Typhus fever and relapsing fever are often associated as regards their epidemic prevalence, although there is no evidence that they bear any etiological relation other than that due to common predisposing causes. That they are specifically distinct is well established, and the clinical history of each is sufficiently characteristic. The eruption of typhus, the continuous course of the pyretic movement, and the fatal tendency of the disease are all in contrast with relapsing fever. A more detailed account of the clinical points of difference is hardly necessary in view of what has preceded, and of the ready means of establishing the differential diagnosis which is furnished by the microscope. The same may be said as regards enteric fever, which disease is also characterized by a less abrupt onset, and a pyrexia which presents peculiar features essentially different from that of relapsing fever, together with special symptoms, such as a tendency to delirium, abdominal distention, an eruption of rose spots, etc. The differential diagnosis in that form of relapsing fever which is denominated by Griesinger "bilious typhoid" may perhaps present greater difficulties, and, before the discovery of the spirillum of Obermeier, much uncertainty existed as to the etiological relations of this fatal form of disease. In addition to the presence of the spirillum it is distinguished from enteric fever by its mode of onset, by the early appearance of jaundice, and by the character of the pyrexia, together with a tendency to hemorrhage from mucous surfaces, a more decided enlargement of the spleen, and the absence of rose-colored spots.

Bilious typhoid might very easily be mistaken for yellow fever in countries where this disease prevails, and we have the authority of Murchison for the statement that this mistake has been made by Graves, Stokes, and Cormack. The two diseases have many features in common, but also essential points of difference. Thus, yellow fever prevails only in certain latitudes and during the summer season, while relapsing fever is quite independent of climatic conditions. Yellow fever is extremely fatal, and a single attack protects from subsequent attacks; the reverse is true of relapsing fever. Relapsing fever is propagated by direct transmission from individual to individual; yellow fever is not, and its extension depends upon external conditions. The negro has a partial immunity from the effects of the yellow-fever poison, but is especially susceptible to relapsing fever. There are also essential differences in the clinical history of the two diseases. In one—yellow fever—the acme of temperature is commonly reached during the first twenty-four hours, and defervescence is gradual; in the other defervescence is rapid and accompanied by a critical discharge, and the acme of temperature occurs, as a rule, shortly before the crisis.

The "stage of calm" in yellow fever is a period of the gravest danger, the urine is scanty and highly albuminous, and complete suppression is a common, and almost invariably a fatal, event; the febrile paroxysm is usually not so protracted as in relapsing fever, and is attended with less distress, but the effects of the specific poison upon the blood, the kidneys, and the mucous membrane of the stomach are of such a nature as to place the life of the patient in the greatest jeopardy. The apyretic interval in relapsing fever is, on the other hand, a period of comparative safety and comfort; the urinary secretion is abundant, the appetite returns, and the stomach resumes its functions. This apyretic interval is, however, not so clearly defined in severe cases of bilious typhoid, as death occurs in from thirty to fifty per cent. of these cases, and most frequently during the initial paroxysm, or as a result of complications which interfere with the normal course of the disease; and as there are jaundice, albuminous urine, and a tendency to hemorrhages from mucous membranes, it is easy to see how mistakes may arise, and the diagnostic value of the microscopic test, demonstrating the presence or absence of the spirillum, becomes apparent. It must be remembered, however, that the spirillum is not found during the reactionary fever which sometimes follows the crisis, or during the pyrexia attending a complication.

Prognosis and Mortality.—The mortality from relapsing fever, in the absence of complications, is low. Out of 2,115 cases admitted to the London Fever Hospital in twenty-three years (1847–70), there were 39 deaths (1.84 per cent.). Murchison, to whom we are indebted for these figures, has also analyzed the statistics furnished by Scotch physicians. In a series of 6,300 cases the mortality was 4.12 per cent., and in a second series of 10,444 cases it was 4.42 per cent. According to Pepper, the mortality in the Philadelphia epidemic was 14.4 per cent., the total number of cases being 1,174. These figures scarcely sustain the statement that relapsing fever is a comparatively mild disease, and the mortality in the cases in which jaundice was a prominent symptom—"bilious typhoid"—which is said to have been not less than fifty per cent., places this form of the disease on a level with yellow fever and typhus, so far as its fatality is concerned. In India, out of 616 cases collected by Carter, there were 111 deaths (18.02 per cent.). It is evident from these figures that it is only by excluding cases complicated by jaundice, pneumonia, etc., that the statement is justified that "the death rate in relapsing fever is low." Death may occur during the initial paroxysm, the apyretic interval, the relapse, or subsequently to this. In an analysis of 99 fatal cases Carter ascertained that in 48 death occurred during the primary paroxysm, and of these 37 died at or about the apparent acme of fever, and at the stage of defervescence 11; 24 deaths occurred during the first apyretic interval; 6 during the first relapse; 11 during the second interval, and 1 in a second relapse. The apparent *cause of death* in these cases is said to have been in 63 cases exhaustion, resulting from the immediate effects of the pyrexia and its attendant symptoms; in 17 cases pneumonia as a complication; in 2 copious gastric hemorrhage; in 1 femoral thrombosis; in 7 cerebral hemorrhage was ascertained by autopsy; there was acute dysentery in 8 cases, and hepatic abscess in 1.

