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# THE COMMON BACTERIAL INFECTIONS OF THE DIGESTIVE TRACT AND THE INTOXICATIONS ARISING THEREFROM*

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IF one examines with the microscope the contents of any portion of the large intestine of a human being or of any mammal, the richness of the material in micro-organisms is strikingly apparent, especially in stained preparations. It is true that if the material is selected from the lowest portion of the gut, many of the organisms can be shown by suitable cultural methods to be no longer living, but rather to be undergoing a process of disintegration, partly owing to a solution in their own juices—a process of autolysis. But even the dead and dying bacteria point to the multiplicity of bacterial life at higher levels of the gut.

The knowledge that the digestive tract is so rich in bacterial forms has led many physiologists to inquire into the biological meaning of this remarkable fact. Pasteur expressed a belief that these bacterial inhabitants are in some way necessary to the life of the individual that harbors them. Nuttall and Thierfelder, in their well-known experiments, attempted to rear guinea-pigs delivered by Caesarian section and fed on quite sterile food. As the animals lived and increased in weight, the experimenters concluded that the intestinal bacteria were not necessary to normal nutrition. Other observers have, however, reached a different conclusion. The experiments of Schottelius with chickens, of Madam Metchnikoff with tadpoles, and the very careful work of Moro with the larvæ

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of the turtle tend to show that intestinal bacteria are essential to normal nutrition.

It must be admitted, I think, that none of these experiments is conclusive as to the necessity of bacterial action in the digestive tract for the maintenance of health in adult mammals of the highest types—man and the various domestic animals. The evidence given by the sterile intestinal contents of certain Arctic animals is apparently conclusive for the conditions in which this experiment of nature has been carried out. Levin examined the intestinal contents of the Arctic animals in Spitzenberg. The digestive tract was found to be in most instances entirely sterile in white bears, seals, reindeer, eider ducks, penguins, etc.

Clearly then, in this case, the intestinal bacteria are not required to carry on the ordinary digestive processes and normal nutrition. It has been supposed that the intestinal bacteria aid in the digestion of cellulose, which they are undoubtedly able to decompose fermentatively. The argument in favor of the importance of this function of the intestinal bacteria loses much of its force if it be true, as lately maintained by Bergman, that most of the cellulose eaten by herbivora is provided with intracellular enzymes capable of decomposing cellulose.

The real significance of the normal intestinal flora probably lies not in any immediate relation to processes of digestion, but in a wholly different direction. It is impossible to avoid the entrance of bacteria into the digestive tract. The obligate bacteria (for example, *B. lactis ærogenes, B. coli, B. bifidus*) adapt themselves to the secretions of this part of the body and ordinarily hold their own against newcomers. By virtue of their adaptation, they are not ordinarily harmful to their host, but, on the contrary, they are, under some circumstances, capable of doing service by giving rise to conditions that discourage the growth of many harmless and harmful species which man cannot readily exclude from his digestive tract. I believe the chief significance of the obligate intestinal bacteria lies in their potential capacity for thus checking the development of other types of organisms capable of doing injury.

### DEFENSIVE ACTION OF THE DIGESTIVE JUICES.

The normal human organism is provided with more or less efficient (though by no means fully understood) methods of defence against these bacterial invaders. The secretion of the gastric juice in normal abundance, after a meal, provides a degree of acidity which acts as an effective check upon the growth of many non-sporulating bacteria, and is actually destructive to most varieties at least in a measure. Probably the proteolytic action of the peptic ferment and the tryptic enzymes leads to a very quick destruction of any bacteria whose vitality has been lowered by contact with the acid of the gastric juice. If, however, bacteria are administered in very large numbers, there is a chance that some of them will find their way into the intestine while still viable. This seems especially liable to happen when bacteria are taken into the empty stomach or into a stomach with defective motility which secretes little gastric juice with a low content of hydrochloric acid—and there are many such stomachs among persons over forty years of age and in fair health.

Exactly what happens when the accidental saprophytic forms of bacterial life—the "wild races," as the French call them—come to close quarters with the "obligate," well-adapted parasitic forms in the intestine, we do not at present know. There are, however, numerous facts which point to well-defined biological antagonisms between the "wild" forms and the representatives of the *B. coli* group.

A long, largely anaërobic intestinal tract permitting gradual resorption of the contents is a physiologic necessity in order that a loss of water and its detrimental consequences may be spared the organism. The presence in the colon of immense numbers of obligate micro-organisms of the *B. coli* type may be an important defense of the organism in the sense that they hinder the development of that putrefactive decomposition which, if prolonged, is so injurious to the organism as a whole. This adaptation is the most rational explanation of the meaning of the myriads of colon bacilli that inhabit the large intestine.

This view is not inconsistent with the conception that under some conditions the colon bacilli multiply to such an extent as to prove harmful through the part they play in promoting fermentation and putrefaction. An alkaline reaction of the medium appears to favor their putrefactive functions if peptones be present.

### INFLUENCE OF REACTION ON THE GROWTH AND PRODUCTS OF INTESTINAL ANÆROBES.

If mixed fæcal flora be grown in sugar bouillon and in sugar bouillon containing calcium or magnesium carbonate for one week at 37° C., it will be found that usually the amount of volatile fatty acid will be greater in the carbonate flasks. This difference in the quantity of acids is probably due to the action of these salts in maintaining a neutral reaction. In a series of such cultures it was found by Dr. A. J. Wakeman that in nearly all instances the molecular weights of the fatty acids were somewhat higher in the neutral flasks. This fact suggests a relatively greater activity of putrefactive bacteria in the neutral media, for it is known that such bacteria tend to form the higher rather than the lower fatty acids. He also found that the proportion of non-volatile acids (mainly lactic) was greater in the cultures that were not neutralized.

These observations and similar ones with pure cultures indicate that in the digestive tract the growth of putrefactive anærobes must be favored by a neutral reaction and restrained by the presence of acid. The favorable influence of milk food, containing lactic acid formers, in controlling putrefaction in the intestine finds its explanation partly in the inhibitory action exerted by such bacteria and in part in the presence of performed lactic acid in the food at the time it is ingested.

### AEROBIC AND ANAEROBIC CONDITIONS IN THE DIGESTIVE TRACT.

There are many conditions which influence the character and extent of bacterial decomposition in the alimentary tract: among them are the chemical character of the food, the solubility of the food in the digestive juices, and the volume and com-

position of these digestive juices. Intimately intermingled with these factors of food and secretory activity is the influence of aërobic and anaërobic conditions in the digestive tract on the nature of the bacterial activities that occur there. The initiation of putrefactive decomposition in the digestive tract, as elsewhere, depends very largely, though probably not exclusively, on the activities of obligate anaërobes. An important portion of the digestive tract is most of the time under anaërobic conditions.

The facts all point to the correctness of the view that we largely owe the initiation of bacterial proteid cleavage there to the agency of the strict anaërobes, but it does not follow that intestinal putrefaction is carried on through the sole activity of these organisms. The intestine abounds with micro-organisms, which are able to attack albumoses and peptones and to effect the further degradation of the proteid molecule, thus entering into a symbiotic action with the strict anaërobes.

