present representative, have of late been incorporating in some of their prescriptions for milk mixtures definite quantities of cereal jellies as expressed by percentage of starch. The ingenious experiments of Dr. Leeds of Hoboken, demonstrating the difference in coagulability of the casein between cow's milk and mother's milk, have stimulated our efforts to still further eliminate the casein without reducing the percentage of proteid substances. This we are attempting to do by replacing a large part of the rejected cow proteid with egg albumin. It has been claimed that egg albumin rendered the mixture unstable and that it could not be protected by Pasteurization because of its ready coagulability. We have not found these obstacles to the use of egg albumin to be insuperable, and are today employing the egg to replace the lact-albumin with satisfactory results. At my suggestion, our prescription blanks have been arranged for the addition of egg albuminoids when deemed advisable.

The milk laboratory, I believe, has come to stay.

ORIGINAL ARTICLES.

THE RELATION OF DISEASES OF THE SKIN TO GENERAL CONDITIONS.

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The modern division of the practice of medicine and surgery into many specialties has been a natural and legitimate sequence to the marvelous development of the science and the art of healing which has been made in late years. The sum total of medical knowledge in various lines has now become so great and extended that few if any can hope to compass and apply it to all satisfactorily in a lifetime; and the development of specialism in the medical profession (as in many other branches of science) has both contributed to this development and has facilitated the practical application of knowledge and experience along many lines. The advances which have been made in connection with medicine and surgery, largely by specialization of work, compare favorably with those obtained in other lines of human activity, even in this age of steam and electricity.

But, on the other hand, all thoughtful men must recognize that in this minute subdivision of thought and practice, and in the enormous aggregation of medical knowledge there is a lack of coördination in its practical application which at times results disadvantageously to the patient. Minute and concentrated attention to separate and individual lines of thought and practice has too frequently resulted in a narrowness of thought and practice, which has prevented the physician from properly recognizing, appreciating and applying many of the broader principles of medicine, which are so often of the utmost importance.

This is especially apt to be the case in connection with diseases of the skin, and yet in almost no branch of medicine is the error more serious; and the error has unfortunately spread from the specialist to the general practitioner, until lesions on the skin are now too often regarded as special and local affairs, quite unconnected with disorders of the general system.

The reasons for the neglect of internal conditions of the system in the practice of dermatology are not

difficult to discover. Much of the work in this branch has, of late years, been done by those who have devoted themselves to it exclusively, almost from their first graduation; they have had little or no practical experience in general medicine, and as their interest and study has been largely concentrated on the lesions visible on the skin, other broader relations of medicine have naturally become less distinct. The feeling that the skin affection is a local one is also largely shared and fostered by patients, who constantly urge that they are in perfect health, and only desire the removal of the local disease which gives them annoyance. Thus, it happens that more and more attention is localized on the portion of the body that gives offense, and varied local applications are used with more or less satisfactory results, and subsequently recommended to others. The profession is thus taught to look upon local measures as the only important feature of treatment.

It must be granted, however, that clinical experience often seems to give considerable support to the errors thus begun. For undoubtedly, very much can often be accomplished by correct and proper local treatment, and the cessation of this or that eruption under local applications does often seem to warrant belief in their great efficacy. On the other hand there is certainly often danger of error in this judgment. For it is possible, and indeed probable that very frequently the local or other exciting cause which produced the eruption has passed away, and thus the local lesion which was left yields readily to local treatment while the general systemic condition which predisposed thereto still remains; the skin then readily succumbs to a renewed irritant and the eruption recurs again and again, until the conditions of system at the bottom of it are removed. This is well illustrated by syphilis, where local mercurial or other treatment may be successful in removing local lesions, which will reappear again and again until the actual disease is overcome by proper constitutional treatment. In certain instances, as in herpes zoster, the eruption is quite self-limited, and so naturally ceases under any proper local application. How readily could a perfectly ignorant person be deceived on seeing the rash of scarlet fever, measles, chicken pox or variola cease after local treatment; the same error could occur in regard to eruptions excited by certain drugs, as quinin, belladonna, copaiba, etc., after the administration had been suspended.

