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HISTORY
OF SALINE
INFUSION
AND
HARVEY'S
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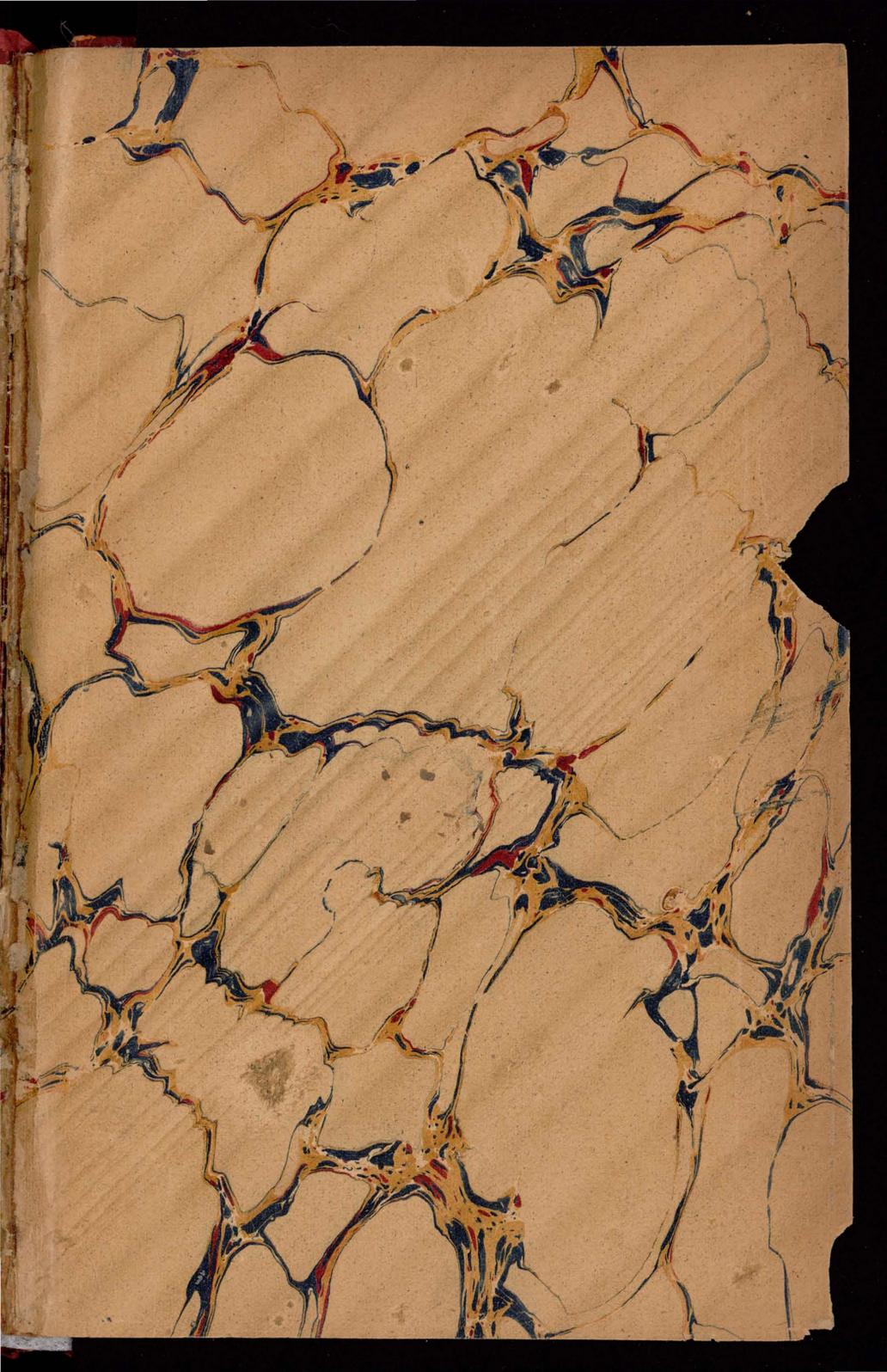
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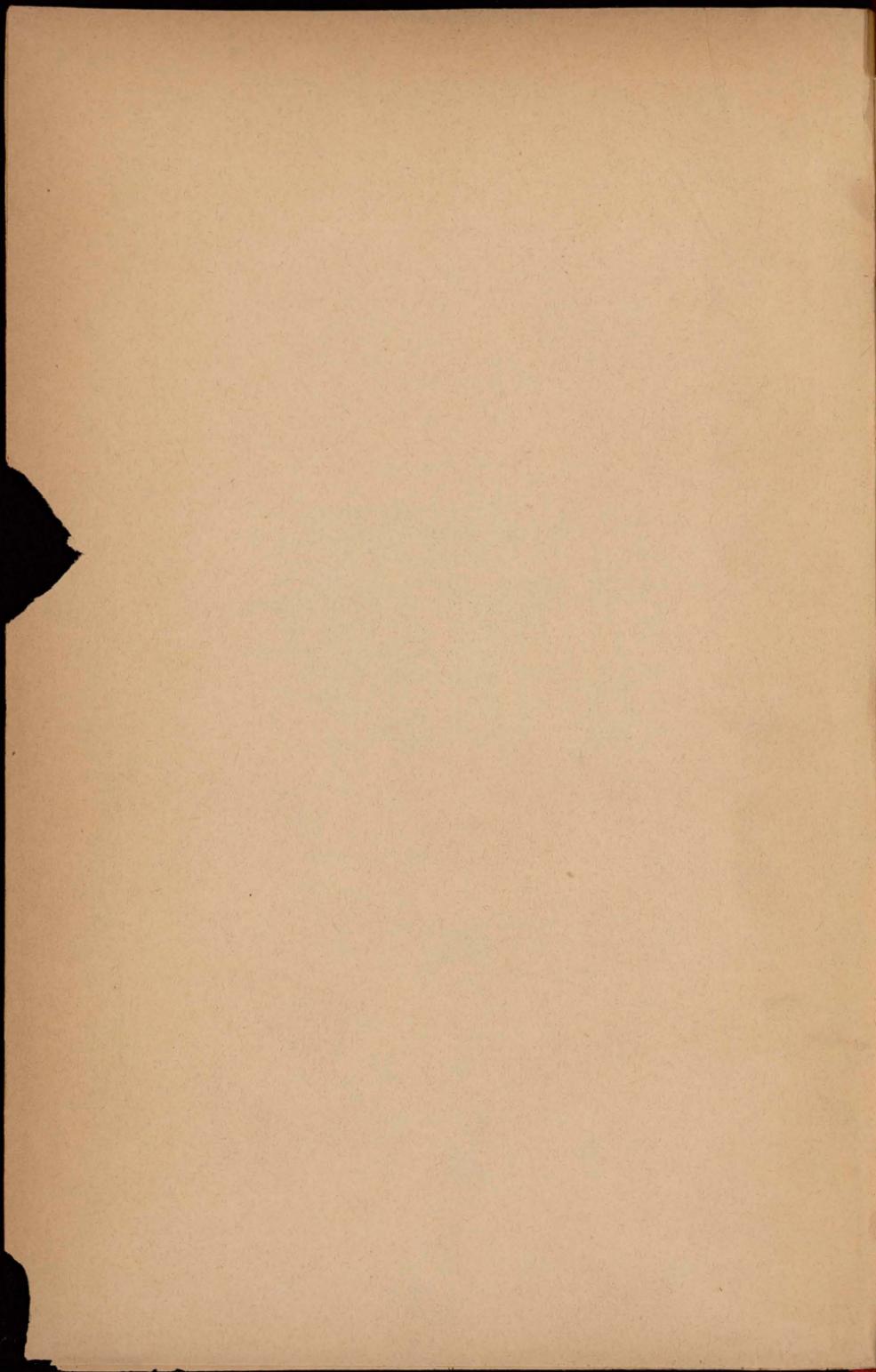