The symbiosis of aërobes and anaërobes is a biologic phenomenon of much consequence in determining the distribution of anaërobic bacterial processes in the digestive tract. Without such symbiotic action, the development of strict anaërobes would be confined to those parts of the digestive tract into which oxygen passes rarely, and then only in small amounts. The large intestine is seldom visited by free oxygen, but it is probably usual in man for the small intestine to contain a little air.

It is probably safe to assume that in the mouth the free presence of oxygen constantly acts as a deterrent to anaërobic growth. In spite of this, however, anaërobic life is possible. Caries of the teeth, which was formerly referred to aërobic bacteria, seems clearly the result of the invasive action of anaërobes on the tooth pulp. In removing decomposing food masses by the intelligent use of a tooth brush, one not merely admits air to the anaërobes, but also removes many aërobes, which, through the symbiotic action already mentioned, facilitate the multiplication of the former.

In a stomach which secretes little or no hydrochloric acid and

which is sluggish in emptying its contents, the chances for anaërobic development are good, and hence we frequently find under these circumstances that there are evidences of putrefactive decomposition of food that has been unduly retained in the stomach (*e.g.*, production of sulphuretted hydrogen, mercaptan, butyric acid, etc.). On the whole, however, I think one may say that in the course of chronic gastric affections the number of anaërobic micro-organisms in the stomach is seldom great.

Of the conditions of bacterial life in the small intestine, very little is known because of the inaccessibility of the contents of this portion of the digestive tract. However, observations at operation after gunshot wounds and at early autopsies have shown that putrefactive micro-organisms are commonly few in the upper two-thirds of the small intestines. In man there is in the ileum within a foot or two of the colon a marked increase, both in the number of bacteria and of their varieties. Hence we find that the mixed fecal bacteria taken from this level of the lower ileum are capable of inducing putrefactive changes in native proteids and in more simple nitrogen-holding media, even in health, and that anaërobic conditions of bacterial life are exaggerated in pathologic states. We may indeed look on the ileum as the debatable land of digestive territory.

In the large intestine we find the most dense accumulation of bacteria and the best conditions for anaërobic growth. The transition from small to large intestine is in this respect very striking. The anaërobic conditions are well maintained throughout the colon and it is here that we find the greatest numbers of anaërobes and the most pronounced evidence of putrefaction. There is, however, a gradual fall in the number of living bacteria beyond the ileocecal valve, so that in the rectum the numbers of cultivable bacteria are very much less than in the ascending colon. It should be noted, however, that the variety of bacteria in this region is often not so great as in the ileum, although their numbers are in excess.

### CHARACTERS OF THE BACTERIAL FLORA OF CARNIVOROUS AND HERBIVOROUS ANIMALS.

In the course of the study of anaërobes of the human intestine it appeared desirable to learn something about the flora of the large intestine of various domestic and wild animals. A study of a grown cat fed upon raw meat showed the presence of Gram-positive vegetative organisms from one end of the digestive tract to the other. Cultures in bouillon from the stomach, the small intestine and the large intestine showed an abundant production of methyl mercaptan as well as of hydrogen sulphide. The numbers of colon bacilli in this case were small as compared with the anaërobes. A large number of the colonies on anaërobic plates were *B. ærogenes capsulatus.*

Observations on other cats, on dogs, lions, wolves and tigers showed in the Gram-stained fields large numbers of free spores, of spore-holding bacilli and of Gram-negative vegetating forms, suggesting *B. ærogenes capsulatus.* Bouillon cultures of the mixed fæcal flora of these animals quickly developed methyl mercaptan. Fæcal suspensions proved to be highly pathogenic to guinea-pigs when injected subcutaneously. The animals died within twenty-four hours and usually in fifteen to eighteen hours. At autopsy the subcutaneous tissues throughout the body were hæmorrhagic and œdematous, and showed necrotic changes which extended in some instances to the muscles.

We may contrast with these findings the observations made upon herbivorous animals, including the buffalo, goat, horse, elephant and camel. In none of these animals were seen any organism suggesting *B. ærogenes capsulatus,* excepting in the case of the buffalo, where the number of bacilli of this type was very small. Spore-holding organisms were not observed, but moderate numbers of free spores were present. In the fields showing the largest number of spores their ocurrence was far less frequent than in the lion, tiger, wolf, or cat.

The mixed fæcal flora of these herbivorous animals grown upon peptone bouillon failed to show the production of methyl

mercaptan excepting in the case of the horse, where a moderate reaction was obtained.

With the exception of the suspensions from the horse, subcutaneous injections of the fæcal suspensions were but slightly pathogenic to guinea-pigs. The guinea-pigs frequently lived two or three days or entirely recovered. The fæces from the horse caused hæmorrhagic and œdematous lesions with necrosis similar to those found after inoculation with the fæces of carnivorous animals, although the lesions were less pronounced.

A further confirmation of the radical differences existing in the intestinal tracts of carnivora and herbivora is furnished by a series of observations with the Welch-Nuttall incubation test. Suspensions were made from the fæces of all types of animals mentioned, and equal quantities of these suspensions were infused intravenously into a series of living rabbits. The rabbits were then quickly killed and incubated. On examination after twenty-four hours it was found that all the rabbits infused with suspensions from carnivora showed in an extreme degree the characteristic putrefactive changes in the liver, cellular tissues, etc., induced by pure cultures of *B. ærogenes capsulatus.* The rabbits infused with suspensions from the herbivora showed similar but very much slighter changes in every case. The results for each group of animals separated the herbivora sharply from the carnivora.

These differences in the appearance and behavior of the bacteria derived from typical carnivora and herbivora suggest that the habit of living upon a diet consisting exclusively of raw meat entails differences in the types of bacteria that characterize the contents of the large intestine. The occurrence of considerable numbers of spore-bearing organisms in the carnivora points to the presence of anaërobic putrefactive forms in great numbers.

Inquiries made of Dr. Blair, the pathologist in the New York Zoological Gardens, elicited the fact that while, upon the whole, the carnivorous animals are apt to live somewhat longer than the herbivorous animals of about equal size, the carnivora are much more likely to develop conditions of advanced anæmia

in the later years of life than is the case with the herbivora. Instances are stated to be not uncommon in which a pernicious type of anæmia has developed in the carnivora. The examples of severe anæmia encountered among the herbivora were said by Dr. Blair to be very occasional and to be in nearly all instances referable to gross animal parasites.

### INFLUENCE OF FOOD ON HUMAN BACTERIAL FLORA OF THE DIGESTIVE TRACT.

That a knowledge of the influence of different foods upon the flora in health and disease would not only be of great biological interest but would also give many indications of a practical sort for the use of foods in pathological conditions, requires no argument. I have observed that the number of Gram-positive organisms in the fæcal fields was much increased when an adult subject who had previously been on a mixed diet began to live on a dietary consisting almost exclusively of meat. An increase in the number of putrefactive anaërobes was largely responsible for the change from a mixed fæcal field to one which was dominantly Gram-positive. In this connection I think the observation noteworthy that the intestinal contents of animals living on a diet of raw meat tend to give mixed or dominantly Gram-positive fields, whereas similar material from herbivorous animals tends to give Gram-negative fields. The numbers of anaërobes is much greater in the carnivora.