But belief in a general local pathology and treatment for all diseases of the skin finds a still further support in the fact that there are certain lesions of the skin which are of a purely local nature, and yield readily to local measures alone. Such, for instance, are certain hypertrophic and atrophic diseases, and some new growths, as also the lesions caused by various local irritants and those produced by animal and vegetable parasites. But even in many of these very careful medical study will determine features or elements where the broad principles of general medicine should be applied. A striking illustration of this is found in ringworm in children, which will persist and luxuriate in those of weak constitution or exhausted by mal-nutrition, and yield much more readily when proper internal measures are instituted.

Finally, recent science has been claiming for the class of microbes an important place in the local causation of skin lesions. But it is more than ques-

tionable if, in many instances which have been claimed, they are more than accidental elements, or even the result, instead of the cause of the diseased process. In some instances, at least, it seems highly probable that the parasites generate and operate only because the soil is suitable and has been previously rendered so by other causes which can and should be removed.

I can not more forcibly illustrate my conception of the relations between local pathology and general causes than by reference to some facts in nature. For a long time it was unknown as to what was the real cause of a certain condition or disease in peach trees called "yellows." It is a disease which attacks the leaves, causing them to become yellow and fall off; the life of the tree is thus impaired, no fruit is produced, and before long the tree itself may die. Careful study finally demonstrated that the disease was caused by a fungus parasite invading the leaves, and thus arresting their vital action. Many and varied local remedies were thereupon advised, and much ingenuity expended upon methods of spraying the trees with various solutions destructive to the parasitic growth. While these means are all effective for a time in some cases, in other instances they fail to save the trees, while in many if not most trees the disease recurs again and again, requiring repeated and frequent applications. Finding local treatment to be but temporary and often ineffective, attention was then paid to other and more general points relating to the life and nutrition of the trees, and now, at the present time the best authorities advise, not the local treatment to the leaves, but improved nutrition to the tree, especially in the way of phosphates to the roots, even though it is yet recognized that the disease on the leaves is parasitic. The increased vitality of the tree enables it to resist the inroads of the parasites which, attacking first the leaves, finally destroyed the life of the tree itself.

At my country home I have a large virgouleuse pear tree which each year has borne a very great number of pears. But when about half grown the fruit becomes attacked by a fungus which thickens and hardens the skin of each pear, and they soon crack and dry up, so that hitherto for many years there has never been a single good pear ripened; the fruit is hardened with deep fissures, and never more than half grown. Finally, I began to systematically reduce the number of pears which were allowed to remain on the tree, removing a third or half of them when they were the size of a walnut, and before showing much signs of the parasite. The result was remarkable. A very great improvement occurred in the remaining fruit, which resisted the parasite very markedly, some of the pears attaining large size and ripening without being cracked and split as formerly. Another year I shall carry the process still further, removing a larger portion of the fruit very early, and the resulting vigor in the remaining portion will enable those that are left to resist the parasite still better. Thus we see the fruit yielding to the attack of the parasite when the strength of the tree was weak from overbearing and resisting it when a lessened quantity of fruit allowed greater vigor to be expended upon each pear.

One more illustration. On a very bad, hilly and stony field on my farm, which had run entirely to red sorrel and brambles, my farmer sprinkled a considerable quantity of wood ashes thickly across one corner.

In the following spring this portion was covered with a beautiful carpet of white clover, it forming a striking contrast with the rest of the field, although no clover seed was sown. This clover was reproduced for several years until the fertilizer was exhausted, when the weeds again gained the ascendancy and have remained in possession of the spot. We see here that with proper nourishment the clover seeds, which are everywhere present, grow luxuriantly, while with impoverished soil plants of a lower order assert themselves. All are familiar with the growth of moss, both upon dead and dying trees and upon those in poor damp ground, and shut in from sunlight, and how it disappears when the best conditions of life are secured; the mistletoe on the oak flourishes when the soil is damp and on the highest branches, where vitality is least.

Illustrations could be multiplied indefinitely to show the resisting power of health over the germs of disease, and yet the principle seems to be applied very little in diseases of the skin. They seem to be regarded on all sides as something peculiar and distinct from other maladies and subject to different pathologic laws. My plea is that the specialist and general practitioner should look at them more as other diseases are considered, namely as being largely evidences of lowered vitality and connected with faulty metabolic processes in the system. Time and space forbid me to develop the matter to its fullest extent. But this I do urge: That the patient should be studied in all aspects and treated more on the broad principles of general medicine than simply by the various local measures at the time in vogue, commonly with the addition of arsenic internally. It would surprise the profession could they but know how universally this remedy is given by the general practitioner when anything whatever is wrong on the skin, and it would be even a greater surprise to know to what a very slight extent arsenic enters into the treatment employed by those best acquainted with and most successful in the practice of dermatology.