The influence of age upon mortality is shown by the following table, which we copy from Wilson (*op. cit.*), who obtained it from the statistics of the London Fever Hospital as given by Murchison.

Of the 2,115 cases admitted there were:

| | Cases. | Deaths. | Per cent. |
|---|---|---|---|
| Under 20 years | 804 | 3 | 0.37 |
| Between 20 and 30 years | 562 | 4 | .71 |
| " 40 " 50 " | 322 | 8 | 2.48 |
| " 50 " 60 " | 119 | 9 | 7.56 |
| " 60 " 70 " | 66 | 7 | 10.60 |
| " 70 " 80 " | 6 | 2 | 33.33 |

The favorable influence of youth, as shown in this table —0.37 per cent. for all cases below the age of 20—is not in correspondence with the data obtained by Carter in India. He says: "The influence of age was apparent in the greater comparative mortality at both extremes of the scale of years; thus, the general mean death rate being about 18 per cent., the rate was 27 per cent. up to the age of ten years, and then in the two succeeding decennia declining to 11 per cent. (11 to 20 years), and 16 per cent. (21 to 30 years), it rose with advancing age above the mean to 24.5 per cent. (31 to 40 years), 29.4 per cent. (41 to 50 years), and 37.5 per cent. (51 to 60 years).

The mortality is greatest at the outset of an epidemic, and the proportion of cases complicated with jaundice is larger at this time. *Sex* has no apparent influence upon the death rate, when we exclude the decided influence of intemperate habits, and take account of the fact that more males than females are attacked.

Anatomical Lesions.—Most authors assert that there are no constant anatomical lesions in relapsing fever, but Ponfick, of Berlin, who has made the most elaborate researches yet published, based upon sixty-five autopsies made during the epidemic of 1872–73, asserts "that certain changes in the spleen, the marrow of bones, the