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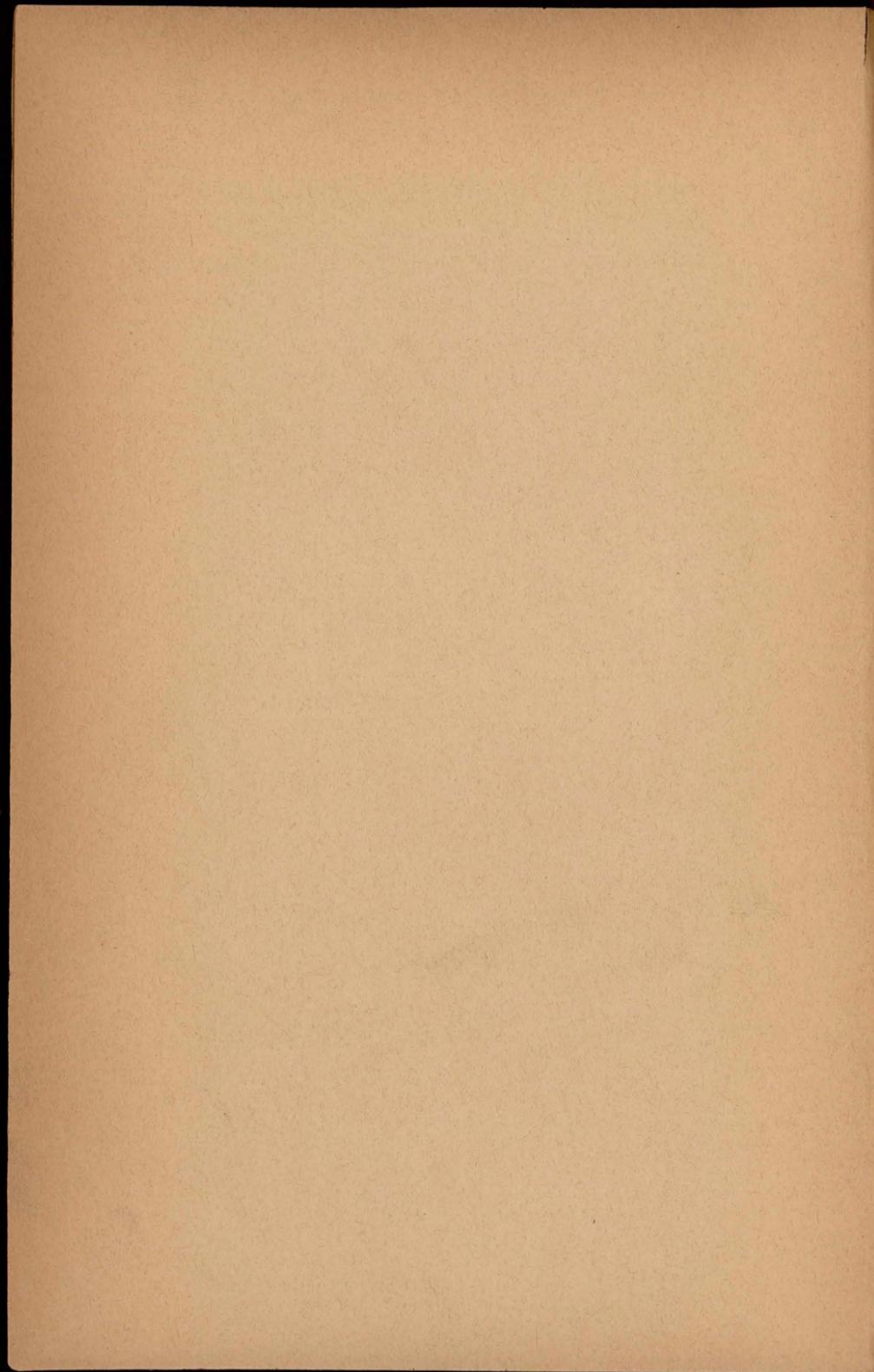
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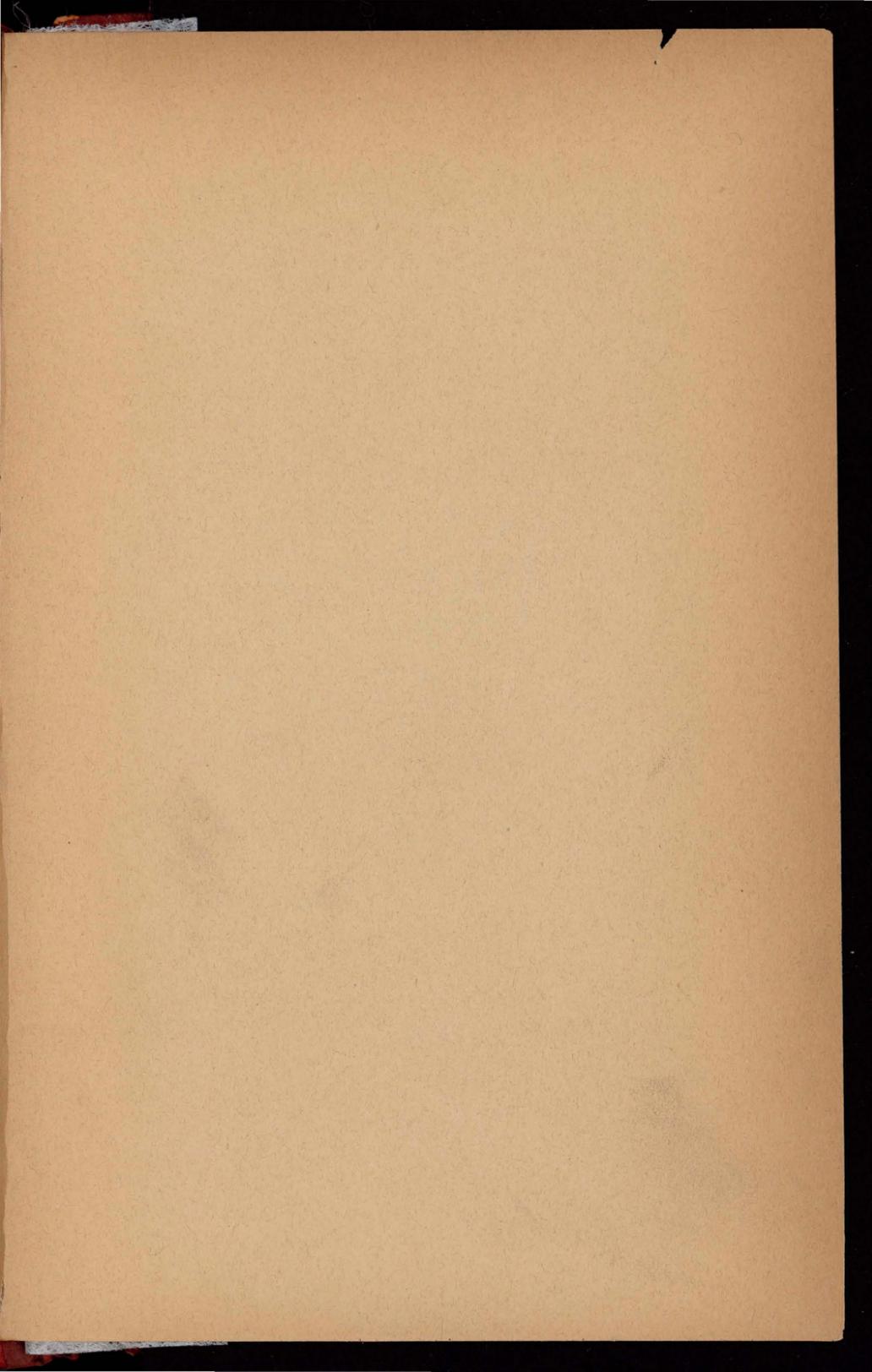
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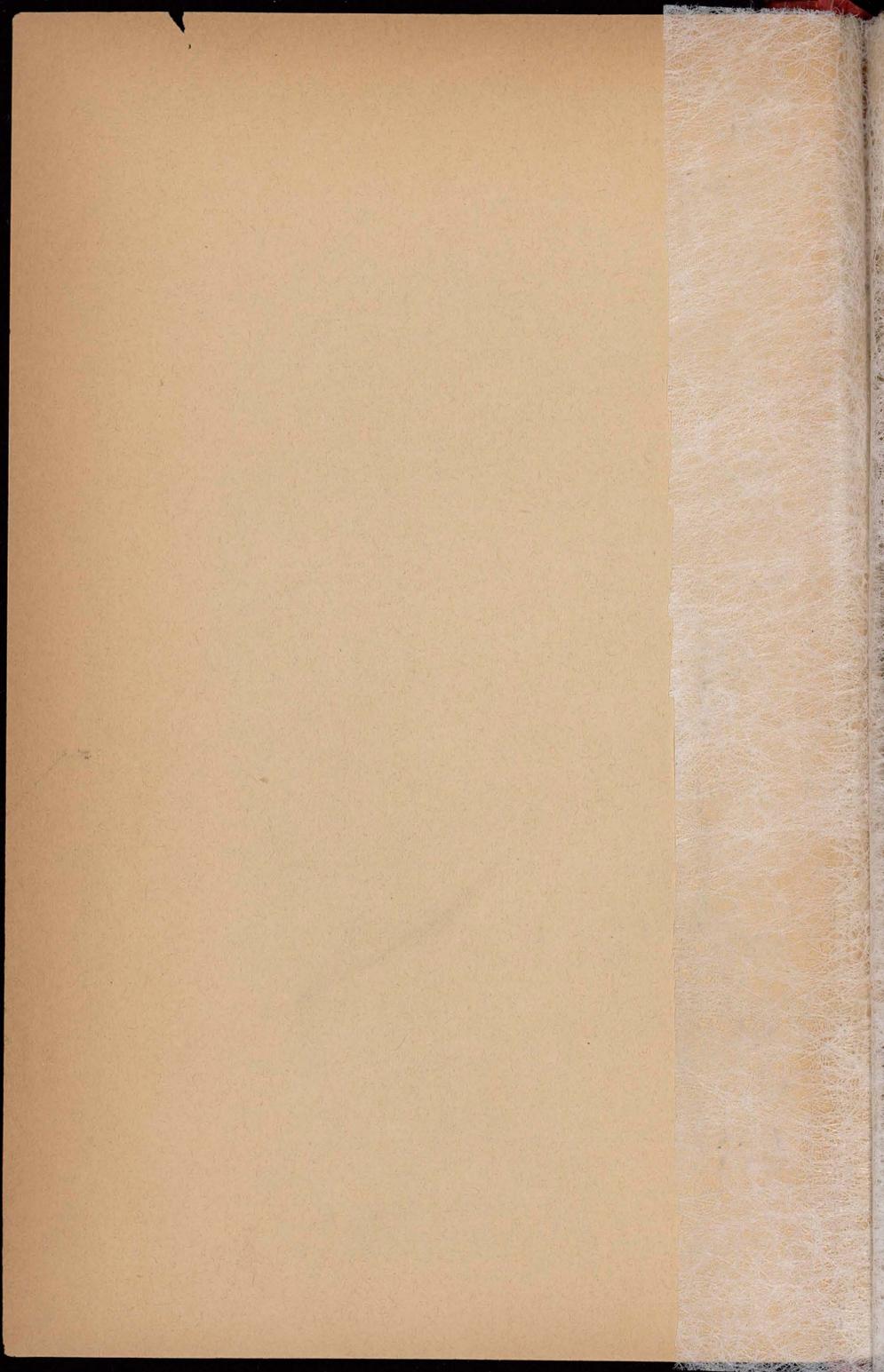
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A STUDY IN RETROSPECTIVE THERAPEUTICS.