It appears probable that in considering the influence of foods upon the flora of the digestive tract one should take into account the factor of rapid digestion and absorption in the upper part of the digestive tract. For example, in cases where a patient takes daily a large quantity of meat which is imperfectly masticated, there is much more opportunity for the development of putrefactive anaërobes in the lower part of the intestine than if mastication is more thorough. I believe also that the influence of diet must be largely modified by the character of the dominant organisms in the intestinal tract and that

this influence may come to the front in a telling way in cases of chronic infections of the large intestine.

### THE REDUCING ACTION OF MEAT.

It seems probable that different articles of food have a different significance in respect to their influence on the presence or absence of oxygen in the digestive tract. It is known that the fresh tissues of animals exert a considerable degree of reducing power much more in general than the reducing action of vegetable cells. The reducing action of fresh liver has been successfully employed by Professor Theobald Smith in rendering the closed arm of the fermentation tube more strictly anaërobic and thus facilitating the growth of certain strictly anaërobic bacteria. In carnivorous animals living on raw meat there seems little doubt that anaërobic conditions may exist throughout the digestive tract. Even in the case of man this factor cannot be ignored, as there are many instances in which large quantities of raw or nearly raw meat are eaten. Moreover meat that has been slightly cooked still retains considerable reducing power. It seems not unlikely that there are cases of excessive intestinal putrefaction dependent on the excessive activity of anaërobes in which the conditions of anaërobiosis are distinctly favored by excessive meat eating.

### THE INFLUENCE OF THE EPITHELIAL CELLS LINING THE DIGESTIVE TRACT.

Every cell has an inherent capacity, if undisturbed by injurious agencies, to live a certain period of time. Every epithelial cell of the digestive tract doubtless has a high capacity for reproduction. This power must nevertheless be limited, and if the cells be injured by too many demands upon them, they may fail after a time to reproduce normally. Superficial cells which under these circumstances have undergone desquamation are thus not so easily replaced, and the epithelial layer may become in some places much thinner than normal. It seems reasonable to suppose that this pathological thinning of the mucous membrane may lead to diminished function in

secretion, in the process involved in transudation and in the capacity on the part of the intestinal epithelium to act on products of decomposition in the intestine. In experiments made many years ago with indol, it was found that the epithelium of the digestive tract possesses in a high degree the capacity to bind indol in such a way that it cannot be recovered by distillation. This action of the epithelial cells is certainly not confined to indol.

### PERMEABILITY OF THE MUCOUS MEMBRANE OF THE INTESTINAL TRACT TO BACTERIA.

There exists some experimental evidence indicating that an intact, fully developed layer of epithelium is an important barrier to the entry of at least some kinds of bacteria into the mucous membrane. Hilgerman, however, is inclined to believe with Behring that the mucous membrane in early life is lacking in natural protective substances capable of hindering this penetration by bacteria. Ficker holds very definitely that in fully grown dogs, in which the intestinal tract is ordinarily little permeable, it is possible through inanition or fatigue or a combination of the two, to facilitate a penetration of the intestinal mucous membrane which is analogous to that observed in the infantile tract and further resembles the conditions present in the dying organism. He also raises the question whether the penetration of the intestinal tract by bacteria may not explain some of the phenomena that have been noted after great fatigue, for example, the so-called "fever of exhaustion," and also the state designated by the older physicians as "autotyphization."

### THE PRESENCE OF PATHOGENIC BACTERIA IN THE INTESTINES IN HEALTH.

Evidence is gradually accumulating which goes to show that pathogenic micro-organisms may be present in moderate or even considerable numbers in the digestive tract under some conditions without giving rise to clinical manifestations of deranged function. This is true of the typhoid bacillus, and dysentery

bacilli and of other forms. It is likely that in all these cases the pathogenic organisms in question are held in check by other bacteria present in the digestive tract or by the bacteria and the intestinal secretions, so that they are unable to multiply in a significant manner or to gain entry into the cells of the mucous membranes. It seems not unreasonable to suppose that this restraint may be overcome by errors in diet, depressed general conditions, or by alternations in the secretions of the digestive tract, and that thus definite infection by the hemiparasitic bacteria that are present becomes possible.

The considerations just mentioned as applying to these bacteria probably hold equally true of the more saprophytic forms concerned in intestinal putrefaction. It is certain that the intestine may harbor considerable numbers of *B. putrificus* and *B. ærogenes capsulatus,* or both of these together, without the development of clinical manifestations. A variety of conditions may be presumed so to favor the development of these anaërobes that their products, instead of being formed in such small amounts as to be harmless, begin to exert a detrimental effect on the organism. Especially important are influences which alter the character of the secretions in the large intestines or bring there unusually large quantities of partly digested proteid food. In certain conditions of the digestive tract an excessive or even a moderate meal of proteid food will precipitate an intoxication or a seizure of vomiting or diarrhea. There are cases classed as ptomain poisoning in which the digestive tract rather than the food is responsible for the observed disorders.

### THE BACTERIA OF THE HUMAN DIGESTIVE TRACT AT DIFFERENT AGES IN APPARENTLY HEALTHY INDIVIDUALS.

While it is true that at all periods of life the human digestive tract is the seat of the life activities of myriads of micro-organisms, it is also true that the biological characters of these micro-organisms are not the same at all times of life. In apparently healthy persons of about the same age living under somewhat similar conditions the resemblances in the biological characters of the bacteria are, on the whole, more striking than the

differences. Comparisons between different persons of unequal ages have been repeatedly made and support the statement that the normal bacterial flora characteristic of different ages, present different biological characters and are responsible for different types of decomposition in the digestive tract.

### NURSLING INFANTS.

In babies fed on mother's milk the alimentary tract is the seat of conditions of bacterial activity that possess a high degree of interest for one who wishes to obtain an insight into the physiology of digestion. For in nurslings one finds a relatively simple bacterial flora which gives a clew to the more complex and puzzling bacterial conditions that characterize normal adult life and many states of disease. Gram-stained microscopical fields, prepared from the normal fæces of a nursling child from any portion of the large intestine, present essentially the same characteristic appearances. The typical field is predominantly Gram-positive and consists very largely of *B. bifidus.* This organism was first described by Tissier. It is anaërobic and its form varies according to the culture medium. Other Gram-positive organisms are *B. acidophilus* of Moro, and small numbers of *B. ærogenes capsulatus* and a diplococcus that sometimes grows in chains. Among the Gram-negative forms may be mentioned representatives of the *B. lactis ærogenes* and *B. coli* groups and small coccal or coccoid forms.