Much could be written on the evils of narrowness of thought and practice in this branch of medicine, and many illustrations could be given of the harm resulting from not studying cases thoroughly and then treating the patient in the directions indicated thereby, instead of by local applications alone.

As well might the neurologist give temporary relief to headache or sleeplessness by sedatives or hypnotics without searching out and removing the cause; as well might the oculist seek to improve the eyesight by glasses alone when syphilis had altered the deeper structures; as well might the laryngologist only relieve a tuberculous laryngitis by topical applications without seeking to overcome the cause by hygiene and proper remedies; as well might the orthopedist only support a lateral curvature by braces and expect satisfactory results, without employing means to strengthen the weakened muscles on which the condition depended; as well might the gynecologist expect to get good results by local treatment in a leucorrhea which was dependent upon debility and constipation without relieving the underlying causes.

The proper treatment of certain diseases of the skin often involves the most extended knowledge and practice of general medicine; and he but poorly serves his patient who prescribes only a local treatment without fully going into the cause and rectifying, as far as may be, the systemic errors which often play a great part in its production and continuance.

It would lead us far beyond the proper limits of this paper to treat fully of all the possibilities which might be presented in connection with the subject under discussion. But I may be pardoned, even if I traverse ground well known to many, in pointing out some of the more common aspects of the subject, as they are presented to me in daily practice. I will, therefore, briefly indicate the lines on which investigation and therapy should be directed in connection with many of the patients presenting diseases of the skin.

How large a proportion of the ordinary run of cases may require general constitutional treatment can be judged from the fact that out of 10,000 miscellaneous skin cases in the writer's private practice, recently analyzed, over 6,000 or more than three-fifths of all belonged to five of the more common inflammatory diseases of the skin, all requiring more or less of general treatment; while there were even less than 1,000, or not 10 per cent. belonging to the three classes of new growths, hypertrophies and atrophies, and only about 10 per cent. of syphilis and parasitic diseases together.

To correctly understand and properly treat a large proportion of the general run of skin cases, therefore, there is need of the physician considering the patient, briefly though it may be, in reference to the action of his entire system. Some of the points to be regarded we will consider under the following heads:

1. Digestive system.
2. Renal system.
3. Cutaneous system.
4. Nervous system.
5. Circulatory system.
6. Respiratory system.
7. Sexual system.
8. Anemia, gout, rheumatism, syphilis, malaria.

1. *Digestive system.*—It is hardly necessary for me to dwell much on the importance of attending to the digestive system in skin patients, for all will immediately recall the intimate relations which every one must have observed between digestive derangements and the skin; and the subject of auto-intoxication from the products of mal-assimilation has received much attention lately at the hands of Bouchard and others, and merits the most serious consideration.

Urticaria and acne furnish, perhaps, the most striking examples of auto-toxic skin disorder, as they are constantly seen to follow promptly upon digestive disturbances. But the same may often be observed in eczema, while psoriasis will frequently be seen to be more active when these occur, and the itching of pruritus is always augmented thereby; falling of the hair may continually be observed to occur with each attack of dyspepsia and even syphilitic skin lesions will frequently appear aggravated when the digestive functions are disturbed. In many cases, however, the connection may not be very apparent at first sight, and it will sometimes require considerable persistence to establish the digestive derangement which is at the bottom of the difficulty.

Primary digestion, either atonic or fermentative, often due to errors in diet and hygiene, is not very infrequent in these patients, but secondary and intestinal indigestion is more common. It is almost needless to remark that the condition of the tongue often affords a most valuable guide in regard to these disorders, and should always be studied, even when the necessity of regarding this aspect of the patient's condition does not seem apparent at first sight.

Constipation in a varying degree is perhaps the most frequent derangement, and is often the source of incalculable mischief in skin cases. But even this may not be easily discernible, for many patients are ignorant of what should be the normal action of the bowels, or are too careless or unobservant to report correctly at first in regard to this function; the affirmative answer so often given to the routine question "Do the bowels act regularly?" will not infrequently be found to be a long way from the actual truth, medically; that is, if it is desired to determine thereby whether the bowels are performing their excretory function in a perfect manner. Far too little attention has commonly been paid to the character and quantity of this excretion, and it is well recognized that there may even be a daily discharge from the bowels while the most extreme state of constipation exists, with vast amounts of concretions past which fecal matter may find exit. Time and space forbid entering more fully into this portion of the subject, which, however, is of the utmost importance in connection with many cases of skin disease.