blood (large granule cells); also those of the liver, kidneys, and muscles (especially of the heart), pertain directly to relapsing fever, and taken together are pathognomonic." The splenic changes are said to be absolutely constant, and this assertion at once disposes of the commonly repeated statement that there are no constant local lesions in relapsing fever. Liver changes, too, were invariable; but some difficulty here arose from the likelihood of prior lesion due to alcoholism. It is evident that the epidemic at Berlin was a severe one, there being seen several examples of *typhus biliosus*. The following is a summary of Ponfick's results. *Liver:* The turgescence ensuing during specific pyrexia may be greater than occurs in any other infectious disease; the individual lobules become enlarged, their outlines indistinct, and tint a grayish-red. Microscopically, the increased volume is due to cloudy swelling of the hepatic cells (always present), to their peripheral fatty degeneration, and lastly, to an infiltration of small cells in the portal canals; from an anatomical point of view, no distinction here is possible between the mild and the severe forms of relapsing fever; jaundice was present sixteen times (twenty-four per cent.), and it results from biliary engorgement. *Kidneys:* Changed without exception, and in correspondence with alterations noted in the urine; they may be doubled in size; parenchyma flabby; the cortex broad and clouded; the Malpighian tufts pallid. Or parts alone may be changed, and when dark streaks are visible, then not only is the tubular epithelium more or less fatty, but the lumen of the tubes is occupied by fibrinous or blood-tinged plugs. Such cylinders with red discs have been found in the urine (not at Bombay, H. V. C.). There is also evident, in the extreme degree of swelling, a copious small-cell infiltration of the intertubular tissue; and besides, an amyloid thickening of the vessels, which may be attributed to previous *morbus Brightii*. *Striated muscles:* Lesion of the myocardium is very frequent, its consistence flabby, tint pale gray or brownish, wholly or in streaks, where the fibres have undergone fatty degeneration; such degeneration may be as extreme as in the most virulent kind of infectious disease, or even in poisoning by phosphorus. Dr. Ponfick naturally applies these data in explanation of certain fatal cases of fever, where death occurs by syncope, and no other lesion is found after death. I have above remarked that the like were not witnessed among the temperate natives of West India. *Spleen:* Changes here are localized or diffused; the latter are always present, and induce a swelling of the organ, sometimes greater than occurs in *leukæmia*. The pulp is then dark, livid, and projecting; the Malpighian bodies much enlarged or even effaced, their tint gray or yellowish; at a later stage of fever their outlines become more defined. In cases of unusually rapid turgescence of the spleen, rupture of its capsule may occur, and death, with or without peritonitis; this change is compared with that taking place in enteric fever. Swelling is due to distention of blood-vessels, and to a great increase of the cell elements, including large multinucleated forms in near relationship to the cavernous veins. Dr. Ponfick could not find any spirilla among these cells. Numerous pulp cells were seen containing red blood discs and pigment; and others filled with bright granules which look like spores, but probably are not such; these structures are not peculiar to relapsing fever, though found here in relatively larger numbers than in other fevers; they may be seen in the blood circulating during life, and when very abundant, may be concerned with death of patient. Cases are quoted such as occurred at Bombay. There is also another contamination of the blood which can be demonstrated during life in severe cases, viz., by vascular endothelium cells in a state of fatty degeneration; this, too, is not absolutely peculiar. As to localized splenic changes, the chief pertain to the venous system and comprise the so-called 'infarcts,' which were present in forty per cent. of all autopsies; they resemble closely embolic infarcts, but arise from another cause than arterial obstruction, and hence are peculiar to relapsing fever." (Quoted from Carter, *op. cit.*)

Ponfick also describes certain changes in the marrow of bones which he considers peculiar to relapsing fever. "These changes consist in proliferation and subsequent degeneration of the lymphoid cells of the marrow, with multiplication of the nuclei in the walls of the minute vessels and fatty degeneration of their coats. As a result of these changes spots of puriform softening may form, chiefly in the cancellous tissue of the extremities of long bones, with the production of localized necrosis, and possibly with extension of inflammation to the neighboring articular cavity." (Quoted from Pepper, *op. cit.*)

In addition to these constant changes, a variety of lesions are found which appertain to the complications which occur in this disease with greater or less frequency. Most prominent among these are the lesions due to pneumonia. Pepper found evidence of lobar pneumonia in thirty-three per cent. of his autopsies, Carter in twenty-eight per cent., and Ponfick in twenty per cent.

Treatment.—All efforts to cut short an attack of relapsing fever by specific medication have thus far proved unsuccessful, and the knowledge that the disease is due to the presence of a minute vegetable parasite in the blood has not resulted in any decided improvement in our therapeutic resources. The evident indication is to destroy or restrain the development of this blood parasite; but in the list of known therapeutic agents there is not one which can be safely administered in sufficient quantity to accomplish this purpose. Quinine in full doses has been tried again and again, but the testimony of Murchison, of Pepper, and of Carter is in accord as to its failure to exercise any specific therapeutic power. The last-named observer says that "the blood spirillum and the febrile symptoms remain unaffected after quinine given largely to cinchonism, after narcotism by chloral, and after the freest exhibition of spirituous liquors; also after the administration of the carbolates and very large doses of the salicylates." We have no precise data showing the action of germicidal agents upon the spirillum of Obermeier; but Carter states that he once found that weak neutral solutions of quinine seemed to kill the spirillum; and Dr. Litten has ascertained that the movements of the parasite are arrested by a one-per-cent. solution of carbolic acid. The experiments of Ceri show that the development of schizomycetes is prevented by the presence of muriate of quinine in the proportion of 1 to 800 in a culture solution. The development of certain species is prevented by a considerably smaller amount, but so far as our experimental data go the indications are that at least one part in two thousand will be required to prevent the development of organisms of this class in the blood. This would require the *constant* presence of something more than a drachm of muriate of quinine *in solution in the blood* to prevent the multiplication of bacterial parasites present in this fluid. The therapeutic possibilities in the case of carbolic acid are not so favorable as this, and the writer has elsewhere estimated the amount of this agent which would be necessary to restrain the development of pathogenic organisms in the blood to be something more than two drachms. Arsenic was fairly tried by Pepper in the Philadelphia epidemic, and his conclusion is that "there seems to be no reason whatever for any further use of this drug in relapsing fever." Large doses of sodium salicylate have been demonstrated by Unterberger and by Riess to exercise a marked antipyretic effect, but to be impotent for the arrest of the febrile paroxysm or for the destruction of the blood parasite. "Unterberger has seen the temperature brought down 3° C. (5.4° F.), yet the attack was not apparently cut short, or splenic enlargement prevented, or the active blood spirillum visibly affected. Dr. L. Reiss, after essay on twenty-six cases, thinks that it is possible to cut short or mitigate the symptoms (especially the temperature) of specific relapses by very large doses (one hundred grains or more daily), noting, however, that even when the heat is reduced to normal or below it, the spirillum still persists." (Quoted from Carter.) Another remedy, tried by Pepper in a large number of cases, is the hyposulphite of