### DISTRIBUTION OF THE BACTERIAL FLORA IN THE DIGESTIVE TRACT OF THE NURSLING.

I have had an opportunity to make microscopical examinations (using Gram's method of staining) of the contents of the digestive tract of nurslings dying within the first six months from conditions not closely connected with the digestive tract (*e.g.*, acute bronchopneumonia). In the normal nursling the mouth contains few bacteria and these are for the most part derived from the skin and the nipple—*Staphylococcus pyogenes aureus,* bacilli of the *B. coli* group and *B. lactis ærogenes.* In the stomach also the bacteria are few and the bacterioscopic

picture shows usually a few positive or negative diplococci or streptococci, or negative coccobacilli, or positive or negative bacilli suggesting the *B. coli* and *B. lactis ærogenes* groups. The normal bacteria of the greater portion of the small intestine are short Gram-negative bacilli of the colon and *lactis ærogenes* groups, mixed sometimes with a few positive and negative coccal forms. In the lower ileum the organisms of the bifidus type appear and at the transition from lower ileum to cecum there is a striking change in the proportions of coli and bifidus types, the former losing their dominant numerical position. The ascendency of the bifidus type increases in the colon to such an extent that in the rectum this type has the appearance of being present in pure culture.

The bacterial flora of the intestinal tract of the nursling is thus only moderately numerous as regards variety. The bacteria are concentrated in the regions that lie between the lower ileum and the anus, the ileocecal junction presenting most organisms capable of being cultivated and the greatest variety. The comparatively small number of bacteria found in the small intestine has its explanation partly in the small amount of food that lodges there and partly, perhaps, in the bacteriolytic action of the succus entericus, which, though moderate, is appreciable. Wherever particles of transformed casein are found there will bacteria also be abundant, but with the exception of the lower ileum the small intestine does not harbor food-masses to any considerable extent. The epithelial cells are said to contain an antitryptic ferment and this passes to some extent into the succus entericus, where it is perhaps capable of exerting a restraining influence on that peptonization of proteid which is the first essential step toward putrefactive decomposition.

A satisfactory study of the products of the mixed fæcal flora from normal nurslings has not yet been made. One fact, nevertheless, stands out, that on sugar-bouillon containing blood the volatile acid or acids produced give a molecular weight corresponding closely to that for acetic acid. The insignificant amounts of the higher volatile fatty acids point to the absence of any considerable numbers of anaërobic putrefactive bacteria.

In harmony with this is our observation that the Welch-Nuttal incubation test with rabbits does not produce the gas-liver from putrefactive anaërobes. The mixed fæcal flora when grown on plain bouillon make indol, doubtless owing to the multiplication of colon bacilli.

### BACTERIAL FLORA OF BOTTLE-FED CHILDREN.

If one makes a comparison of the bacteria of the digestive tract of children fed on cow's milk with the flora which has been described as characteristic of the digestive tract in breast-fed children, one finds many points of resemblance, but also some typical and important differences. Even where the cow's milk has been sterilized, the number of bacteria is considerably greater. Where sterilized milk is employed the increase in the number of bacteria is dependent, at least in part, upon the presence of anaërobic bacteria or facultative varieties capable of forming spores.

Many of the bacterial forms which have already been described as regular inhabitants of the nursling's intestinal tract are also inhabitants of the digestive tract of bottle-fed children. The place of preponderance is, however, occupied by organisms of the *B. coli* type, and we thus find that the stained fields are Gram-negative instead of Gram-positive as is the case in nurslings.

### PRODUCTS OF DECOMPOSITION IN THE INTESTINAL TRACT OF BOTTLE-FED CHILDREN.

The products of intestinal decomposition in normal nurslings are remarkably small in amount, and almost the same thing holds true of the intestinal tract of bottle-fed children. If we make extracts of the contents of any part of the large intestine from a normal bottle-fed child, we find by the most delicate methods, merely a trace of indol, or even no trace at all. Only a moderate amount of volatile fatty acid is obtained from the distillate of an acidified watery suspension from any portion of the intestinal contents, and of this acetic acid forms by far the larger part. The scantiness of the higher fatty acids indi-

cates that such bacterial processes of decomposition as occur within the intestinal tract are of a fermentative rather than of a putrefactive nature.

### THE BACTERIAL CONDITIONS AFTER INFANCY.

The bacterial conditions in the digestive tract between the period of childhood and that of old age differ in health so considerably from the conditions that exist during the period of milk feeding that they call for separate consideration. The difference depends mainly on the character of the diet, which grows more varied at the end of the milk period. With this comes increased opportunity for the entry of bacteria of many sorts into the digestive tract. It is impossible to briefly picture the bacterial conditions in the digestive tract in such a way as to take account of the many individual peculiarities which are met, but fairly typical descriptions may be given. It must be distinctly understood that these descriptions are based on well-cared-for individuals and not on the study of neglected persons or persons following peculiar occupations which subject them constantly to irregular conditions of life.

During childhood and adolescence one sees a slow transition from the conditions of infancy to those of adult life. *B. bifidus*, although present, is much less numerous, and other types are more numerous. Still the numbers of putrefactive anaërobes are small and putrefactive processes in the intestine are not active. This is shown by the presence of only a very small amount of indol and phenol in the feces, and, in the urine, by low ethereal sulphates and the absence or small amount of indican and phenol. The reaction with dimethylamidobenzaldehyd ($(CH_3)_2N.C_6H_4.CHO$) is slight or moderate—often so slight that its existence is questionable. During temporary derangements of digestion there may be an increase of the ethereal sulphates or indican, but this is very transitory.

Toward adult life great differences exist in the habits of different persons, and these are in a degree reflected in the nature of the bacterial processes of the digestive tract. In adult life the individual experiences new responsibilities, new dangers,

an enhanced emotional life and often a large proportion of indoor life and more sedentary habits. The dietary is apt to undergo an alteration in the direction of increased and frequently injudicious liberty and the use of tea and coffee. Also the use of tobacco and alcoholic drinks is either increased or begun. Sooner or later these things lead to slight derangements of digestion which manifest themselves clinically. One occasionally meets with persons of unusually robust physical and mental health in whom the bacterial conditions of adolescence persist until the fiftieth year, or longer. A large proportion of persons, however, by the time they reach the age of 50 present different physical conditions, although they are in no sense in a state of invalidism, but work hard and most of the time feel well. While in such persons the fecal flora shows nothing striking, it is usually not difficult to demonstrate that the number of putrefactive anaërobes in the intestine is larger than in healthy adolescents. In short, we find in middle life a large number of persons whose health is good or fair, in whom the putrefactive processes are distinctly more active than is the case with most younger persons of normal health.

These persons, though in good health, are not robust. A period of sustained hard work is followed by considerable mental and physical fatigue. Dining out and the use of alcoholic drinks are indulgences quickly followed by unpleasant consequences. Exercise out of doors becomes more and more a necessity. The individual is conscious that it requires careful living to keep him in a condition compatible with the performance of his duties.

