is masked, and the effervescent salts have therefore come into great popularity. The widespread use of nostrums of this type, instead of the official effervescent salts prepared by the pharmacist, illustrates an unfortunate condition which exists without a sufficient reason. There is too much distrust of the pharmacist by certain physicians, who complain that pharmacists are unable to supply preparations equal to those of the nostrum-maker. This may possibly be true in isolated cases, but the proof to the contrary is furnished by the extreme simplicity of the preparation of the effervescent salts which the average pharmacist can prepare quite as well as the large manufacturer. Nevertheless the proprietaries of this class have an enormous sale.

It is unfortunately true that the physician often lacks confidence in himself and prefers to use the ready-made mixture rather than to exercise his own choice. This is degrading alike to medicine and to pharmacy.

It is a part of our present purpose to illustrate the ease with which the physician may choose his own agents in the proportion which seems best adapted to each individual case, with the assurance that any honest pharmacist can compound his prescription in a form equal in efficiency and elegance to the nostrums.

The preparation of the effervescent salts depends on the fact that tartaric and citric acids and sodium bicarbonate may be kept in contact without change when dry, but unite with effervescence when they are dissolved in water.

As an example of the ease with which effervescent salts are prepared, we give directions for making one, which, though extremely simple, is still the most complex of those which are official. The Effervescent Magnesium Sulphate. The same directions, with slight modifications, are used in preparing the other official granular effervescent salts and may be used when it is desired to include other salts or even caffeine and similar substances.

The magnesium sulphate is dried over a water bath, powdered and mixed with powdered citric and tartaric acids, then with the sodium bicarbonate; the mixture is heated to about 95 C. in a dish placed in an oven until it becomes moist; it is then rubbed through an ordinary tinned iron sieve (which forms it into granules). These are then dried at a temperature of 54 C.

Does it seem credible that any pharmacist is unable to make so simple a preparation as that?

Many of the nostrums that are offered to physicians as effervescent saline mixtures are not even granulated, and some of them, at least, depend entirely on the use of the cheaper tartaric acid and sodium bicarbonate to produce effervescence. Mixtures of this kind can be prepared extemporaneously quite

* We have received letters calling attention to an apparent discrepancy in the dosage of codein as given in Chapter II of this article, Dec. 23, 1905, p. 1953, and in Chapter III, Jan. 13, 1906, p. 118. In Chapter II, the dose is given as 1/20 of a grain, and in Chapter III it is given as 1/2 grain. In the first instance referred to it was the intention to give the dose of codein as 3 mg. (1/20 grain), when the drug is used as a sedative in expectorant mixtures. The average dose, of course, is generally double that of morphin, or 30 mg. (1/2 grain).