soda; his verdict is that "it is certain that it exerted no specific effect upon the disease."

In the absence of any known specific, our therapeutic resources are reduced to those measures which are best adapted to the control of the most distressing symptoms, and to that watchful care and anticipation of complications which enables us so often to tide a patient safely through the critical stages of an infectious disease, and to save many lives, notwithstanding our acknowledged inability to cure these diseases. Although the high pyrexia is not so immediately dangerous to life as is the case in certain other continued fevers, it will always be advisable to keep it within bounds, and the tendency to death toward the close of the febrile paroxysm, primary or secondary, should be borne in mind. The evidence on record is in favor of sodium salicylate, rather than quinine, as an antipyretic medicine; it may be given to the extent of one hundred grains, or more, in the twenty-four hours, and is said to be well borne. Its persistent use, however, interferes with the patient's appetite, and it will be best to reserve it for those cases which are marked by a specially high pyrexia, and to administer it, in full doses, only when the temperature approaches 106° F. For a more moderate elevation of temperature, cold sponging of the surface, and the administration of simple febrifuge remedies, such as effervescing draught, or solution of spirit of nitrous ether, will suffice. Aconite, in small and repeated doses, may be given—one drop every two hours—in combination with moderate doses of spirit of nitrous ether, and if any routine treatment for the fever is considered necessary this may be recommended, as less liable to disturb the stomach than certain other drugs which are sometimes used in similar conditions, *e.g.*, veratrum viride, digitalis. There is a tendency to constipation, and a mild aperient will commonly be required at the outset of the attack; a dose of castor oil, or a simple saline purgative, will answer the purpose; later the bowels may be moved, if necessary, by enemata; emetics, as a rule, do more harm than good. *Headache* is to be combated by cold applications to the head. *Insomnia* is a marked and distressing feature of the disease; Carter prefers to administer chloral and bromide of potassium for the relief of this symptom, rather than to give opiates. Pepper, on the contrary, says that "opium and morphine must be regarded as the basis of the rational treatment of relapsing fever. It is called for by the insomnia, the severe headache, and the pains in various parts of the body, the nausea and vomiting, and the pyrexia." One-fourth of a grain of morphine, given at intervals of six to twelve hours, was found by the author last mentioned to relieve pain and vomiting, and often to induce refreshing sleep. It is contraindicated in those cases having a typhoid tendency, as shown by a disposition to stupor and deficient urinary secretion. In the experience of Pepper during the Philadelphia epidemic, bromide of potassium in full doses failed to produce sleep or relieve headache, and chloral, in doses of twenty to forty grains, could not be depended upon, although it sometimes gave relief. In view of the tendency to heart failure in this disease, the author named very properly points out the possible danger which may attend the administration of chloral. For the relief of excessive *tenderness of the liver or spleen*, Carter recommends hot fomentations and poultices in preference to cold applications, "which are seldom grateful to the patient." To control excessive *irritability of the stomach*, Pepper advises the use of small doses of calomel, gr. $\frac{1}{4}$–$\frac{1}{8}$ every two hours, or gr. $\frac{1}{16}$ of nitrate of silver, dissolved in thin mucilage of acacia, administered at intervals of three or four hours. *Hiccough* is a distressing symptom, which often defies all remedial measures. In Pepper's experience, chloroform is the most useful remedy for its relief. As death from *heart failure* may occur at the acme of the pyrexia, or during the depression, often amounting to collapse, which follows crisis, it will be necessary to watch carefully for the slightest indications of such failure, and to guard against it by the administration of digitalis, or strychnia, and the early use of alcoholic stimulants. When the symptoms of *collapse* are developed, it will be necessary to resort to the subcutaneous injection of ether, or of strychnia, and to apply artificial heat to the surface of the body.