The main difference between the putrefactive conditions found at 50 and at 70 is that at the latter period they are a little more marked in their intensity and affect a much larger proportion of the population. The subjects in question at this later period of life are not ill, but in order to keep fairly well have to be very careful as to their habits of living. They are moderately anemic and easily develop slight disorders of digestion. They weigh less than formerly and, though they may still be well nourished in appearance, are conscious of losing

strength from year to year. They are undergoing what is usually regarded as normal involution. It may be confidently asserted that the onset of senility may be distinctly accelerated through the development of intestinal infection in which the putrefactive anaërobes are prominently represented. I have observed this in cases where it has appeared certain that other toxic causes of premature senility could be excluded.

### METHODS OF INVESTIGATION.

It is desirable to speak briefly here of the methods of investigation that have been employed in some of the investigations with which this lecture deals. Some of these methods are well known, others are new. They relate in part to the study of the morphological and cultural characters of the bacterial organisms found in the digestive tract under different conditions, but they have to do mainly with the products of the life activities of these bacteria upon different nutrient media.

By far the most helpful method of studying the microscopical fields is with the aid of the Gram stain. From the use of this stain one obtains as a rule an indication of the dominant flora of the lower part of the intestine. Of course it alone does not suffice for the identification of the micro-organisms but it must be supplemented by series of cultures.

I shall not attempt here to discuss fully methods of isolation and identification of individual bacteria. The usual methods have been employed. In this research the fermentation tubes are extremely helpful, as first pointed out by Professor Theobald Smith. Anaërobic organisms in general grow much better in the closed limb of the tube on sugar bouillon in the presence of bits of sterile tissue, and in some cases, as in that of *B. ærogenes capsulatus,* they do not grow in the absence of this aid. The identification of anaërobes involves the study of their cultural characteristics, of their ability to form gas on sugar media, and the determination of their gas formula, that is of the ratio between the hydrogen and the carbon dioxide formed. The influence of the growth of anaërobes on milk is easily studied in the fermentation tubes and gives considerable aid in identifi-

cation. The pathogenicity of the isolated anaërobes is also a point of importance in establishing their identity. Finally the Welch-Nuttall incubation test is often very helpful. This method has apparently never been used heretofore in connection with the study of human fæces, but I believe that it has here an important clinical application.

It was obviously impracticable to isolate in every instance the dominant micro-organisms of the fæces and therefore the action of the mixed fæcal flora was studied. A 10 per cent. suspension of the fæces in physiological salt solution was used to inoculate fermentation tubes. The tubes contained dextrose bouillon, levulose bouillon, lactose bouillon, saccharose bouillon, peptone bouillon and plain bouillon. The gas production in the sugar tubes gave most information. The tubes contained concentrations of the sugars already mentioned equal to 2 per cent. in each case. The quantity of gas produced in conditions of health by the mixed flora is somewhat variable but may be roughly stated as varying ordinarily from 15 to 30 per cent. taking the average of the four tubes. In normal children the amount of gas is often somewhat less than in adults. In conditions of disease the gas production was found to be usually considerably less than the average production in health, both in adults and children. In well-marked examples of saccharobutyric putrefaction the quantity of gas produced may be one-half or even one-fifth of the normal. I am disposed to attribute this mainly or wholly to an elimination of the colon bacilli. This has been supported repeatedly by the results of plating on litmus gelatin. The diet is not without influence in this connection. An abundance of carbohydrates leads to a greater gas production, while a meat diet may occasion a fall of from 40 to 50 per cent. in the amount of gas produced.

From the peptone bouillon tube it is possible with suitable reactions to form an estimate of the amounts of indol, of ammonia and of sulphuretted hydrogen.

It has been found useful to examine regularly the sediments of the fermentation tubes which have been inoculated with the mixed fæcal flora. The appearance of the Gram-stained fields

gives, as a rule, but not always, an indication of the dominant flora in the lower part of the intestine. One can not rely on it alone, but in connection with data derived from other methods it helps us to form a conception of the bacterial types present.

In addition to the study of the mixed fæcal flora in the fermentation tubes, as a routine procedure, four flasks, each containing about 500 c.c. of medium, have been inoculated with a suspension of the mixed fæcal flora and incubated seven days. The media employed have been peptone-bouillon, peptone-bouillon with calcium carbonate, sugar-bouillon and sugar-bouillon with calcium carbonate. Under the conditions prevailing in these flasks a large part of the growth has been anaërobic and a high degree of anaërobiosis has been maintained, owing in part to the formation of reducing products, such as hydrogen, incidental to the fermentative and putrefactive cleavages. It has been found in general that the anaërobes grow more abundantly in the flasks which were kept neutral by the presence of calcium carbonate. The chemical examination of the seven days' flasks has included two different series of procedures. The peptone-bouillon flasks were examined for hydrogen sulphid, methyl mercaptan, volatile fatty acids, ammonia, indol, skatol, phenol, alcohol and acetone. Quantitative determinations have regularly been made in the case of the volatile fatty acids, ammonia, indol, skatol and phenol. In the sugar-bouillon flasks the contents have been examined for alcohol and acetone, volatile fatty acids and the non-volatile organic acids. The molecular weights of the barium salts of the volatile fatty acids have regularly been determined. An interesting observation has been made that in the flasks containing calcium carbonate the molecular weights obtained for the volatile fatty acids have nearly always been somewhat higher than in the case of the molecular weights obtained from the volatile fatty acids of the sugar-bouillon flasks. This fact confirms the evidence of the microscopic fields and shows the greater abundance of the putrefactive anaërobes in the neutral flasks than in the sugar-containing flasks that are allowed to become acid. Methyl mercaptan has been determined by the isatin-sulphuric acid

method. I have published elsewhere the method used for the determination of indol and skatol and their separation by means of β-naphtha-quinone-sodium-monosulphonate and the dimethylamidobenzaldehyd reaction.

The chemical methods of studying the fæces and urine are those that are fully described in the text-books relating to these subjects. To these known methods has been added the color reaction of the filtered watery extract of the fæces with Ehrlich's aldehyd and also the urinary reaction with this reagent.

### THE CHEMICAL PRODUCTS OF INTESTINAL FERMENTATION AND PUTREFACTION.

I shall use the word fermentation to designate the decomposition of carbohydrate and fatty substances and the word putrefaction to apply to the cleavages of proteid and allied substances. The products of putrefaction include the substances containing sulphur or nitrogen or both sulphur and nitrogen. The fermentative and putrefactive processes overlap in the sense that they furnish some products in common, such as carbon dioxid and volatile fatty acids, and, furthermore, they are linked by the fact that excessive fermentation in the digestive tract nearly always leads to excessive putrefaction. Of the products of fermentation the carbon dioxid acts mainly as a cause of flatulence in the stomach or small intestine. The acids formed—chiefly acetic and lactic—are irritants and may be exciters of vomiting and diarrhœa. When in excess the acids may be excreted, unburned, and thus withdraw alkali from the tissues. It is possible that a mild degree of acidosis may thus result from fermentative processes in the intestine.

