conditions. This test has been used continuously by one of the authors for the last ten years, and shews the absence of any clinical degree of ketonuria in normal pregnancy*.

If all pregnancies or a very high percentage of pregnancies shew glycosuria and are physiological in character it seems unnecessary from the purely clinical standpoint to distinguish between a glycosuria and a lactosuria, as usually recommended. If the distinction between glucose and lactose were readily and clearly made, we should advise otherwise, on the grounds of completeness of data. In view of the uncertainty of the distinction by the present suggested tests, we think the wiser course is to assume the presence of a glycosuria.

*Le Nobel Test. To 6-10 c.c. urine add 2 or 3 small crystals of sodium nitroprusside. Shake until most of the crystals are dissolved. Add 2-3 c.c. *glacial* acetic acid. Mix, and then freely overlay with *concentrated* aqueous ammonia. A purple or permanganate colour forms where the liquids are mixed, and spreads upwards into the ammonia layer. The significance and value of this test was first pointed out by Harding and Ruttan[11]. While not so sensitive as the more popular Rothera test, it is not so liable to misinterpretation.

The authors wish to acknowledge the assistance of the Burnside Metabolic Ward of the Toronto General Hospital under the direction of Professor W. B. Hendry.

REFERENCES

1. KUSTNER, *Zentralbl. f. Gyn.*, 1922, **46**: 1238.
2. WALLIS AND BOSE, *J. Obst. & Gyn. Brit. Emp.*, 1922, **29**: 274.
3. WILLIAMS, *Boston M. & S. J.*, 1925, **192**: 163.
4. CROOK, *The Lancet*, 1925, **1**: 656.
5. WILLIAMS, *Am. J. M. Sc.*, 1909, **137**: 1.
6. JOSLIN, *Boston M. & S. J.*, 1915, **173**: 841.
7. RABINOWITCH, *Canad. M. Ass. J.*, 1924, **14**: 375.
8. POWELSON AND WILDER, *J. Am. M. Ass.*, 1931, **96**: 1562.
9. ROCKWOOD AND DODGE, *Surg., Gyn. & Obst.*, 1928, **47**: 660.
10. HARDING AND VAN NOSTRAND, *J. Biol. Chem.*, 1930, **85**: 765.
11. HARDING AND RUTTAN, *Biochem. J.*, 1912, **6**: 445.

A DISCUSSION ON THE ETIOLOGY AND SPECIFIC TREATMENT OF ARTHRITIS*

BY FRED. T. CADHAM, M.D.,

Professor of Bacteriology and Immunology, Faculty of Medicine, University of Manitoba, Winnipeg

IN some European countries arthritis ranks first among all diseases as a cause of disability, and in America the disability from this disease is estimated to equal that caused by tuberculosis. One would expect in view of such an incidence that public health organizations would be greatly concerned with this problem. However, especially on this continent, public health activities in reference to arthritis have been quite limited.

Chronic polyarthritis constitutes one of those medical paradoxes, a subject about which so much and at the same time so little is known. A literature almost unequalled by that on any other disease in medicine adds to the complexity. One reason for this is the difficulty of classification. Gibson, in a preliminary report of this work, has emphasized this aspect of the problem. The term "arthritis" covers varying changes in and about the joints, the result of the action of different agents, and indicates no more specific etiology or pathology than the general terms rheumatism, influenza, or pneumonia.

*Read at the meeting of the Canadian Public Health Association, Regina, May, 1931.

PREDISPOSING CAUSES

Certain observers hold that the familial incidence of this disease is marked. It may be accepted that in some instances this acts as a predisposing cause. However, in weighing the importance of this factor it must be remembered that the law of averages is to be considered, for the incidence of chronic arthritis is high in the general population. Also, an infectious agent may be common to certain family surroundings; moreover, a familial failing, such as a lack of oral hygiene, frequently exists, and hence supplies a predisposing focal factor. Definite evidence of a hereditary diathesis is mentioned by Gerrard in that rare disease, alcaptonuria, a condition in which homogentisic acid is present in the urine, the joint cartilage turns black, and osteo-arthritis develops.