The Evolutionary Processes through which have Traveled Transfusion, Infusion, Subcutaneous Injection, Enteroclysis, Peritoneoclysis, and Cystoclysis in the Treatment of Asiatic Cholera, from 1830 to 1895.

BY P. C. REMONDINO, M.D.,
of San Diego, Cal.

IN medicine, as in other arts and sciences, we advance, profit and improve by noting the mistakes, failures, and successes of those who have gone before us in the same field of investigation, study, and practice. The intelligent physician will not be satisfied with the simple knowledge that is restricted within the superstructure of his medical education, but will inquire into the foundation, supports and evolutionary processes, so as to familiarize himself with all of their details. He will then not only be in a better position wherefrom to judge, compare and criticise and form well-founded opinions upon medical subjects, but he will also place himself in a position from whence he can the more safely and securely advance, especially if he be of an enterprising and progressive spirit. To do this he must thoroughly familiarize himself with the study of the history of his art and science.

The study of the evolutionary processes through which any one given subject of medical research, or any disease and its therapeutics has passed to reach a certain point of development or excellence, forms a most instructive as well as an interesting occupation, as in so doing one must necessarily closely follow the changes and advances made from period to period, groping from thick mists into bright sunshine in the

study of pathology, chemistry, and therapeutics, as sought for and demonstrated by the theorists and warring sectarians and the experimentalists in physiology and pathology in the past. The remark made by Sir William Hamilton in regard to the study of medical history in general "that however uninteresting the prospect of a history of medicine may appear at a distance, it will be found gradually to improve and become full of interest, wonder and animation as we proceed," is peculiarly applicable to the detailed and connected study of the history of a single subject of medicine, as we have there a more continuous tale through which the changes and improvements made possible by the increasing light thrown upon our art have traveled, either to reach a stage in their journey or their climax of excellence.

Moderns seem to overlook the fact that the teachings which we can cull from the pages of medical history is a material that has been well culled, sifted, and refined, having had to pass the severe ordeal of refining at the hands of unfeeling and unprejudiced critics who were as careful to give us only the gold as they were to well exclude the sand and worthless debris, whilst on the other hand much of the new material upon which we base so much of our modern superiority has yet to be tested and to go through that severe refining process, although it requires no very close observation to discern that even in the course of a modern decade we learn and adopt much, as the late Professor Goodell would say about gynecology, which we soon learn that we have to unlearn—and that in every branch and specialty in practical medicine.

When, in 1831-32, London was greatly exercised over the disputes concerning the relative merits of the saline treatment of cholera (a treatment adopted, as will be seen, under a variety of guises), Dr. J. Hancock, of London,¹ held that the fundamental principles involved in the discussion were by no means new, as the practice of administering salines in acute malignant distempers was as old as Hippocrates, who advised it in the treatment of the plague. Hancock

¹ *Lancet*, August 18, 1832.

cited Van Helmont—a contemporary of William Harvey—who insisted that the vital spirit of arterial blood resided in its salinity. This erudite critic, who was somewhat annoyed at the unseemly disputes and wrangles over the claims to priority of the discovery of the values of salines in these malignant distempers by the Englishmen of the nineteenth century, quotes the work on the plague of Laurent Joubertus, a professor of medicine in Montpellier in the middle of the sixteenth century, who also recommended the use of salines as being both prophylactic and curative, as well as the later works of Isbrand de Diemberbroeck, of the University of Utrecht—another contemporary of Harvey—who in his work on the plague counseled a like form of treatment. This author had further observed that laborers who fed much on salt fish enjoyed a peculiar immunity from pestilential diseases—an observation which has more than once been made by moderns in connection with the immunity to epidemic cholera enjoyed by the tanners, who are of necessity more or less constantly impregnated with tannin, a circumstance which might long ago have suggested the practice of Chitty of Ceylon, and the still later experiments and practice of Cantani—thus showing us the suggestions that the experimentalist and practitioner may profitably receive from a study not only of medical history, but even from that seemingly untherapeutic branch of medicine which deals with general medical demography and hygiene, but more especially with the diseases of occupation.