Liver disturbance plays an important part in many skin disorders, as it does in those of other portions of the system, and should always be considered and treated in this connection. The great value of small and repeated doses of calomel and of nitric acid in many conditions of the skin needs only to be seen to appreciate this point.

2. *Renal system.*—Next to the exhalation from the lungs, that of the kidneys is the most important of all the excretions, as far as relates to the life of the patient. Its total suspension for a day is fraught with great danger, for a much longer period it is death. Its derangement is both a cause and a sign of disease. At the present writing no account is taken of organic disease of the kidney, for practically this is not very often found among skin patients. But functional disorder of the urinary secretion is a most common occurrence among those presenting diseases of the skin, and will often prove to be a very important element in their treatment; careful investigation of this function should never be neglected in skin cases of any importance.

It is not possible to enter here largely into the consideration of all the changes which may be found, and their significance in different cases, for many pages would not suffice to cover the subject, and a few hints must suffice.

Not only may transient albuminuria and glycosuria be of importance, and the grosser appearance of the urates, uric acid and the oxalates and phosphates have their significance, but the bile salts and pigments and indican may point to disorders requiring correction, while the percentage of urea is always an item worthy of consideration. This latter constituent of the urine, urea, suggests what is perhaps the most important element to consider in this connection, namely, the total quantity of the kidney secretion in the twenty-four hours, not only as relates to the watery element, but mainly as to the total solids, or excrementitious products which are thus eliminated, for it has been shown that urea bears only a certain relation to the other solids and to the toxicity of the urine.¹

While the acidity and specific gravity of separate specimens of urine are often of some value in the guidance of the case, the true indications of the workings of the kidneys can only be obtained from a

¹ Transactions of the Medical Society of the State of New York, 1897.

knowledge of the total amount excreted in the entire day and the estimate thereupon of the solid excreta. When thus tested it will be found that many patients presenting obstinate affections of the skin suffer from an insufficient kidney excretion, either as to its watery or solid constituents, or both, the relief of which will prove of the utmost advantage in managing the eruption on the surface. The researches of Haig and others have shown also, I think, conclusively that the relations of uric acid to the system are of the greatest importance, and have much to do with the production of disease in the skin, as well as in other organs; although few will entirely agree with all that author has claimed in this direction.

3. *Cutaneous system.*—The importance of the skin as an emunctory organ and as a regulator of the heat of the body should never be forgotten, and its general condition should always be inquired into and appreciated in connection with skin cases. It is well known that many general diseases have their origin in a chilling of the surface, or check of perspiration, and the relations between the excretion from the skin and that of the kidneys is well recognized.

Therefore the general condition of the skin, its harshness or dryness, the tendency or not to active perspiration with heat or exercise, are all elements which have much to do with the general health, as well as with special eruptions on the skin. It is not at all uncommon for skin patients to present some of these departures from health in the general expanse of the skin.

With these may be mentioned the general appearance as to sallowness or vascular derangement of the skin. The condition of the subcutaneous and adipose tissues is also important, with which may be mentioned the weight of the patient, whether there has been loss or gain, etc. It may thus be remarked incidentally that the weight of the patient is an element to be taken into consideration in connection with the dosage of internal remedies, even as age is to be considered in the therapeutics of childhood.

4. *Nervous system.*—Many observations of most careful clinicians have demonstrated beyond question the intimate connection between many affections of the skin and the nervous system, and even in many eruptions which are not distinctly recognized as "neurotic" great benefit may result from a proper attention to this feature of the case.

Sleep is one of the most important elements to consider in connection with many diseases of the skin, for without proper and refreshing sleep it will often be impossible to effect much permanent benefit. As the writer has recently discussed this subject at length² it will not be necessary to enter upon it very fully on the present occasion. Suffice to say, that while in certain instances the disturbance of sleep, as by itching or pain, will be a marked feature calling for relief; in a far larger number of instances the faulty character of the sleep will only be learned after some patient investigation. Very often it will be found to be dependent upon errors of assimilation and occasionally upon circulatory disturbance; sometimes it is purely psychic, and it may be that even external causes can be found, which, by preventing full and refreshing sleep, have contributed largely to the continuance of the eruption. A case has recently occurred to me where the prolonged illness of a child so disturbed the father's sleep that this formed an

important element in the continuance of a neurotic eczema on the backs of the hands.