It is now well established that various molds and bacteria are capable of acting on media containing sugar in such a manner as to give rise to the production of oxalic acid. Dr. Helen Baldwin has shown that by prolonged feeding of dogs with large amounts of sugar a mucous gastritis is incited and that oxalic acid is present in the stomach and urine. It was also found that in media containing beef extract and sugar, oxalic acid was produced after inoculation with the contents of the

stomachs of persons showing marked grades of oxaluria. Although gastric fermentation is not the chief source of oxalic acid in the body, it is possible that it may have an influence in causing the condition known as oxaluria.

When we turn to the consideration of the nitrogen-holding and sulphur-holding products of putrefactive cleavage, the scantiness of our knowledge comes into view with almost discouraging clearness. That putrefactive processes are attended by the formation of bases such as ammonia, amines, diamines (such as putrescin and cadaverin), cholin, neurin, sulphur compounds and various aromatic bodies, has been known many years and something has been learned, though by no means enough, about the media and the bacteria which determine the presence and proportions of these substances. When, however, we ask ourselves what we can safely say of the conditions under which such substances arise in the human intestines and of their pathologic effects, we are able to give in most instances only very inadequate answers.

*Basic Substances.*—Although ammonia is regularly formed in the course of putrefaction in the intestines, it is probably present in too small quantities to be toxic. The organism is well adapted to care for moderate quantities of ammonia which, as is well known, is united with carbon dioxid in the liver and elsewhere to form urea. It is possible, however, that ammonium butyrate may act as a local irritant in the intestine. Likewise we know nothing of any toxic action from methylamine or other alkyl amines. Cholin and, perhaps, neurin have been found in the intestinal tract in experiments on animals, but we lack positive evidence that they can under these conditions exercise their poisonous effects on the organism.

*Putrescin and Cadaverin.*—Although the study of the conditions under which putrescin and cadaverin are formed in the intestinal tract is of much biologic interest, there is at present little evidence that these diamines are ever formed in sufficient quantities in the human intestine to constitute in themselves factors in the production of states of intoxication. The association with cystinuria is a striking fact, and the further investi-

gation of this condition will doubtless give us the explanation of the relationship between the production of diamines and the formation of cystin, if, indeed, there be any necessary relation.

*Sulphur Compounds.*—The sulphur compounds resulting from putrefactive decomposition in the intestines have received little attention from the standpoint of their pharmacologic action. It is very difficult at present to form a just estimate of their importance in intestinal intoxications.

There is reason for thinking that the production of hydrogen sulphid in the digestive tract is of more importance to the organism than the formation of mercaptan. This gas is regularly formed in the intestines and its presence can be demonstrated in freshly voided fæces. The mixed fæcal flora, both in health and disease, produce hydrogen sulphid in cultures containing partially hydrolized proteids (bouillon). In health probably hydrogen sulphid is formed only in the colon and perhaps in the lower part of the ileum. There are, however, pathologic conditions in which it occurs in the stomach. It is not necessary to assume the presence of a pathologic organism in these cases, as it is well known that *B. lactis ærogenes* and colon bacilli liberate it when growing in certain media. In marantic children I have found organisms capable of producing hydrogen sulphid in pepton-bouillon in the stomach and the first part of the small intestine; while in children dying of bronchopneumonia, such results were obtained only from the flora of the lower ileum and colon.

We have at present very little satisfactory knowledge of the influence of hydrogen sulphid on the organism in cases where the gas is liberated in the intestine. Senator and others have described poisoning by this gas. Among the symptoms which have been met with in such cases there have been prominent those pointing to disordered function of the central nervous system, including headache, dizziness, delirium, mental depression, drowsiness, stupor and collapse. Somewhat similar manifestations have been observed in experimental poisoning by hydrogen sulphid in animals and men.

*Aromatic Products of Putrefactive Decomposition—Phenol*

*and Cresol.*—In some pathologic conditions attended by excessive putrefaction in the intestine these substances are found in the intestinal contents in quantities considerably above the normal amount, which is always small. But one never, however, finds them in large quantities—never so much, for example, as in the case of indol. Notwithstanding this, the quantity excreted in twenty-four hours in the urine as phenol potassium sulphate may be fairly high owing to the fact that phenols are produced in the organism in the course of the metabolism of normal cells. In certain putrefactive cases I have found these substances in considerably greater amounts in the urine, but even here, however, it does not appear that the phenols can be regarded as important toxic agents, although it is likely that the continued absorption of moderate quantities from the intestine over a long period of time may harm the cells of the liver and other structures concerned with the pairing of phenol and sulphuric acid, especially if the cell protoplasm of the liver has previously been somewhat damaged.

*Skatol.*—This substance is formed in very small quantities from time to time in some normal persons and very abundantly in some persons suffering from excessive intestinal putrefaction. In persons with marked intestinal or nervous disorders I have occasionally found in the fæces as much as 8 or 10 mg. of skatol in 100 gm. of fæces. Usually the amount is much less than that of indol, but this rule is not invariable. Like indol, it is derived from tryptophan, but what are the conditions, bacterial and other, that determine its formation rather than the formation of indol, we do not at present know. I have found that the administration of skatol to monkeys by the mouth and by subcutaneous injections has been followed by the appearance of a substance in the urine giving the Ehrlich dimethylamidobenzaldehyd reaction and that the administration of 0.1 gm. of skatol to man has heightened the Ehrlich reaction in the urine. In most cases in which the fæces contain considerable skatol the urine gives a strong reaction with Ehrlich aldehyd. Skatol behaves in the organism much like indol as respects its toxic properties, but it is somewhat less poisonous. There is

seldom reason to attribute to it any definite pathologic effects. It is possible, however, that, like phenol, it may, under some conditions, play an auxiliary part with other substances in damaging living cells.

*Indol.*—Indol is not a product of tryptic digestion of proteids and probably cannot be formed in the course of physiologic processes without the intervention of organized ferments such as bacteria. The indol produced in the intestine is, like skatol, derived from tryptophan. In early life the production of indol in the intestines is in general very slight and there are some older persons also who, even while suffering from disorders of digestion, do not form indol. On the other hand, the production of considerable quantities of indol in the large intestine is a feature of many instances of intestinal putrefaction and in some cases the quantity formed is large. That indol may be absorbed in considerable amounts is shown by the appearance of large quantities of indican in the urine of persons in whom the intestine contains large amounts of indol.

While it is true that in general the aromatic compounds are resistent to oxidation, it is probable that whenever indol is introduced in moderate quantities into the organism of carnivorous and omniverous animals, a portion of it is burned completely in the body. It may be regarded as settled that the liver, muscles, intestinal epithelium and other cells normally exert a protective action to the nervous system in screening it from the effects of an injurious percentage of indol in the blood, by the ability of these structures to quickly bind any indol which comes to them. The differences in the observed toxic effects are probably dependent on inequalities in different persons in their ability to oxidize indol and to pair it with sulphuric acid. As to the effects of absorbed indol on the organism in disease, it is necessary to speak with caution, since there is no evidence that indol is the only toxic substance absorbed in those cases where it enters the organism from the gut.