In this as in other specific febrile diseases running a protracted course, it is necessary to commence with a *supporting treatment* at an early date. As soon as the stomach will retain it, liquid nourishment should be administered at stated intervals—every two or three hours; meat broths, milk, or gruel may be given if the condition of the stomach admits of their being retained; if not, koumiss, chicken water, or skimmed milk diluted with lime water, may be given in small quantities and at shorter intervals. When the stomach is very irritable, it is probable that iced champagne, or a teaspoonful of good brandy poured upon broken ice in a glass, and taken as cold as ice will make it, will be found the best form of stimulant. Whiskey toddy or milk punch may be given during the apyretic interval, or until convalescence is fairly established, or a good wine may be substituted for these if the patient prefers. In this disease, as in yellow fever, sudden death is liable to occur from cardiac syncope, as a result of very trifling exertion made when the patient is apparently out of danger. It therefore becomes necessary to insist upon absolute quiet and the maintenance of a recumbent position until such time as the strength of the patient is fairly restored. This precaution is especially imperative at the time of crisis, and during the period immediately following it, when there are a subnormal temperature and other evidence of a state of collapse. *George M. Sternberg.*


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**REMITTENT MALARIAL FEVER.** See *Malarial Diseases.*

**RENNIN.**—This name for the milk-curdling enzyme of the gastric juice was first proposed in Foster's "Textbook of Physiology," and is now in common use in English-speaking countries. The name of *chymosin* was that given to it by Deschamps; it was later termed *lab* by Hammarsten, and this name is occasionally used by English writers.

The most valuable researches into its mode of action and isolation are due to Hammarsten, who was the first to show that it is distinct from pepsin. This view is now almost universally accepted, although it has recently been stated by Pawlow that rennin and pepsin are identical. Pawlow's experiments, which consist chiefly in a demonstration of a parallelism of intensity of action of gastric juice in digesting proteid and coagulating milk, are not, however, very convincing against the careful experimentation of Hammarsten in the separation of the two enzymes, as described later on in this article.





Rennin and milk-coagulating ferments allied to it are very widely distributed, for rennin occurs not only in the mucous membrane of the stomachs of all mammalia which have been tested for it, but is also found in the stomachs of birds and fishes where its function is at present unknown. A similar if not identical ferment is found in the cell sap of many plants, such as the butterwort, fig-tree, and artichoke, and in certain of the Schizomycetes.

It is usually prepared commercially as rennet in the form of solution, powder, or tabloids, preserved with boracic acid, from the fourth stomach of the calf; carefully prepared products preserve their power of coagulating milk almost indefinitely, and long after proteid decomposition may have taken place in the other constituents admixed with the rennin.

Rennin is present in man at birth, and in this respect differs from pepsin. In its distribution in the gastric mucous membrane it closely resembles pepsin, being present only in small quantities at the pyloric region. Like pepsin, also, it is present in the gland cells as a zymogen; in fact, it was in the case of rennin that a precursory form or zymogen (Labzymogen) was first demonstrated by Hammarsten in 1872, some years before a similar demonstration was made in the case of pepsin by Langley and Edkins.

The zymogen appears to exist in a more stable form in some animals than in others, for while a neutral extract of the mucous membrane of the sheep or calf contains the enzyme in an active form, similar extracts from birds, fishes, and certain mammalia exert an action upon milk only after these extracts have first been treated with very dilute acid and again neutralized.

Rennin and pepsin and their corresponding zymogens behave very similarly on treatment with dilute alkalies; thus both rennin and pepsin are very rapidly destroyed by traces of caustic alkalies. The active ferments are also destroyed in both cases much more rapidly than their zymogens by the alkaline carbonates in dilute solutions, and this fact has been utilized, especially in the case of pepsin and pepsinogen, for proving the existence of the zymogen.

Rennin differs from pepsin in that it will act in a neutral or even in a faintly alkaline medium, but it acts most quickly when the medium possesses a slightly acid reaction. Excess of acid destroys its activity.

The *optimum* temperature lies at 37° C. to 40° C.; at this temperature the reaction takes place with three times as great rapidity as at 25° C.; activity ceases at 50° C., but the enzyme is not destroyed very rapidly at this temperature, and becomes active again as the temperature is lowered toward the optimum. The enzyme is destroyed, however, in five minutes when heated to 70° C. in neutral solution, or at 65° C. in acid solution. Its activity is also removed by standing under alcohol, but less rapidly than is the case with pepsin.