SEX AND AGE

Females appear to be at least three times more susceptible to rheumatoid arthritis than males; but in England since the War the incidence for males is steadily increasing. In osteo-arthritis the rate is approximately equal;

however, peculiar variations exist in the incidence of mono-articular arthritis, such as that of the hip, which is far more common in men than in women.

Rheumatoid arthritis has been noted at all ages, from one to eighty-five, but the usual age when the patient seeks treatment is between twenty-five and forty-five. To determine the date of onset in such an insidious disease is a much more difficult task. Careful inquiry will frequently elicit the fact that the patient had twinges of pain in the affected joints even years before actual disability occurred.

ANTECEDENT DISEASES

At least 15 per cent of all patients with chronic arthritis give a history of having suffered from an attack of acute rheumatism; also, tonsillitis, sinusitis, puerperal fever and other complications of pregnancy, influenza and gonorrhœa, are frequently mentioned as antecedent causal diseases. On the other hand, in the majority of cases, no such history may be obtained. Chronic arthritis is often found associated with scleroderma, and gout with psoriasis, and, conversely, chronic arthritis and tuberculosis or carcinoma seldom exist concurrently in the same patient.

Charcot and others hold there is a close association between pregnancy and some forms of arthritis. No reason is applied for this association, but one should remember that a lowered resistance of the gums and teeth frequently obtains during the puerperium. Hence an infectious agent may then take advantage of a favourable opportunity. Then too, there is that peculiar association of arthritis with the menopause, so-called "climacteric arthritis," described in the time of Hippocrates. Here again the question of a lowered resistance at this period of life must be taken into account as a possible factor. Hench suggests that the arthritis of the menopause may be a static arthritis following increased weight, the result of the obesity which is coincident with the climacteric.

Trauma of a joint is occasionally followed by arthritis of that joint; this may subsequently extend to involve other joints. Also arthritis develops more frequently in those joints which, because of a certain occupation, come under the greatest stress.

Some writers dwell on the relation of this disease to disordered metabolism. The endocrines, in diseases of ill defined etiology, generally come under suspicion as a possible etiological factor. The positive evidence supporting arguments in favour of such an origin for chronic arthritis is exceedingly slight. Cawadias[3] stresses the variation in sulphur metabolism, and Ellis[5] holds that there exists an inability to utilize phosphorus. The blood calcium remains normal or slightly above normal, and the blood urea holds close to normal values, though it may be found high in gout. Barr[1] states that true rheumatoid arthritis follows a prolonged mild acidosis. Pemberton,[14] in an investigation of 400 cases of arthritis, found but little variation in the basal metabolic rates. True, a lowered sugar tolerance is noted in many cases, but such a condition also prevails in the presence of known foci of infection; further, this tolerance returns to normal limits after the removal of such foci. Moreover, there exists no definite evidence that diseases believed to be caused by disorders of metabolism are especially associated with arthritis. Usually an infection gives rise to marked symptoms in some particular anatomical part, which does not signify that other areas escape. Why should the endocrine glands be immune to bacteria or their toxins? That infection may so interfere with metabolism as to favour a joint infection is far different, as Rolleston[16] states, from postulating a primary error of metabolism.

Many investigators believe that the character of the food has little if any effect in this disease; others, again, advise the use of a low protein diet; still others a high protective diet. Considerable experimental evidence now exists that a deficiency of vitamins, particularly vitamins A and B, predisposes the tissues to infection or possibly the continuance of an infection. The relation of vitamins to immunity in this and other diseases promises a hopeful field for further investigation.