The idea that the circulation of free indol in the blood may act in a depressing manner on the muscular structures is sug-

gested by the rapid muscular fatigue which comes on in some persons who have suffered for a long period of time from a high grade of indicanuria. Professor Lee has shown experimentally that indol has this effect in dogs. In some cases of excessive intestinal putrefaction in childhood associated with retardation in growth and abdominal distension there is clearly a poisoning of the muscular system. These children show signs of fatigue very rapidly, and in some cases where the condition has come on in early life they are slow in learning to walk. Their urine contains not only a large amount of indican, but a considerable quantity of phenol. It is likely that phenol in these cases plays a part in the muscular depression. Perhaps in some instances it is as much a factor in inducing fatigue as is indol.

### INDIVIDUAL SUSCEPTIBILITIES AS POSSIBLE FACTORS IN DETERMINING CLINICAL TYPES.

Instances are many in which clinical experience has made it clear that two persons of approximately the same weight react differently to the same drug and do so regularly. Of individual human susceptibilities and reactions to the action of enterogenous poisons almost nothing is now known. Nevertheless, one cannot fail to recognize the possibility that such individual susceptibilities and reactions may play an important part in determining the clinical manifestations of intoxications. It is well known to clinicians that there are some persons who promptly develop a widespread urticaria after indulgence in certain foods or drinks, such as shell-fish or strawberries or champagne. In some persons the indulgence in a single glass of champagne is followed within twenty-four hours by manifestations of gout. In others champagne causes headache and the excretion of increased amounts of uric acid.

The explanation of these different effects is to be sought in the individual cellular reaction of the patient rather than in the poison. There are probably many similar examples of individual susceptibility, but when we come to study the question in relation to processes found in the digestive tract we

cannot make close comparisons between different persons because we cannot say what substances are being absorbed. We may know that a certain group of patients are alike in having intense indicanuria, but we cannot say that the intoxications may not be different in these cases owing to differences with respect to the absorption of other substances than indol. Among half a dozen persons suffering from extreme indicanuria one suffers from headache, sometimes migraine-like; another is prone to lumbago; another perhaps has epileptic seizures; another has mental depression; another progressive muscular atrophy, and still another suffers from cyclic vomiting. There is good reason for suspecting that very similar bacterial processes in the digestive tract lead in one case mainly to digestive disturbances and in others, owing to a lesser sensitiveness in the digestive tract itself, to better absorption of poisons and the development of more remote consequences, such as acute arthritis, anemia or nervous disorders. While it is possible that these very different manifestations are always connected with different and perhaps specifically different types of gastroenteric infection and intoxication, the possibility is not excluded that even such very different derangements may have much in common in their etiology. That the mental and emotional peculiarities of individuals have a large part in fixing the type of nervous reactions that occur in consequence of intoxications has become apparent to careful students of pathologic conditions.

### TYPES OF CHRONIC EXCESSIVE INTESTINAL PUTREFACTION.

The variations in the clinical manifestations and pathologic accompaniments of chronic excessive intestinal putrefaction suggest that the etiologic conditions vary in different patients. The three types that I would suggest are:

1. The *Indolic Type* of chronic excessive intestinal putrefaction. This is marked by striking indicanuria and probably is due to members of the *B. coli* group.

2. The *Saccharo-Butyric Type* of chronic excessive intestinal putrefaction, which seems to be initiated chiefly by the anaë-

robic forms. In its simplest examples there is very little indol in the gut.

3. A *Combined Type,* or cases combining the characteristics of Groups 1 and 2.

*Indolic Type of Chronic Excessive Intestinal Putrefaction.*—In these cases the members of the *B. coli* group form indol in considerable quantities and they probably invade the small intestine in large numbers. The bacterial cleavages seem largely to replace normal tryptic digestion.

Provisionally we may classify here that type of chronic intestinal indigestion found in marantic children with large abdomens. In the treatment of these children much patience is necessary. At first their digestive processes must be improved. Carbohydrates should be greatly restricted and should be given as rice or Huntley and Palmer biscuits. The milk may be peptonized to promote its earlier absorption. Chicken, beef and mutton are permissible, but they should be finely divided. In a child 5 or 6 years old it may be advisable to give only two meals a day. Considerable benefit seems to follow daily irrigation of the colon, which facilitates the removal of the putrefactive products before they are absorbed. The children should exercise, but should be spared fatigue. They should rest much. Because they stand cold badly, they do best in a mild climate during the winter. Improvement may be possible after several years of rigid régime. The retarded growth, however, is evident even at puberty. Some of these patients seem always susceptible to intestinal disorders, and may never become strikingly robust.

*The Saccharo-Butyric Type of Chronic Excessive Intestinal Putrefaction.*—In this type the seat of the putrefactive process is the large intestine and lower ileum. It is due to the activity of the strictly anaërobic butyric acid producing bacteria. Although our study is not yet exhausted it may confidently be stated that in many cases *B. ærogenes capsulatus* is largely responsible. With this form may be assoeiated *B. putrificus* and possibly sometimes the bacillus of malignant edema,

although often these forms are not found in cultures on any of the ordinary media.

The abundance of putrefactive anaërobes, especially of *B. ærogenes capsulatus,* gives a peculiar character to the intestinal contents. The organisms attack carbohydrates and proteids vigorously and butyric acid is formed from both, together at times with propionic, caproic or valeric acid. These acids are largely responsible for the odor of the stools. From proteids, besides these acids, hydrogen, carbon dioxid and perhaps methane are formed. As a consequence the fæces have a low specific gravity and often a decidedly light color. The presence of hydrogen leads to the extensive reduction of bilirubin and other pigments. The Schmidt test with mercury bichlorid gives a strong pink color. The stools have an acid reaction, although the acids are neutralized in part by ammonia and other bases formed in the process of putrefaction. It is probable that the ammonium butyrate acts as an irritant to the gut, causing soft stools or diarrhœa. Indol is absent, or present in small amounts. Phenol occasionally is found in slight excess. In the urine the ethereal sulphates at times are excessive, although the reason for this is not clear. Mercaptan may be present in the fæces as a trace; it is also found in cultures by means of the isatin-sulphuric-acid test. It has been noted that as the patient improves the mercaptan becomes less or disappears, but the explanation of this phenomenon is at present unknown.

In nearly all adults the *B. ærogenes capsulatus* is present in the intestines in small numbers. It is possible that this organism is responsible for repeated slight attacks of intestinal putrefaction, although it may not in these mild cases lessen the duration of life. In some persons in whom a high grade of putrefaction is present, a condition of actual invalidism may be induced and life may be definitely shortened as a consequence of the intoxication.

The presence of ammonium butyrate may give rise to irritation of the intestine and this may be associated with an excessive desquamation of the epithelium, not only in the

intestine, but in the mouth and stomach as well. We have evidence of this in the presence of a large number of nuclei in the fæces, and it is well recognized that excessive desquamation of the lingual epithelium is associated with digestive disorders. The patients suffer from flatulence. They tolerate carbohydrates and acids badly, and are very liable to attacks of diarrhœa after a meal of carbohydrates. Acids may be formed in the mouths of these patients through the influence of anaërobes. This adds to the irritability of the intestine. It is possible that in advanced cases the *B. ærogenes capsulatus* may invade the small intestine and there find sugar from which to form butyric acid, etc. After the carbohydrates are thus exhausted, the anaërobic forms in the large intestine set up putrefactive processes in the proteids which exist there.