A physician at all times should cultivate an independent and unprejudiced habit of thought, and not allow himself to rely too much on the dictum of others, even upon that of a collection of men, who by position and experience are supposed to have become oracularly infallible in matters medical, as such bodies are too apt at times to be guided or influenced by that too strict conservatism, which of necessity honest and conscientious responsibility imposes upon those whose opinions and utterances are adopted as final by the rank and file of the profession. The conscientious and conservative report of the committee of the College of Physicians of Philadelphia

upon the advisability or practicability of the Latta treatment of cholera is a case in point, as the very able men who framed that report, if living today, and in the light of intervening events, would undoubtedly materially change the tenor of that report.

Cases of sporadic cholera, bearing all the vehemence, rapid course and fatality that attend the worse form of cases occurring during an epidemic of Asiatic cholera, appear now and then from an accidental or unknown cause. The general disposition on the part of the physician is then too apt to glide into the practice of attempting to relieve the suffering patient by the administration of such antispasmodics and anodynes as are at hand and generally in use, and from these glide unconsciously into seeking assistance from stimulants as the patient becomes weaker, while the distracted relations and friends are in a fair way to relieve the poor patient of some of his skin by their well-intentioned but inconsiderate attempts at relieving the cramps and the impeded circulation by vehement frictions. This is no fancy sketch, as I have been in that position in years past, and have also seen others as uselessly laboring away on obsolete and ineffectual methods, while the patient gradually sank into death; while such means as would not only have more speedily granted a relief from the sufferings, but even life, were simply neglected, either for the want of some more defined general knowledge on the subject or for that want of the exercise of the power of comparative reasoning which points out analogies and the general rules that govern them.

Whatever remedy or method has once given relief, and that, whether at the hands of an Hippocrates, a Galen, a Brown, a Sydenham, a Boerhaave, or a Rush, can generally be counted on as being fully able to repeat the like good results when employed under conditions that are analogous, so that I feel that the following pages will not be written without some resulting practical use and value aside from their historical interest and the processes of new thoughts they may engender.

No subject in medicine furnishes a more varied or interesting set of events than the history of transfu-

sion and its many derivatives, as studied in connection with the evolutionary history of our ever-changing and never wholly satisfactory ideas concerning the treatment of epidemic cholera. This partnership has existed for more than 60 years, and during that period—beginning with the impracticable blood-transfusions in cholera first suggested and attempted by Dieffenbach—the variation experienced by transfusion have been as varied and as changing as the colors of the kaleidoscope. Dismissing the original ideas that entertained solely the item of blood-transfusion, and at once coming down to its substitute, the saline intravenous injections practised by Latta, our subject enjoys the distinction of being the first form of treatment employed in any stage of cholera that had for a basis the careful experiments of practical physiologists and for its sponsors the first experimental chemists of Europe.

It would be useless to attempt the history of transfusion in its various connections with the treatment of cholera, without at times treading into the fields that are beyond the boundary and making either comparative allusions or discussing some collateral points in its pathology and other forms of treatments. To obtain a full understanding of the subject, of its uselessness here, and of its extreme usefulness there and to understand why the subject has been adopted by some, disapproved of by others, and misunderstood by the many, explanations must be made and details are here, although at times seemingly irrelevant, unavoidable.

It would be idle to expect any form of treatment for cholera to give perfect or universal satisfaction that would fall short of saving at least 95% of the attacked. This can only be looked for in prophylaxis. Our present state of science is inadequate to formulate a plan of comprehensive treatment covering all the stages of the disease that could by any means be called satisfactory to the many. The most that we can expect at present is to materially and visibly modify the usual mortality of the past epidemics and to learn as well as possible to relieve the sufferings of those who are so fortunate as to recover.

Aside from the many routine treatments, embodying the administration of remedies by the mouth, frictions, warmth, etc., there are at present three therapeutic means that may be said to have earned for themselves the position of being recognized and established forms among the more observing of the European nations.

Taken in the order of priority of introduction or of existence and application in practice, we may first mention the intravenous injection of an artificial serum, a plan first tried in 1832 by Dr. Latta in his practice in Edinburgh. This plan has undergone many modifications, although the original plan, both as to application and as to infusion, is still largely practised in Europe. The second of these consists in the modifications originated by Cantani on the catechu enteroclysis system inaugurated in 1847 by Dr. Chitty, of Ceylon, and now known under the name of Cantani's tannin treatment. The third and last of these series of remedies is the anticholerin of Klebs, a remedy belonging to the antitoxin group of medicines made from attenuated cultures of the germs of the disease which it is intended to treat.

These three forms of treatment have each their peculiar applicability, and unless an epidemic should present a virulence and that rapidity of onset and of disintegration on the patient which belongs purely to the foudroyante order of some diseases, it would seem as if between the three, and the judicious and timely selection and administration of these as they are respectively called for, that the cholera mortality should be greatly reduced.

Prior to the systemic and well-based investigations of 1831-32, all cholera treatments had been unfounded except on the crudest of empiricism. There had existed no regular system of research, nor any comprehensive or uniform ideas. The battle against the cholera, had, prior to this period, resembled one of the battles of the days of the feudal barons, before the establishment of national or regular armies, and when each count or baron yelled his battle-cry, and surrounded by his retainers he fought on, utterly regardless of what was taking place on his flank or on his rear.

Medical men then met the disease as best they could, and as the mariner of old was wont to ascribe his safety to the saint devoutly implored and prayed to just at the breaking up of the tempest, so our medical men were wont to ascribe their cures to the last remedy employed just before the disease had exhausted its violence. Calomel, opium, morphia, and the whole list of the *materia medica* were thus all brought in as successful therapeutic agents or competitors, and confusion reigned supreme, as in the danger of rapid dissolution that threatened the patients, physicians must often have exhibited a lightning rapidity of skill in dodging from a tried remedy to another recommended, but still untried.

Physicians and pathologists now drew comparisons to the similarity of the pathologic conditions found to exist in the closing stages of the many forms of tropic fevers, of yellow fever, and of epidemic cholera, conditions where, to use the description of some of the physicians of the period, "after death the anatomist often cannot detect any trace of disease, either in the brain, stomach, the intestines, or any of those organs whose derangements are generally supposed to be the cause of fever, and from these drew their inference as to treatment." In other words, it was then the consensus of medical opinion that the seat of the disease, and the parts that suffered, and whose sudden disintegration caused death, were the fluids, this being the blood, and that the other pathologic conditions were secondary to this; an opinion that seemed to be verified by the subsequent success of the treatment evolved out of the various investigations and experimentations upon the blood that these conclusions engendered.

This was a busy period for the experimental physiologist, for the experimental chemist, and the investigating physician. Having decided that the blood was the part attacked and put to ruin by the cholera-poison, they all began their investigations of this fluid, hoping, if possible, to find a prophylactic, and failing in this, then at least to discover some rational and scientific mode of treating the disease after it had attacked its victim. The most active and best-

equipped of the many investigators who entered the field was Wittstock, of Berlin, who carried on his researches at the instance of and under the liberal protection of the Prussian government. Russia furnished Hermann, who carried on his work in Moscow, while in France, Marcet, Denys, and Lecanu labored industriously at the same problem. England contributed Latta, O'Shaughnessy, Clanny, Stevens, Wright, and a little later, Begbie, Garrod, and many more. Rayer, of London, assisted the Londoners by his experiments on the respired air from cholera patients.