Headaches are a very common symptom in those coming for the treatment of skin affections, being often closely related to the disease itself, and should always receive solicitous attention from the physician.

Neurasthenia, or a general nervous debility, is also very frequently met with in these subjects, and must be overcome, as far as possible, in order to obtain satisfactory results in many cases. There are many points in this connection which could be easily and profitably enlarged upon, but time and space forbid. In approaching a rebellious skin affection, however, due consideration should always be given to the condition of the nervous system.

5. *Circulatory system.*—While this may seem of less importance than some of the other portions of the subject, its bearing in certain cases is often very marked. Digitalis and aconite, as representing the therapeutics of two very opposite conditions of the circulatory system, may often, with other kindred drugs, play a very important part in the treatment of some skin affections. Palpitation and flushing of the head and extremities, as well as cold and clammy hands and feet, are constantly met with in connection with many diseases of the skin, and must receive attention, either as indications of other disorders or on their own account. Purpura is an affection where blood vessel disease is strikingly exhibited.

The indications afforded by the pulse are most important in many patients affected with disease of the skin, and the time-honored practice of judging of the patient's general condition by the character of the pulse should never be neglected in this class of cases.

6. *Respiratory system.*—While relatively little is known as to the variations in the performance of the work done by the lungs, or their effect on the general system or special diseases, there are often features relating to the respiratory system which may be of much importance in connection with some skin cases. The most notable illustration is the occurrence of tuberculosis, in the patient or family, in connection with which we find lupus, tuberculosis cutis, and forms of scrofulous eczema, etc.

But certain other conditions of the respiratory tract are also not infrequently found to be associated with or even related to diseases of the skin; such are asthma, hay fever, bronchitis, catarrh, etc., and in certain instances their existence and continuance may have a very important bearing on the case. The occasional alternations of asthma or bronchitis with attacks of eczema and psoriasis is sometimes very striking.

Chronic catarrhal conditions of the upper air passages may be observed in a very considerable share of patients with eczema and acne, and the continuance of this causing (as well as indicating) disturbance of the digestive tract will aid in making the case rebellious. In this connection may be mentioned the breath, which by its varied and often offensive odor may indicate various deranged conditions both of the upper respiratory passages and of the alimentary canal.

7. *Sexual system.*—The common observation of the development of acne at the period of puberty in both sexes, as well as the increase of the eruption at each menstrual epoch in females, especially in those exhibiting any disorders of this function, call attention to the fact of the relation between the skin and

² The Medical Record, New York, Nov. 20, 1895.

the sexual system. Instances are also multiplying in literature where other eruptions have been found to be distinctly dependent upon such relationship, and the present writer is constantly meeting these in practice. Perhaps the most striking example of all is found in what is known as "herpes gestationis," where, with each recurring pregnancy an acute, intensely irritating papulo-vesicular eruption appears, vanishing abruptly after the uterus is emptied of its contents.

The condition of the menstruation is, therefore, a very important one to consider in connection with many diseases of the skin, and the various disorders of it will often be found to improve greatly with the carrying out of wholly proper treatment for the latter.

Not only should the character of the menses be known and appreciated, but often physical or other changes in the female generative organs may have their influences in diseases of the skin, and should be rectified. Leucorrhea is also always of great importance, both as a sign and cause of weakness, and its existence should always be known and the trouble remedied. Also in certain females there may be an amount of pruritus vulvæ, perhaps dependent upon the leucorrhea, which may so depress the patient and prevent sleep to such an extent, as to prove a hindrance to the cure of the skin affection.

The occurrence of acne at puberty in the male, as already mentioned, shows that the sexual organs in this sex also have some, though less, influence on the skin. But the connection between stricture of the urethra and herpes genitalis and pruritus ani is also well recognized; and undoubtedly masturbation can cause rebellious acne. Sexual excess can likewise influence unfavorably many eruptions.

8. There remain yet several more general matters requiring consideration in patients with diseases of the skin. These are: 1, *anemia*; 2, *gout and rheumatism*; 3, *syphilis*, and 4, *malaria*.