It is also noteworthy that many patients who suffer from severe intestinal putrefaction are distinctly anemic. The first change in the blood seems to be a decrease in its volume; then the hemoglobin falls somewhat and finally the cells themselves are reduced in number. The grade of anemia varies extremely, from a moderate secondary anemia to the most serious grades of the progressive pernicious form.

*The Combined Indolic and Saccharo-Butyric Type of Chronic Excessive Intestinal Putrefaction.*—Examples of this type of intestinal putrefaction are common. There are many putrefactive anaërobes in the gut, and also a persistent and well-marked indicanuria, which is but slightly influenced by diet. The nervous symptoms are relatively prominent and appear early. They are emotional irritability and periods of mental depression; muscular or mental activity soon induces a striking fatigue. Later the blood disturbances may appear. Although these patients have intervals of improvement that continue for months, on the whole the general tendency is downward. They become less robust and recuperate less promptly from every succeeding attack. They may run along for ten or fifteen years in a weak condition, with periods of slow improvement, and finally may present the picture of a pernicious anemia. In others the nervous symptoms increase and the patients may

need treatment in a sanitarium or in an asylum for the victims of melancholia.

These various manifestations in different individuals may represent merely a differing reaction to the same poison. Whether the nervous system or the blood shall bear the brunt of the attack is determined by the relative vulnerability of these tissues in that particular individual. It is noticed also that under treatment one group of symptoms may improve quite independently of the other.

There is a more rapid advance of invalidism than is the case of either type (1) or type (2) alone. The atrophy of the fat and muscle and the blood changes are present, and perhaps also there are chronic parenchymatous changes in the kidney and liver as a result of the constant poisonous action.

### THERAPEUTIC CONSIDERATIONS.

The difficulties that beset our efforts to control and modify excessive intestinal putrefaction are obvious. Although the cases arrange themselves in groups, every one presents certain points of difference. Our experience is so incomplete that as yet our efforts are more or less experimental. Notwithstanding this, one may lay down rules for partial guidance that are based on certain principles, but a careful regard for individual traits is imperative.

The mild cases often show a rapid improvement and lose the evidences of putrefaction. The patient feels well, yet he can hardly be called normal, because he has deficient reserve power and will easily relapse to his former condition after an indiscretion in eating or excessive fatigue or worry. The long-standing cases improve slowly at best. The chemical products of putrefaction may be reduced in amount, but the symptoms often persist, and even under most favorable circumstances the patient is liable to frequent and protracted exacerbations.

The following principles must be regarded in treating all the three types of putrefaction: (1) Avoidance of continued reinfection that follows the ingestion of putrefactive bacteria with the food; (2) the promotion of prompt digestion and rapid

absorption from the small intestine; (3) the reduction of the number of putrefactive anaërobes in the ileum and colon.

1. To avoid infection and reinfection the mouth must receive scrupulous care. Carious teeth and gingivitis must be treated carefully by the intelligent use of the toothbrush and of washes containing peroxid of hydrogen. In conditions of gastric atony a process of putrefaction begins in the stomach that normally starts in the colon. Gastric fermentation and putrefaction are controlled by lavage every day, perhaps best in the morning. The reduction of the number of bacteria here leads to lessened damage to the bowel at lower levels.

In the preparation of food ordinary cleanliness is very effective. It is probably better to use cooked food as much as possible. Fruit is not above suspicion, for Dr. Rettger has determined that the bacillus of malignant œdema is commonly present on banana peel. This suggests the advisability of peeling all fruit that is eaten. Milk always contains a large number of bacteria and often some of the putrefactive forms, especially *B. putrificus.* The lactic acid formers abound, but their action is rather beneficial in that they antagonize other and harmful forms. Sterilization of the milk is of little value. Pasteurization or the ordinary boiling kills the lactic acid formers, but does not harm the spores of the putrefactive organisms. Cheese, except fresh home-made cheese, contains many putrefactive forms, and is best avoided, particularly inasmuch as many of these patients lack the protective action of the normal amount of hydrochloric acid in the stomach.

2. With rapid digestion and prompt absorption little pabulum for the putrefactive organisms reaches the colon. These processes are facilitated by measures that improve the secretory and motor functions of the stomach. Chief among these is proper mastication, which largely determines the ability of the body to utilize food. When large masses of meat are swallowed, they commonly appear in the fæces. Comminution of food outside the body is not an adequate substitute, for the patient then loses the emotional stimulus to gastric secretion and also the digestive action of the saliva itself. The admin-

istration of hydrochloric acid often helps for a time, but in long-standing cases, especially those of the combined indolic and saccharo-butyric types, it is of little use. Ferments, such as pepsin and pancreatin, are of doubtful value, although they cannot be said to be always useless. Diastase gives better results, as it enables the patient to utilize more extensively the carbohydrates of the food. If, as often happens, the stomach is irritable, it is advisable to give small meals and to administer flaxseed or other demulcent before eating. The best pancreatic stimuli, aside from the quality of the chyme, are cheerful emotional accompaniments of eating, and rest, physical, mental and sexual. Prompt absorption is promoted by restricting the amount of food, especially of proteid food. Meat should rarely be eaten more than once a day.

3. To reduce the number of putrefactive organisms in the colon, one turns naturally to intestinal antiseptics. While these drugs may act efficiently on bacteria in the stomach, evidence of their continued action in the intestine is variable. Perhaps the salicylates are most likely to check fermentation and putrefaction in the stomach and small intestine. It is conceivable that certain oxidizing substances which are slowly dissociated, such as manganese bioxid, may reach the colon in time to liberate their oxygen there and thus, in part at least, remove the anaërobic conditions that obtain in this part of the intestine.

The use of laxatives may be followed by temporary benefit, in that they lessen absorption from the gut, as is shown by a decrease of the ethereal sulphates in the urine, after their use. They must, however, be given with caution, lest they increase the irritability of the bowel and lead to diarrhœa and loss of strength. On the whole, they are useful in acute and subacute cases only.

There are certain very tempting methods which aim to substitute harmless bacteria for the putrefactive organisms, but more evidence is needed as to the value of this procedure. It is a common practice to introduce lactic acid formers in kumys and kefir and also in bacillac, a fermented milk introduced

by Metchnikoff, which is free from yeasts. Irrigation of the colon two or three times a week is often followed by a decrease of the ethereal sulphates in the urine and by relief from symptoms, including both the mental symptoms and the anemia. This procedure is more efficacious in the saccharo-butyric and combined types of putrefaction.

### PROGNOSIS.

In considering the prognosis in these patients, the duration of the condition is as important as its intensity. Better results are obtained in those cases induced by gross errors of life, the correction of which is followed by improvement or complete recovery. In a highly neurotic person the outlook is less hopeful. A protracted rest for two or three years, with careful attention to the principles of treatment laid down, offers the best hope of health.