Although there existed many discrepancies between the details of many of the researches, the results of the various labors did, in the main, tend to the same general conclusions. After a series of well-regulated experiments, Wittstock determined, after a comparison of his results with those gathered from the analysis of normal healthy blood previously made by Berzelius, that on an average a patient laboring under a severe attack of cholera lost 19% of the watery particles of the blood, or estimated to be a loss of about 5 pounds for an average-sized person. Among the British experimenters, O'Shaughnessy found that, in addition to the serious loss of watery parts, the blood parted largely with its saline constituents, and in two cases he found in the remaining blood an utter deficiency of soda carbonate.

The experiments of Wittstock, O'Shaughnessy, and others, led to the belief that if the large loss of the watery and saline parts of the blood could be replaced, the chances of recovery would be greatly augmented. For this purpose solutions of common salt with some soda-bicarbonate were at first administered both by the mouth and by rectum, but owing to the loss of the power of absorption the practice was soon abandoned. The *Medico-Chirurgical Review* called this practice "carrying coals to Newcastle," and quoted Dr. Latta of Leith in asserting that the introduction of the saline solution into the intestines of cholera patients "aggravated the tormina, vomiting, and purging," and explained the sporadic success

of the practice in the hands of some London practitioners by observing "that any remedy, however inert, or even absurd, may gain great reputation towards the close of an epidemic, when Nature herself is generally equal to the cure."

Dr. O'Shaughnessy, who, as a result of his researches, first suggested the employment of the saline solution in cholera, made some further experiments upon the blood of cholera patients who had been subjected to the injection into the veins of the saline infusion and obtained some interesting results. In one of these cases he examined some blood taken 4 days after the injection of 2 drams of soda-carbonate and 3 of sodium-chlorid dissolved in 4 pounds of water; in the interval, the diarrhoea had continued, but the patient had not passed urine; the quantity of the watery particles in this case were, however, exactly in the normal quantity, or 778.76 per 1,000. The quantity of coloring matter and of albumin was also normal, but that of the salts was only one-half of the normal quantity, and the serum of the blood contained $2\frac{1}{10}$ grain of urea per 1,000 parts. This, and the following conclusions were reached after a number of blood-examinations made in cholera patients by Dr. O'Shaughnessy appeared in the *Lancet* of August 11, 1831-32.

He found that no changes occurred in the blood in the premonitory symptoms. In trivial cases, at least, those with slight purging but still with hard cramps, the blood was still unchanged. The blood-alterations as found in its great loss of water and saline matters only occur in the collapse cases that are preceded by excessive rice-water discharges. From a minute analysis made upon the blood of unaffected persons residing in infected houses or districts, he concluded that in the unaffected no blood-changes occurred. Owing to the suppression of urine in the attack and the secondary fever, choleraic blood is more than usually charged with urea. From these results it was demonstrated that the saline treatment, which was considered so useful in the course of the disease, was altogether useless as a prophylactic or in the first stages of the disease, as the changes in the blood

were the results of the gravity of the disease and of its violence, and not the cause of the disease.

It is interesting to observe in many instances the evolutionary processes of pathology and therapeutics, or how the former makes suggestions to the latter, and how these suggestions work around by the most circuitous route to combine with some other evolving therapeutic process to merge into something rational and practical. It had long been the practice in the West Indies and in many of the tropics to treat the pernicious tropical fevers by bloodletting, with the patient in the warm bath, in association with the internal administration of salines; this combination being intended to overcome the very pathologic blood conditions found in those fevers, which resemble in every way the blood-conditions found in serious cholera cases.

At first it was suggested by Dr. William Stevens, of London, to employ the saline part of this treatment for cholera, and this became known as the Stevens' treatment. In London and elsewhere it proved a failure. In Norway, where, in addition to rice-water discharges, there was often added a very fatal bloody diarrhea, which was ascribed to the use of saline administered internally, it also was experimented upon, but it there also proved a failure. The Stevens treatment was still used in some late epidemics.

Poor Dr. Stevens, aside from the general failure of his treatment at the time—which Dr. Hackett said Stevens had borrowed from, but never gave credit to, Jackson—had the misfortune at the same time to write a book on the blood, which, being rather more verbose, assertive, and theoretic than practical, or based on actual observations, experiments, or facts, handed him over to the incisive and merciless pens of the critics, who even in those serious cholera times had no end of sport with the rash and inconsiderate doctor, who had very much underestimated the prodigious abilities of the average British medical critic. For once, all critics and journals stopped berating each other, and laid aside all discussions to join in the chase after the hapless Stevens, who was scurry-

ing ahead like a panicstricken and unclaimed canine in a strange land.

Profiting by the experiments on morbid blood of Wittstock, Clanny, O'Shaughnessy, Denys, and others, and by the previous analysis of the blood in its normal state, the new experimenters were now enabled to construct and prepare an artificial serum in every way suitable to repair the losses of the blood as experienced in the latter stages of cholera, the experiments previously made not only giving them a full idea of all quantitative and qualitative ingredients required, but through the elaborated experiments of Wittstock have been able even to approximate the required quantity for the mass. With this knowledge, and the adoption of Dieffenbach's ideas of transfusion to point out the best way of placing this artificial serum into the circulatory channels, and the additional employment of the steam-bath by Latta, finally placed the subject of saline-infusion on quite a triumphant basis.

There are no doubts but that the adoption of the steam-bath by Latta, of Leith, was itself an outcome of the evolutionary process of the principle of Jackson employed in the West Indies in the shape of a warm bath. The low temperature of the patient as he approaches the collapse state, has necessarily always been a subject of much concern to the physician, and when the new saline-infusion intravenous treatment was proposed on the heels of the failure of the Stevens treatment, with the knowledge that the enema was returned quite cold from out of the chilled body, although administered at blood heat, various means were sought for looking to a maintaining of the warmth of the injections thrown into the veins. There is no doubt that Latta himself tentatively felt his way in this matter and learned much by dire experience—of which he has not left us the details—and when he speaks of the evil effects of the warm-water bath and of the intravenous injections heated up to 122 F., although he does not mention it, it is very probably the relation of the evolutionary processes experienced by himself before reaching the level of the steam bath that he is relating.

The chilled condition of the patient's body in this disease is something accompanied with very strange and paradoxical attendant conditions, for while the body is icy cold to the touch, the patient will often experience a pungent heat and seek relief from its torments by exposure to the cold air. With a cold, clammy skin, likened, as observed by Latta, to the back of a frog, or to a cold, damp hide, the patient often feels, nevertheless, as if about to die of heat and of thirst. The hot-air bath first adopted to relieve the reduced bodily temperature was only a further torment, and the good effects of the warm-water bath were not only transient but with subsequent evil results. In the use of the saline intravenous injections some had injudiciously raised their temperatures to 12° , 16° , and 24° above the normal temperature of the blood in the hope of overcoming the loss of heat experienced by the injections when introduced into the cold body and of maintaining them at a normal temperature, a procedure, as observed by Latta, which "has been with the indiscriminating, a source of error, and doubtless in many cases produced bad consequences." After much discarding, the steam bath was reached, and Latta was able to record some very successful cases treated by the combined solution and steam bath treatment.