1. *Anemia* is a fertile cause of many skin complaints, as it is constantly observed that many eruptions return whenever this state recurs; it should, therefore, always be recognized and treated when present. It is, of course, not infrequently associated with, or dependent upon derangements of some of the systems of the body which have been already considered, but very often it is due largely to erroneous diet and hygiene; the latter should always be very closely looked into and cared for in patients with diseases of the skin.

2. *Gout and rheumatism*.—These, as well as certain diseases of the skin, are often only the expression or result of some of the systemic disturbances which have been already considered; but as they may be such definite and commonly well-marked conditions, and represent such a well-recognized train of systemic changes, it is well always to know whether they have been present in the patient or his ancestors. Much has been written in regard to the part played by uric acid in many diseases, and it is certain that the recognition of the lithemic state, or *uricacidemia*, is of very great importance in connection with certain diseases of the skin. Whether we are to look upon the uric acid itself as the real cause of any of these troubles is still somewhat of an open question; certain it is, however, that it forms one link in the chain, or one easily demonstrable sign of the faulty metabolic process which may result in gout and rheu-

matism. Hence these diseases are important to recognize and treat in connection with many diseases of the skin. The beneficial results from the internal administration of salicylate of soda in some of them points strongly to a connection of this nature.

3. *Syphilis*.—This great poison has reached out until it has influenced countless lives, and today is represented by nearly 10 per cent. of all cases which come to public skin clinics, or appear in private dermatologic practice. It should, therefore, always be considered in all its possible bearings on this class of cases; although, fortunately by practice its features can generally be recognized without much mental effort and without much interrogation of the patient. But, on the other hand, caution is necessary not to suspect this cause too strongly in skin cases, for, as remarked, less than one-tenth of all cases are of this nature. When present, and properly treated, the results in this class of patients is most satisfactory whereas, if unrecognized, but little benefit can result from local or wrong internal treatment.

4. *Malaria* is regarded by some as productive of many skin diseases, and certain cases of urticaria are unquestionably of this nature, and cured only by quinin in efficient doses. It is certain also that by its depressing effect and by the liver and other disturbances which it may cause, it can act prejudicially in many diseases of the skin. It should always be looked for and treated when present.

There is very much more which could be said with advantage, both in connection with the points already considered and with many other items pertaining to the general medical relations of diseases of the skin. But already this paper has probably far exceeded what many would have expected from the subject. Enough has been said, however, to show that dermatology is an important study, not only because of the great interest which the varied conditions of the skin may present, but also on account of the very many vital relations which they may bear to other disorders of the economy.

It is quite probable that much that has been said is entirely familiar to many present, but, unless I am much mistaken, these principles are not universally put in practice in connection with the ordinary treatment of diseases of the skin. As remarked at the opening, local therapeutics has been so much advocated and arsenic is so universally believed to be "good for diseases of the skin," that the former are too often pushed to an unreasonable extent and the latter is too wholly relied on. In many, many instances, as my notes of cases abundantly show, Fowler's solution has been the only internal remedy which had been previously prescribed, even when proper investigation showed the most palpable departures from health, which were of the greatest causative importance to the eruption.

To be a good specialist in dermatology, or in any other specialty, one must be a good general practitioner. The specialist who confines his study and thought only and exclusively to his own branch, and can not or does not embrace the entire field of general medicine, can never succeed in the highest degree, and certainly can not serve his patients in the best manner possible.

I beg to assure my hearers that all this has not been written in any captious spirit, nor from any theoretical standpoint. All that has been said comes from the practical experience of over a quarter of a century

contact with just such conditions as have been mentioned, and all is written from a profound feeling and belief that only by proper attention to the matters here indicated can the most good be done to those coming under our care with many of the diseases of the skin.

4 East Thirty-seventh Street.

DIABETIC COMA AND THE TREATMENT OF DIABETES MELLITUS.