THE BLOOD PICTURE

Chronic arthritis is associated with anæmia, which most authorities believe to be secondary. The blood picture, however, fails to disclose the degree of anæmia one would expect from the pale waxy appearance of so many of these

patients. The leucocyte count and content varies; generally, a leucocytosis occurs in osteo-arthritic forms of the disease. Since achlorhydria is associated with anæmia, it should be noted that this condition is not an unusual finding in patients with chronic arthritis. Is such a condition in itself, then, responsible for the arthritis, or does the lack of the acid in the stomach allow the effect of oral sepsis to reach the bowel? Such questions illustrate the difficulty of determining the exact influence of these so-called antecedent causes.

FOCI OF INFECTION

Here we stand on more solid ground. A multiplicity of experience exists which shows that the removal of some focus of infection is frequently followed by the relief of an arthritic condition. Whether the focus is responsible for the entrance of organisms into the circulatory system with a subsequent location in the joint, or whether the arthritis is the result of toxins absorbed from the focus, remains to be proved. Probably one or both conditions obtain in different cases.

As a focus of infection it is conceded that the greatest responsibility lies with oral sepsis. Early destruction of the teeth and modern civilization apparently progress hand in hand. A highly mechanized dental surgery may add fuel to the flames, as witnessed by that physiological folly, the "whited sepulchre", the sealed devitalized tooth.

Some authorities would place more responsibility on the tonsils as the source of sepsis in its relation to chronic arthritis. What constitutes a pathological tonsil is a matter of opinion, but it is suggested that even the small and innocent-looking tonsil needs to be viewed with suspicion, especially in those cases of chronic arthritis where no other obvious foci of infection may be demonstrated. Again, to illustrate the complexity of the question, certain investigators have pointed out that an equal or slightly higher incidence of arthritis pertains in those who have had their tonsils completely removed in early life compared with those who have retained them.

Sinusitis may be overlooked as a focal factor, and it is well to bear in mind, in considering these foci of infection, that oral sepsis frequently supplies the original source; subsequently diseased tonsils and sinuses occur, and not infrequently all of these; and possibly more similar conditions exist coincidentally in the same patient. Hence it follows that the removal of a single focus may fail to give therapeutic benefit.

Many authors stress intestinal infection as an important etiological factor, especially in rheumatoid arthritis. Also, infections of the genito-urinary tract, prostate and cervix, are associated with this disease, or special types of this disease. Nor is the lung to be overlooked; the bronchi may furnish an efficient incubator for certain pathogenic types of bacteria. The French view, however, that many cases of arthritis are caused by toxins from a tuberculous focus is not generally accepted.

BACTERIOLOGY

The frequent use of the term "infective arthritis" indicates how entrenched has become the opinion that the disease is, or at least many types of the disease are, of microbic origin.

Abundant evidence is available to prove that acute arthritis may be caused by various organisms, such as the tubercle bacillus, the gonococcus, the typhoid, paratyphoid dysentery bacillus, the spirochæte of syphilis, and others. These infections commonly burn themselves out, but on occasion certain types of acute inflammation of the joints become chronic. Not so clear is the evidence that any single bacteriological factor exists in the majority of the chronic cases. The literature contains an amazing amount of clinical observation, of experiment and investigation, incriminating a considerable number of different bacteria. If we do not allow the present terminology to cloud the issue, and granting that certain cases of the disease are probably non-infective in origin, then it would only appear logical to consider that chronic arthritis may be produced by the action of a number of widely different organisms. How may these be determined, and what is their relative importance? Naturally we would expect that cultures taken direct from the joints would solve the problem, but here we encounter difficulties. As a rule cultures from the joints prove sterile. The synovial fluid is practically always free of

organisms, although an increased white cell count persists, ranging all the way from 80 cells to 40,000, and Forkner[7] points out that the number of polymorphonuclears was distinctly higher in the small group in which positive cultures were obtained from the joint, while those with negative cultures showed a relative increase of mononuclears. Then, too, the examination of the immediate tissues about the joint also fails in the great majority of cases to reveal the presence of organisms, a feature not easy to explain. Hence, the determination of any single causative bacterium, provided we accept that etiological theory, demands further study.