In a communication to the *Lancet* of November 3, 1832, Dr. Latta points out the probable causes of the failure of the saline infusion in many of the cases, this being that, in his estimation, its use should be preceded or supplemented by a steam-bath at a temperature of 100° F. In his practice the solution was usually injected into the vein while the patient was in the bath. This injection consisted of water saturated with protoxid of nitrogen, with half a dram of sodium chlorid and eight grains of soda subcarbonate to the pint of water, the whole gently heated to blood warmth and strained through a piece of porous leather. Of this he injected into the veins in quantities varying from 32 to 105 ounces. The heat of the solution which quickly cools when injected into the body with its subnormal temperature—warm enemas introduced into the bowels being returned quite cold—was con-

sidered by Latta a question of the greatest importance, and the steam bath materially assisted to prevent a loss of proper heat.

He mentions one very interesting case, showing the effect of the temperature of the solution on the body, in that of a very dissipated woman of 45 years of age upon whom he was practising the infusion of salt-solution in the second stage of cholera, who was relieved of sickness, vomiting and purging by 32 ounces of the solution. He proceeded, however, with a second 32-ounce infusion, and was slowly pumping it in, when suddenly the patient lost all the color she had gained by the previous injection, her skin turned blue, her eyes sank into their sockets, her pulse ceased, and all the vomiting and purging reappeared. In testing the temperature of the infusion with the thermometer, he found to his dismay that by some accident or carelessness it had fallen down to below 90° F.; it was quickly raised to 110°, and the temperature of the steam bath was also raised, and hot liquids administered, and the induced sudden spurious attack of cholera was at once overcome. This seemingly hopeless case, although occurring in an habitual drunkard, epileptic, and afflicted with diarrhea for many months previous to the choleraic attack, did, nevertheless, survive until the evening of the sixth day after being taken with the disease. At the postmortem examination her stomach and liver were found to have been diseased, and the cavities of the heart contained fibrinous deposits.

When Dr. O'Shaughnessy first heard of the results of the experiments of Dr. Latta and of Dr. Lewins in the Edinburgh cholera, he stated in a note to the *Lancet*, published in that journal in May, 1832, that the results of the practice exceeded his most sanguine expectations, especially as under the circumstances the experiments could only have been carried on in cases that were considered out of the reach of the ordinary remedies and otherwise altogether hopeless. In this note, however, he further suggested the combination of some slight astringent to the injection, as Caspard's experiments had proved that weak decoctions of vegetable astringents could safely be injected

into the general circulation. He also recommended, in cases of necessity for stimulation, the addition to the injection of minute doses of carbonate of ammonia, Depuy, of the Veterinary School of Alfort in France, having used this stimulating remedy in the veins of horses with advantage.

Dr. O'Shaughnessy did not expect the suggested saline infusion to remove "the unknown *remote* cause" which would "require to be remedied before a perfect cure could be performed;" he simply looked upon the suggested remedy as something that would "restore the deficient fluids of the body." It is very evident that this intelligent physician possessed an insight into the nature and remedial wants of cholera that was not far surpassed by his professional brothers of 1894, and he certainly possessed a clearer view of the scope of the saline injection than was possessed by many who practised during the prevalence of epidemic cholera between his own and the days of Hager at Hamburg.

In addition to Dr. Latta, Dr. Robert Lewin and Dr. Thomas Craigie, all of Leith, practised intravenous injection. The latter physician reported to the *Lancet* the details of a most interesting case treated by the infusion, in addition to other remedies. This case was that of an intemperate woman, aged 38, who, in addition to the misfortune of being a noted drunkard, had the additional misfortune to be attacked with malignant cholera whilst in the sixth month of her pregnancy, while from this last cause, and in consequence of her debauched spells which had probably prevented her from properly nourishing herself, she was thin and debilitated.

This unpromising and forlorn case, Martha Smith, was admitted to the hospital at 8 P.M., on May 16, 1832, having begun to vomit and purge on the morning of the 12th. When admitted she was still rcamping in both legs, and discharging profuse rice-water evacuations from stomach and bowels; eyes were sunk, tongue cold, pulse hardly perceptible at wrist. She was first placed on a heated tin mattress, and a saline enema of some chlorid and carbonate of soda, dissolved in 6 pints of water, was administered.

At 11.30 A.M., of the next day, she was sinking rapidly. Three pints of the saline infusion were now prepared to be injected into one of the veins of the arm, and by noon, when one pint (at a temperature of 105° F.) had been introduced, there was a fluttering pulse at the wrist, and as the injections increased the volume of the circulating fluid she increased in strength. By the time the whole amount was injected she was able to converse quite freely.

At 1.30 she was found to be sinking again, and at 2 P.M. 7 pints of the injection were prepared and injected with the former results. She now ceased purging, but still vomited a serous fluid, and expressed herself as being otherwise quite comfortable. Another saline enema of 3 pints of saline infusion with 1 ounce of diluted alcohol was administered by rectum; this she retained for an hour and a half. The surface of the body was now warm, and stool passed at 4 P.M. only contained the amount of the enema. At 5 o'clock she fell into a soft sleep—the first sleep for days; at 9 P.M. she again exhibited signs of collapse and complained of great debility; breathing had also become difficult. Two pints of saline infusion were again prepared and injected into the veins. The injection was thrown in too rapidly, or some bubbles of air had now entered the pipe, as she complained of a sharp pain in the epigastrium, and of faintness, the pulse being seemingly much perturbed. The working of the syringe was stopped until the passing away of the pain and the recovery of the pulse, and when the injection was renewed she expressed herself as being much relieved.

At midnight she was still vomiting; a blister was now applied over the region of the stomach, and effervescent drinks given. Next day she passed some 16 ounces of urine of a normal color, but her stomach continued irritable, and she continued to eject billious-looking matter. She was gradually mending, however, and labor coming on by the 21st, she was delivered of a still-born child. Some inflammation of the veins at the places of the injection occurred, but yielded promptly to treatment at the time of the report.

The Central Board of Health of London addressed a list of questions to the Leith physicians, inquiring into the details and results of the practice, and into the condition of the patient at the time of the transfusion and subsequently. To the question as to the existence of complete suppression of urine in the cases operated upon, and as to the effects of the transfusion on this secretion, Drs. Latta and Lewin answered that in all but two of the cases, suppression of urine had existed for hours. "In all the successful, and in some of the unsuccessful cases, the effects of the injection in restoring the secretion of urine was most evident."

As to the mortality—this was the report that Drs. Bell and Condie quoted in their "Material Facts" concerning cholera, without taking into consideration the nature of the cases operated upon—out of 15 cases upon whom transfusion had been performed, 5 were saved. Those which died, did so, as observed by Dr. Lewin, "under such circumstances as do not detract from the general merits of the practice," as was evident from the history of the cases. In one of the successful cases, a woman, most desperately ill, already pulseless, sightless, and about lifeless as well, 284 ounces of the infusion were injected.

The *Lancet*, of July 14, 1832, contains the interesting relation of a case somewhat similar to the one of cholera and pregnancy reported by Dr. Craigie, occurring in the practice of Dr. David C. Carruthers, of Dundee. Impressed with the rationality of the suggestions of Dr. O'Shaughnessy, whom he had met in Newcastle, he determined to put them to a test on the first hopeless case of cholera that would permit of the trial.

A woman, aged 36, pregnant 6 months, and her husband, were brought to the cholera hospital in Dundee in the lowest stages of collapse. The doctor attempted a transfusion, using for the purpose an anatomic apparatus which had served in its palmier days in the dissecting-room for the preparation of the subjects. Failing to make it work—probably a lucky mishap for the patient—the doctor repaired to Perth by mail-coach, and borrowing a transfusion apparatus,

from Dr. McFarlane, of that place, returned to Dundee. On his return he found that the husband had died, while the wife was not expected to survive long. Hastily preparing the infusion, he slowly injected into the median basilic vein 3 pints of the saline solution at a temperature of 110° F., taking a half-hour to inject the 3 pints, the temperature of the solution being kept in the meantime up to the above temperature.