That the action is a truly enzymic one is shown not only by the above-mentioned destructions of activity, but also by the fact that it can occur in the presence of antiseptics, and by the infinitesimally small amount necessary to evoke the coagulation, one part of "purified" rennin being capable of coagulating, according to Söldner, ten million parts of casein.

The most successful attempt at its isolation was made by Hammarsten, who utilized Brücke's principle of mechanical precipitation by first neutralizing a gastric infusion with magnesium carbonate which precipitates the greater part of the pepsin. The filtrate was then partially precipitated by solution of acetate of lead to remove the remainder of the pepsin, and finally the rennin was thrown out by further addition of lead acetate and ammonia. This last precipitate was dissolved in very dilute sulphuric acid, and the rennin again mechanically thrown out with stearic acid by the addition of a solution of an alkaline stearate. The rennin was then finally obtained in solution in water by suspending the stearic acid in water and shaking up with ether, which dissolved the stearic acid and left the rennin behind in the aqueous layer.

The solution obtained finally did not act at all upon fibrin, but powerfully coagulated milk in neutral solution. This solution behaved in many important respects differently from a proteid solution, viz., it was not coagulated by heat, did not give a xantho-proteic reaction, and was not precipitated by alcohol, tannin, iodine, or neutral acetate of lead.

The chief facts as to the chemistry of the action of rennin upon milk are to be ascribed also to Hammarsten's researches upon the subject. When milk clots the greater part of the proteid separates in an insoluble form as casein (paracasein of Hammarsten), which entangles all the fat in its meshes as it contracts and so expresses a clear fluid called the whey, while the coagulated casein and entangled fat are called the curd. The whey contains the inorganic salts, lactose, and a small amount of albumen and globulin, which are called lactalbumin and lacto-globulin. Hence the casein is that important constituent which is chemically concerned in the process of coagulation.

The proteid from which the casein is formed in the act of clotting is termed *caseinogen* (casein of Hammarsten), and is present, according to some observers, in suspension in fine globules, and, according to others, as a colloidal solution. This proteid body has the properties of a very weak acid which is in fresh milk present as an alkaline salt; when it is set free from its combination it becomes insoluble. It is naturally so set free in the souring of milk, when lactic acid is formed by bacterial action on the milk sugar, and it is for this reason that sour milk curdles. For experimental purposes, such as the study of the properties of caseinogen and its changes during coagulation, it is best precipitated by the addition of a few drops of acetic acid. It can then be redissolved, after washing away the acetic acid, with distilled water, by the addition of water containing traces of alkali or by rubbing up with precipitated chalk.

As in the formation of fibrin from fibrinogen in blood clotting, it is found that calcium salts are necessary for the coagulation to take place, but more exact research has demonstrated that the rôle of the calcium salt is different in the two cases. For while the calcium salt has been shown by Hammarsten to be necessary for the formation of the *thrombosin* which acts as a ferment in blood coagulation, the same observer has also demonstrated that the calcium salt in milk coagulation does not share in forming the ferment, but has its purpose in a second stage of the reaction in actually combining with the caseinogen which has been modified in the first part of the reaction (soluble casein) to form the insoluble casein.

Hammarsten's two stages can easily be demonstrated by taking either a solution of caseinogen, or pure milk to wh'ch a few drops of ammonium oxalate have been added to throw down the soluble calcium salts, adding in either case a few drops of rennet, and then warming in a water bath to body temperature for ten to fifteen minutes, when no apparent change will be observed. Still a change has occurred, for if the milk be now boiled so as to throw the ferment out of action in the subsequent operation, and then a few drops of calcium chloride be added so that there is a calcium salt in solution in the fluid, on warming again for a few minutes a clot forms. Here no ferment action can take place in the second process, and as the addition of calcium salt only, and subsequent warming, produce no effect upon milk which has no been treated with rennin as in the first part of the process, it follows that the rennin must in the first portion of the experiment have formed some soluble modification of the caseinogen, which is then thrown out as insoluble casein in the second portion of the experiment.

Working with caseinogen solutions Hammarsten further demonstrated that in the action of rennin upon caseinogen there is detached from the caseinogen a soluble portion, which he termed "whey-proteid," that does not undergo any coagulation, and hence is found afterward in the clear fluid, or admixed in the whey with the lactalbumin when milk is used instead of caseinogen