It has been suggested that the change which takes place in the joints as a result of the action of micro-organisms is an anaphylactic one. That is to say, a hæmatogenous infection of the joint had occurred, then the organisms died out or were destroyed, and subsequently toxins originating from some focus of infection of the same organism elsewhere in the body, acted on the joint in an anaphylactic manner. The analogy for the reaction of the joints to foreign proteins is illustrated in the joint symptoms of serum disease.

A number of investigators strongly incriminate the streptococcus, especially that type found in foci of infection. Hastings, and, later, Burbank and Hadjopoulos, carried out extensive complement fixation tests with the blood of arthritic patients against a selective group of the streptococci. They obtained a large percentage of positive results. This is a significant finding, and one would like to determine and compare the results with the results of such tests in a large number of healthy controls.

The organism most frequently reported in such positive cultures that have been obtained from the joints and from neighbouring lymph-nodes, is the streptococcus. We may add to this evidence that of recent workers who have obtained this bacterium in blood cultures in as high as 60 per cent of the cases examined. Then, too, the experimental work of Rosenow[17] and others showed that arthritis developed in rabbits following inoculations with cultures of this organism, when taken from foci of infection; besides which a beneficial response often follows the use of a vaccine prepared from such a streptococcus.

This makes a strong case against the streptococcus; however, other organisms, according to many investigators, apparently share the responsibility. Crowe[4] claims that a special staphylococcus, which he calls the "micrococcus deformans", dominates the picture. Again, other observers place weight on the toxic properties of the coliform organisms of the bowel. Ely[6] ascribes osteo-arthritis to a protozoon infection, which organisms, he states, enter the system from a focus around the tooth sockets. He claims that protozoa were found in the stools of approximately 40 per cent of the arthritic patients examined. Then, there is the diplococcus of Poynton and Payne,[15] an organism which these workers describe as having isolated from the diseased joints. Also the presence of the pneumococcus in the bowel of a considerable number of arthritic patients has been noted, and some authorities stress the importance of the association of this disease with the gonococcus.

PERSONAL INVESTIGATION

In our own work here we have become interested in an apparently different organism. The method we adopted in attacking this problem was to investigate the bacteriology of the regional lymph-nodes. A patient with arthritis is prepared for operation. The regional lymph-glands, as a rule the inguinal, are removed, sectioned into fragments, and at the operating table, are immediately dropped into tubes of serum broth, plain, lactose and dextrose. These tubes are incubated sixteen days, then examined. Portions of the nodes were also placed on Sabouraud's medium, to determine if fungi were present.

These lymph-nodes vary in size, and one unexplained macroscopic characteristic, noted in the majority of cases, was the peculiar colour; the gland or a part of the gland was a bluish purple. On section, some glands showed a hyperplasia of the reticulum, but as a rule little pathological change could be noted.

In the cultures from 34 cases thus investigated a peculiar diphtheroid organism was isolated in twenty-seven. In 5 cases we found staphylococcus, and in 1 case a Gram-negative bacillus in symbiosis with a staphylococcus.

The latter case was eventually diagnosed as leukæmia. Glands removed from 3 patients without arthritis proved negative on culture.

The diphtheroid organism which was isolated is a pleomorphic bacillus, averaging ½ micron by 1½ microns in size, and showing as a rule deeply staining granules resembling cocci. The organism is oblong and flat, the granules, usually six in number, are located three on each margin. These characteristics were only determined by examination under the dark field, for, curiously enough, upon fixing and staining the micro-organism, the granules appear to extend across the diameter, nor is the flattened character of the bacterium to be determined in the fixed smear. Apparently, there are different stages in the life history of this organism. In some cases a coccoid form, resembling a minute streptococcus, appears in the primary cultures, and the bacillary form in subcultures, but in others the single type, that is, the coccoid or the bacillary only, is seen. Some of the bacilli grow to 3 or 4 microns in length. The bacilli may always be developed from the coccoid form. The latter is Gram-positive, the bacilli partly Gram-negative in young cultures, becoming Gram-positive with age. It is not acid-fast, and stains with all aniline dyes.