At the beginning of the operation the woman was pulseless and cold, hands and feet livid, mouth open and tongue cold and white, eyes glazed, sunken and turned upwards, with eyelids half closed, face collapsed and dusky. Towards the conclusion of the injection her pulse returned and she revived in every way. In 3 hours the effect of this transfusion had passed off, and a second was administered in the same vein, this time 5 pints being used. A short time after this last injection she improved so much as to go straight on to a convalescence. She was injected on a Thursday morning, and on Saturday, June 23, at 3 P.M., she was safely delivered of a stillborn child.

Dr. Carruthers stated in his note to the *Lancet*, that according to the rule of the hospital, the above two cases, being considered moribund, were refused admission to the hospital by the medical gentleman who first visited them, but that they were sent by the landlord whose property they rented, as he did not wish them to die on the premises. The doctor further informs us that in the other cases upon whom he had attempted transfusion he had not met with as good success. Considering the condition of the only two cases considered fit subjects for the trial, the failures should not be a matter of great wonderment.

Latta, who in reality was first led to consider the subject of transfusion in connection with cholera after O'Shaughnessy's experiments, labored hard to improve the method, fully believing that in the artificial serum judiciously administered, a proper and rational treatment for cholera had at last been found, was very enthusiastic as to its outcome. Some of his cases which he reported to the *Lancet*, printed in

the issues of November 3 and November 10, 1832, and the immediate favorable results, most certainly formed grounds for a strong faith in the treatment.

The first of his recorded cases, but not the first operated upon, was that of a male, aged 33, who was taken to the hospital some 12 hours after being taken with the cholera. He was then in a state of complete collapse, pulseless in the axilla, and as cold as an icicle. At half past 11 P.M. he was placed in a vapor bath of a temperature of 96° F. for an hour. The body here slowly regained its temperature but not its pulse. Sixty ounces of the saline infusion at a temperature of 98° F. was then slowly injected into the veins, which restored him. He was left in the vapor bath for 2 hours longer and then removed to a warm bed. All symptoms of cholera had disappeared, but in 8 hours he ejected from the stomach some dark bilious matter and passed some feculent stools. In 24 hours more the functions of the kidneys were restored, and on the fourth day from his admission he was convalescent.

In many cases the treatment was applied too late. In his later cases he employed a stronger infusion—one-third stronger in its saline constituents—and injected less than formerly, finding that owing to the assisting action of the vapor or steam bath, less fluid was required to arouse the system. The protoxid of nitrogen with which he saturated the water, was employed for the purpose of conveying into the circulation a quantity of oxygen. In most of the cases that did well, the effects of the saline solution were immediately visible. Of all the forms of treatment then suggested or employed, either in private practice or in the hospitals, that of Dr. Latta certainly appeared the most rational both in theory and in results.

In May of 1832, at the solicitation of the Secretary of the Central Board of Health of London, Dr. Latta addressed a letter to the Board explaining his methods. From this letter it appears that in the first cases he used an infusion at the temperature of 112° F. "If the temperature is as low as 100°," observes Dr. Latta, "it produces an extreme sense of cold, with rigors; and if it reaches 115° it suddenly excites the heart;

the countenance becomes flushed, and the patient complains of great weakness. At first there is but little benefit felt by the patient, and the symptoms continue unaltered, until the blood, mingled with the injected fluid, becomes warm and fluid; the improvement in the pulse and countenance is almost simultaneous; the cadaverous expression gradually gives place to appearances of returning animation, the horrid expression of the precordia goes off, the sunken, up-turned eye, half covered by the palpebrae, becomes gradually fuller, until it sparkles with the brilliancy of health, the livid hue disappears, the warmth of the body returns, and it regains its natural color, words are no more uttered in whispers, the voice first acquiring its true cholera tone, and ultimately its wonted energy, and the poor patient, who but a few minutes before was oppressed with sickness, vomiting and burning thirst, is suddenly relieved from every distressing symptom. Blood now drawn exhibits, on exposure to air, its natural florid hue."

In conjunction with the intravenous injection, he advises the use of astringent injections to check the diarrhea—the precursor of Chitty and of Cantani in this remedy—and on the failure of the pulse or shrinking of the features, he advised a recurrence to the saline infusion. In injecting he counselled only using from 2 to 3 ounces per minute.

He relates in his letter to the Board the history of the recovery of a woman, aged 50, who was seized with cholera at 4 P.M. and was, by 9.30, reduced to a hopeless state; pulseless in the axilla, and so near dead that Dr. Latta refused to attempt the infusion injection, not wishing to give the opponents of the measure, any more than necessary, opportunity for fault-finding. At the extreme solicitation of friends, the attempt was at last undertaken, and 120 ounces was injected, "when, like the effects of magic, instead of the pallid aspect of one whom death had sealed as his own, the vital tide was restored, and life and vivacity returned; but diarrhea recurred, and in 3 hours she sank again. Then 120 ounces more was injected with the same good effect. In this case 330 ounces was so used in 12 hours, when reaction was completely rees-

tablished, and in 48 hours she smoked her pipe, free from distemper."

In the light of late events it seems strange that Dr. Latta's system was not more universally employed or tested at the time; still, when we consider the panicky state of minds in times of epidemics, we need not be surprised, as it is a poor time for cool comparisons, reflection, or judgment. In England it certainly did not meet with the consideration, confidence, or commendation it really deserved, something which was probably partly due to the signal failure and the disrepute of the primary saline treatment of Stevens. From the report of Dr. Wright it seems, however, to have been given a trial in various parts of England. One element that will always militate against the general adoption of this measure is "time," as in the hurry and bustle, excitement, and press of business, it would be almost impossible for a physician to be on hand just at the right moment, with his completely arranged and properly temperatured apparatus; expend the required time for its administration, and then watch the case properly, so as to judiciously administer a second, third, or fourth transfusion if required. Such attention and care is only possible and practicable in a well adapted hospital.

Drs. J. Macintosh and George Meikle (*Lancet*, September 15, 1832) gave the practice a trial in the same epidemic in the Drummond Street Hospital, in Edinburgh, where, although not doing miracles, it did, nevertheless; and in the language of Dr. Meikle, "apparently snatched many, as it were, from the very jaws of death." In one of the recovered cases mentioned by the doctor, a woman, 474 ounces—nearly 30 pints—were injected in the first 14 hours, the patient receiving in the course of treatment 138 ounces more, this being the amount of the fourth and last infusion practised on this one case, making a total of 612 ounces, or over 19 quarts. "This case," observes the doctor, "shows that the practice is not only perfectly safe, but that a great quantity can be thrown into the circulation in a very short time; it also shows how we must persevere in some cases. Had the injection been repeated a fourth time, the poor woman would

to all appearances have sunk within an hour." She had been in a state of complete collapse for hours before her admission into the hospital. As this remedy was only used in the hopeless cases that came to the hospital, all those that were saved may really be credited as owing their lives to this method.

Dr. Thomas Weatherill, of Liverpool, reported the case of John Stevenson (*Lancet*, September 1, 1832), treated in the collapse state by Latta's method, infusion injected at a temperature of 110° F., upon whom were made 7 infusions, of about 2 quarts each, each injection being administered to rescue the patient from serious relapses of the collapsed condition. In addition he was given an injection, per anum, with half an ounce of alum dissolved in a quart of water, to which were added 2 ounces of turpentine, this being administered between the fourth and fifth infusions. The man made a good recovery.