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The disease diabetes mellitus has long furnished the science of medicine with some of its most difficult and obscure problems, one of the most interesting of which is that symptom-complex called diabetic coma, which in many instances brings this affection to a fatal termination. It was at first believed that this condition was induced by an effusion of serum into the arachnoid but later investigations failed to confirm this theory. The idea was then advanced that the phenomena of diabetic coma were due to the action of some toxic body on the organism and a large number of substances have from time to time been considered as the essential factors in the production of this condition. Urea was long believed to play an important part in this as in other affections characterized by marked nervous and cerebral symptoms. Repeated experiments have shown, however, that if free diuresis is maintained, as is the case in diabetes, it is almost impossible to produce any untoward symptoms by the injection or ingestion of this body. It has been repeatedly shown that urea, under such conditions, is no more toxic than common salt. Frerichs then advanced the theory, on observing the presence of large quantities of ammonia in the urine previous to or during the occurrence of coma, that coma was produced by a so-called ammonemia, the ammonia being produced from the urea by an abnormal ferment by which it is broken up in the production of ammonium carbonate. Experiments on animals, however, showed that enormous quantities of alkalies could be tolerated by the system without the production of any severe symptoms, although it was possible to produce convulsions by the continued injection of large amounts of alkalies. About the same time Petters (*Prager Vierteljahrsschrift*, 1857, III, S. 81) noticed the occurrence of acetone in the urine of certain cases of diabetes and believed that this body was the cause of the peculiar odor of the breath and urine in certain cases of this affection. Acetone, however, is by no means present in a large proportion of cases of diabetic coma and is symptomatic rather of the early stages of diabetes. It was soon shown by Kussmaul that doses of from 4 to 6 grams continuously administered had no harmful effects whatever. Experiments by the writer showed that single doses reaching as high as 36 gm. had but slightly stimulant and intoxicant effect upon the system.

Gerhardt (*Wiener Medicin. Presse*, 1868, No. 28) then discovered a reaction which he believed to be due to the presence of ethyl aceto-acetate, a body which was soon shown to possess no toxic properties whatever. It was then advanced that ethyl aceto-acetate was toxic from the free acetone which it yielded in its decomposition, but the harmlessness of the latter body in the system was soon after demonstrated,

while later proof that ethyl aceto-acetate did not exist in diabetic urine showed the entire falsity of this theory. Diacetic acid, the body which gives the well known reaction with ferric chlorid in the urine of these cases, was soon after discovered by Tollens and more completely investigated by Jaksch ("Ueber Acetonurie und Diaceturie," Berlin, 1885), who in almost every case of diabetic coma was able to demonstrate its presence in the urine. He believed that it was formed in the intestine by the union of acetone and formic acid and attributed to it the production of diabetic coma, in what way he was unable to state. Experiments on animals and men, however, made by Frerichs and Kussmaul (*Deutsch. Arch. für klin. Med.*, 1874, S. 11) have shown that 10 to 20 gm. of this acid could be given in health without the production of any grave toxic symptoms and that it therefore possesses no poisonous properties in itself. It is interesting to note that after the administration of such large doses of this acid none whatever appeared in the urine although considerable amounts of acetone were present, thus showing that in the healthy organism a higher oxidation of this acid takes place.

About this time investigations made by Coranda and Halleworden proved that the ammonia in the system fulfills two functions: 1, to contribute to the formation of urea, and 2, to neutralize all acids introduced into the system or produced there in the metabolism of the organism. It was also demonstrated by them that the ammonia excretion furnished an exact estimation of the acid out-put. On extending these researches to various morbid processes it was found that in certain fevers, etc., there was a great increase in the ammonia excretion, the patients becoming carnivorous by feeding upon the albumins of their own systems. In diabetes especially very large ammonia excretions were noticed, showing that in such cases there was a great excess of acid produced in the system which was neutralized by the available ammonia of the organism. At this point Stadelman, Minkowski and Külz discovered in the urine of diabetics with a large ammonia excretion an acid heretofore unknown, which was found to be identical with beta-oxybutyric acid. It was noticed that patients with a large ammonia excretion were especially liable to die of coma and this suggested to Stadelman his theory that diabetic coma is an auto-intoxication, produced by an excess of acids within the body. So he at once began a series of experiments upon the introduction of acids into the circulation, using only those which could be potent through their affinity to alkalies and which in themselves possessed no toxic properties. The moment such an acid enters the circulation it attacks the first alkali available. In the case of man and the carnivora this will be the ammonia, in combination with which it becomes inert and is thus carried out of the system. Herbivorous animals, however, have no such ammonia production and the acid must at once attack the sodium and potassium of the blood and tissues. By such injections it has been found that symptoms identically resembling those of diabetic coma can thus be produced in those animals and that a prompt neutralization of this acid by a further injection of alkalies will at once restore consciousness. It has been therefore believed that after the production of the acid bodies in diabetes for a certain time they are neutralized by the available ammonia. At last, however, there comes a time when the production of ammonia can not keep pace with