It grows well on human blood agar, fairly well on Loeffler's serum, and in glucose serum broth. Gelatin is not liquefied. It ferments dextrose, maltose and dextrin. Primary colonies are exceedingly minute and discrete, becoming confluent with age; at first greyish white, with yellowish tinge after three or four days. Primary cultures take 14 to 21 days to develop; subcultures show pin-point colonies in 24 hours. Variations in the type of colony are to be noted. At one stage the organism is filtrable, and the diphtheroid again develops in the filtrate, apparently from the minute filtrable bodies. Rabbits which we have inoculated with a living culture of this organism developed a polyarthritis.

References to the isolation of a peculiar bacterium occur throughout the history of the bacteriological investigations of this disease. It has been variously described as a diphtheroid, a pleomorphic bacillus, or a peculiar coccoid bacillus. In 1892, Schueller[18] obtained such an organism from the joints in a case of chronic arthritis. In 1900 it was isolated from the synovial fluid. Rosenow[17] found it in 9 out of 38 regional lymph-nodes examined, and Burbank[2] has isolated such an organism from the blood stream of arthritic patients. There is every reason to believe that it would have been noted more frequently had investigators incubated their cultures over a longer period of time.

No one seems to have attached any particular significance to its presence. Apparently this bacterium has a definite etiological relationship to certain types of so-called rheumatoid arthritis. Then, too, the peculiar characteristic it exhibits, that is, the ability to develop from a minute filtrable form into a bacillus might throw light on the reason why direct microscopic examination of tissues from about the diseased joints and also of the synovial fluid proves negative; the minute coccoid form in such tissues would easily pass unrecognized. While we were able to produce polyarthritis in rabbits by inoculations of living cultures of this organism, yet the same results may be obtained by the inoculation of streptococci, and occasionally of staphylococci and other organisms, again illustrating the probability of the varied etiology of the infective type of arthritis.

A study of the diphtheroid bacillus isolated at once plunges us into the entire question of the biology of bacteria. Bacteriologists have been content to believe that bacteria multiply simply by binary fission. Mellon,[13] following long intensive study of a diphtheroid, states that in the life history of bacteria certain special forms are evolved which are possessed of genetic possibilities, and suggests that these cyclo-stages of a bacterium play an important part in infection, immunity and epidemiology. More recently, Hadley, Delves, and Klimek[10] have presented an extensive report of their work on filtrable bacteria. They obtained the filtrable stages in a stable pure culture. The minute bodies are mentioned by various workers, under the terms granules, spores, micro-gonidia or gemmules. Hadley and his co-workers suggest that these bodies are reproductive, and are given off by the bacteria, although they state that they have never seen the process. Under the dark field I have observed the "firing" of these granules from diphtheroids which we have isolated from lymph-nodes. They are motile; moreover this motility is apparently in part con-

trolled. Frequently these minute bodies come in contact with the granules of the bacteria for a moment, and then disperse rapidly.

TREATMENT

The prevention of arthritis depends on hygiene, school and pre-school inspection of children, and periodic health examinations for the elimination of those minor ailments which eventually lead to major disabilities.

The specific treatment, at present confined to the use of foreign proteins and vaccines, offers some hope. Shock protein therapy with typhoid vaccine, horse serum, or other proteins, occasionally gives rise to such immediate beneficial results as to astonish the observer. However, with rare exceptions, the patient reverts, and the second intravenous inoculation of foreign protein frequently fails to bring any relief, and may be accompanied by considerable distress.

Subcutaneous inoculation with vaccines is of value. Such authorities as Wright and Wilcox[19] stress the beneficial reaction that may thus be obtained. Rolleston states that autogenous and not stock vaccines should be employed. The best results follow the use of an autogenous vaccine prepared from the organisms obtained from an obvious focus of infection, or from the joints, or the lymph-nodes. The correct preparation of a suitable vaccine demands experience of a highly specialized procedure, and I should like to emphasize that such vaccines need to be made and administered with the greatest of care.

Now the logic of immunity indicates that the value of vaccines exists only in prevention, and when we endeavour to cure disease with vaccines, we institute a method of therapeutics full of immunological pitfalls. However, in such a condition as chronic arthritis, the inoculation of a suitable vaccine may, and evidently does, stimulate the production of antibodies, which then afford immunity against a further attack, but immediately following the treatment it must be borne in mind that the existing condition is frequently aggravated.

I have had the opportunity to observe the effects of treatment with autogenous vaccines of some ninety patients suffering from chronic polyarthritis. In over eighty of these patients the use of the vaccine was followed by some amelioration of the symptoms, and in many cases by complete relief; a few patients showed no benefit. Some may advance the argument that 30 per cent of these patients will recover when left to their own resources. This argument demands consideration. It may also be applied to the other methods of therapy, and the value of the results obtained by any method needs to be carefully weighed in the light of such knowledge. Then, too, specific therapy should only be carried out in conjunction with other well recognized procedures.

When we approached this problem we had two aims in view; first, to discover if possible if the bacteriological findings in the regional lymph-nodes would throw any light on the etiology, and secondly, if bacteria were present, to utilize them for the preparation of a serum with specific antitoxic properties. While awaiting the development of an antiserum in animals inoculated with a vaccine prepared from the organism recovered, we treated the first of these patients with some of the vaccine. The response to this method of treatment proved so encouraging that the serum treatment was not instituted in any of these cases. The 34 patients who had glands removed were treated with the vaccine; these patients were afflicted with polyarthritis in an advanced stage. Of these 34, 6 are at present undergoing treatment, 17 have recovered and returned to full duty; 7 showed considerable amelioration of symptoms; 3 bed-ridden patients recovered sufficiently to be about; 1 received no benefit, and 1 patient, a child with Still's disease, who was showing considerable improvement, unfortunately died of intercurrent measles. There are patients with chronic arthritis in whom the condition has advanced to such a stage that to remove a focus of infection resembles the act of throwing away the empty cartridge after the shot is fired, the pellets are already scattered throughout the body. Also, in many such cases, specific treatment fails because the tissues are so damaged that they are unable to respond to the immunological stimulant afforded by this treatment. The blood complement in these patients falls below 50 per cent of normal, and when it reaches that low level the prognosis is grave. Also a certain type of case occurs, fortunately few in number, in which the patient, after an early and supposedly complete examination, and with the advantage of all modern methods

of treatment, continues to progress to complete disability and a pitiful end. In this type of case we hope to continue our investigations with serum therapy.

In conclusion, it may be stated that there is a tendency for the profession to hold a pessimistic view of chronic arthritis. One cannot stress too much the importance of the early recognition of this disease, and the value of prompt treatment by both general and specific means. I believe if such conditions are fulfilled, the outlook in this, a major disease of medicine, will be changed to one of optimism.

REFERENCES

1. BARR, *Brit. M. J.*, 1925, **2**: 603.
2. BURBANK AND HADJOPOULOS, *J. Am. M. Ass.*, 1925, **84**: 637.
3. CAWADIAS, *Brit. M. J.*, 1925, **2**: 602.
4. CROWE, *The Lancet*, 1913, **2**: 1460.
5. ELLIS, *M. J. & Rec.*, 1927, **126**: 599.
6. ELY, *J. Am. M. Ass.*, 1923, **81**: 1762.
7. FORKNER, *Arch. Int. Med.*, 1928, **42**: 675.
8. GIBSON, *J. Bone & Joint Surg.*, 1928, **10**: 747.
9. GLOVER, Great Britain Reports on Public Health & Medical Subjects, 1928, p. 52.
10. HADLEY, DELVES AND KLIMEK, *J. Infect. Dis.*, 1931, **48**: 1.
11. HENCH, *M. Clin. North Am.*, 1928, **11**: 1603.
12. HASTINGS, *J. Exp. Med.*, 1914, **20**: 52.
13. MELLON, Contributions to Medical Science, Ann Arbor Press, 1927, p. 271.
14. PEMBERTON, *Arch. Int. Med.*, 1920, **25**: 231.
15. POYNTON AND PAYNE, *Brit. M. J.*, 1902, **1**: 79.
16. ROLLESTON, *Brit. M. J.*, 1925, **2**: 589.
17. ROSENOW, *J. Am. M. Ass.*, 1914, **62**: 1146.
18. SCHUELLER, *Am. J. M. Sc.*, 1906, **132**: 231.
19. WILLCOX, *The Lancet*, 1928, **2**: 207.

INTESTINAL EREPSIN AND PHOSPHATASE OF INFANTS WITH ACUTE INTESTINAL INTOXICATION*

BY G. E. HALL, E. J. KING, J. R. ROSS AND M. M. SHAW

Toronto

THE purpose of this paper is to present a report on the intestinal erepsin and phosphatase (nucleotidase) of children dying from acute intestinal intoxication. In 1929 it was shown by work done in this laboratory[1], that the amounts of trypsin were markedly reduced in the stools in this condition. When these estimations were made on successive days it was found that this reduction followed closely the clinical condition of the infant. This work suggested that perhaps other enzymes were depleted or reduced during the course of the disease. As a result, the present investigation was undertaken.

During the late summer and early fall of 1930, while the seasonal incidence of this disease of infants was at its height, a number of these cases were studied in order to obtain information regarding any disturbance in the erepsin and phosphatase content of the intestinal wall. Acute intestinal intoxication (cholera infantum) is a definite clinical entity, the chief symptoms being diarrhœa, vomiting and, later, drowsiness. The history is of short duration, usually three to five days, but occasionally the onset is very sudden and the infant becomes acutely ill within twenty-four hours. The stools become very frequent and watery; there may be as many as eight or ten in twenty-four hours. Vomiting may occur after many of the feedings. Dehydration is a constant feature of the disease and may be of different degrees of severity, as shown by loss of elasticity of the skin. The temperature rarely exceeds 102°-103° F. Complicating conditions develop in many of the cases. In some there may only be mild infections of the upper respiratory tract, such as nasopharyngitis or otitis media. In others, broncho-pneumonia may be a terminal feature, or kidney lesions may develop and contribute toward a fatal issue. For a complete clinical description of this condition see Brown and associates, 1930[2].

Intestinal erepsin was discovered by Cohnheim in 1901[3], and has been extensively studied by Willstätter, Waldschmidt-Leitz[9] and others. It is secreted by the glands of the small intestine and has the property of hydrolyzing the peptides (formed by partial digestion of protein by trypsin) to amino-acids, in which state they are absorbed. Waldschmidt-Leitz and Hartneck[8] have shown that erepsin is not only secreted by the intestinal glands but also by the pancreas. It is now accepted that intestinal and pancreatic erepsin are identical enzymes.

Phosphatase occurs in small intestine, bone, kidney and other tissues. The enzyme is capable of hydrolyzing various organic compounds of phosphorus, such as nucleic acid, which is formed when nucleo-proteins are digested by trypsin. Intestinal phosphatase has been investigated by numerous workers with reference to its action on various substrates and its optimal reaction con-

*From the Department of Medical Research, University of Toronto, and the wards of the Hospital for Sick Children, Toronto.