Dr. William John Thomas, of Liverpool, felt that the latter treatment had established one important point, this being that the mere stimulus of mechanical dilation would often abruptly rescue the patient from the grasp of death; to make the effect more permanent he suggested that the blood-transfusion should follow the saline, this suggestion being based on a somewhat similar form of reasoning as that which instigated Dieffenbach and Scuttenten to suggest blood-transfusion in cholera in Germany, Dieffenbach then believing that the cholera blood had lost its globular structure.

In the *Lancet* of February 9, 1833, Dr. T. G. Wright, of Stockton-on-Tees, collected the reports in 105 cases of cholera patients treated by the intravenous injection of salt-infusion. Of this number 15 had been ill from 4 to 12 hours, and had each received from 24 to 305 ounces of salt-infusion; of these, 1 was cured, 2 were then convalescing, and 12 had died; 13 had been ill from 12 to 27 hours before resorting to the injection, and of these 3 recovered, 4 were convalescing, and only 6 had died. The remaining 77 cases were unclassified; of these 60 died. In these latter cases, from 1 pint to 5 gallons were injected in each case.

"The method," observes Dr. Wright, in speaking of saline injection, "has not often been successful, and seems now pretty well generally to be abandoned. It has been by relying on the injections as a permanent instead of a temporary relief that much of the failure of that system has probably been attributed."

Could Dr. Wright have lived some 60 years longer he would have thought that either those of his day had failed to recognize a proper and successful mode of treatment or that those of three generations thence totally lacked originality in being obliged to take up the cast-off ideas of the unenlightened of his own day. The above statistics would lead us to infer that the poor cholera-patients who had in various transfusions received 5 gallons of salt infusion into their circulation, must have experienced a most thorough *lavage du sang*. The subject was then evidently in its infancy, and it still required years of experimenting for its perfecting.

In America the suggestions made by O'Shaughnessy did not meet with a Latta to put them into practical operation; on the contrary the prominent men in the profession of the United States at the time did not even coincide in the views expressed by the London investigator. In Philadelphia, when the epidemic had reached England, and was daily expected to visit our shores, the College of Physicians issued a report containing the history, pathology and treatment of the disease, intended to furnish the laity and the profession all possible enlightenment and guidance. The report was prepared by Dr. John Bell and Dr. Francis Condie, both men of eminence and ability, who, when discussing the subject of transfusion, observed as follows:

"Aqueous and Saline Injection into the Veins.—In speaking of this kind of medico-chirurgical treatment last, we believe that we give it the place to which it is entitled, whether regarded on the score of safety or remedial value. The hypothesis on which it is founded is briefly told. It is that, owing to the immoderate fluid discharges from the digestive mucous membrane and the skin, the bloodvessels have parted with an undue quantity of serum, by which the blood, now thick and fibrinous, becomes prone to coagulate in the great vessels and cavities of the heart, and cannot be circulated, hence asphyxia, with its concomitants of the collapsed or blue stage. The indication, therefore, is, we

are told, to replace, by artificial means, this loss. Unfortunately for this speculation, it happens in many cases that collapse is not preceded either by copious serous exudation from the skin or from discharges from the stomach or bowels; of course, the blood cannot, in such cases, have lost its fluidity, or rather, its changes cannot be the effect of a loss of its watery and saline parts, or of serum. At no time is there a well-ascertained or admitted proportion between the prostration of the functions generally, and the discharge of serum by the channels just mentioned. The change in the blood is, in fact, an effect of preexisting derangement of important organs, those to which we have already directed attention, viz., the digestive and respiratory mucous membrane and the skin, and unless we alter and amend the morbid condition by appropriate means, they will neither act nor be acted on by the blood with any chance of permanently good effect."

"Our attempts to modify directly one of these surfaces, the respiratory mucous, or that of the lungs, by means of oxygen, nitrous-oxid gas, chlorine, ammonia, or ether, have not indeed proved very encouraging. . . . In relation to the present topic, we may however observe that some, while admitting the hypothesis of the alarming symptoms in cholera being mainly the effect of the loss by the blood of its watery and saline portions, have thought to supply a remedy by administering repeated doses of saline medicines dissolved in water, with a view to their absorption from the stomach and intestines.

"Some of the objectors to the use of saline medicines by the mouth have, however, expressed a favorable opinion of a more direct method of introducing them into the circulation. This has been done by injection into a vein previously opened for the purpose. Before resorting to so hazardous and daring a practice, we ought to ask ourselves whether, first, in the particular state of the patient at the time, there are not other remedial means which present any fair chance of reviving him? And, secondly, if this practice does not, though affording temporary relief, introduce fresh causes of subsequent disease, and more certainly seal the patient's final doom?"

The report then goes on to state that the few cases upon which the injected infusion had been tried in Philadelphia had died, and that out of upwards of 30 upon which it had been made in New York, only 2 had survived. The experiences in Edinburgh had up to that time only given 5 cures out of 15 cases operated upon, but not to appear to be dogmatically objecting or prejudiced, the American physicians, with commendable fairness, added Dr. Latta's letter to the Central Board of Health in London to their report.

In addition, Drs. Bell and Condie give in the report the somewhat ambiguous relations furnished by Dr.

Anderson, of Rochester, England, detailing the partial history of 5 cases treated by the saline injection which, from its incompleteness and Munchausenism, tended rather to bring the practice into ridicule and disrepute than into respect and use, and which led the American commentators to observe that Dr. Anderson "is trifling too much with his professional brethren."

Whatever other indication we may consider important, there are no doubts but that the one concerning the repair of loss of water of the blood made by O'Shaughnessy, as embodied in his suggested saline-infusion treatment, is as well founded and as imperative as any. Austin Flint's first case made a recovery after being abandoned, by drinking copiously of cold water; and Prof. Thos. D. Mitchell, when lecturing to his class on the remedial virtue of water in the Jefferson Medical College in my student days, was wont to relate among his experiences that of a lady in Kentucky, who had apparently died of cholera, recovering by draining a large pitcherful of water left by her bed while the two negro servants had gone from the room in search of something else, both going because either one feared being left alone with the corpse. The woman opened her eyes, and beholding the pitcher—having been placed there for the purpose of washing the corpse preparatory for burial—she seized it and drained it to the last drop, thereby saving her life. In the epidemic of 1832, Dr. Hardwicke Shute, of Gloucester, England, treated 48 cases by the exclusive administration of cold water, saving 28 out of the number. The practice was adopted by a number of English gentlemen, who rationally looked upon it as the least harmful of all the modes of treatment, and followed it with more or less success.

In the later editions of Good's "Study of Medicine," we find the editor quoting from Paine's "Letters on Cholera Asphyxia," to the effect that transfusion and infusion had been abandoned from their uniform failures, and that their good effects were only transient, while the mortality was not diminished. The editors did admit, however, "the power of this injection," referring to an intravenous injection of 24

grains of soda carbonate and 2 drams of sodium chlorid to the 5 pints of water, "in restoring the pulse and giving the natural color to the skin," as being promptly made manifest after the receipt of the injection into the veins. They are, however, in common with many other critics, somewhat ambiguous in their censure, and they leave us in a quandary as to whether their disappointment results from the fact that one injection did not in the majority of cases give all the expected relief, or whether it was owing that to a recurrence of the collapse another infusion became necessary; as we have seen in the relation of a case by Dr. Latta, a little carelessness on the part of the operator will make the infusion a deadly auxiliary to the cholera. Like to blood-transfusion, none but practised and intelligent hands should have attempted the use of the infusion.

Dr. Francis, of New York, who is extensively quoted in Good's "Study of Medicine" in relation to the details of the cholera of 1832 in that city, says as follows concerning the treatment of Dr. Latta as tried by the New York physicians: "Of about 42 subjects, in which our practitioners have had recourse to this method of treatment, only 4, as far as I can learn, have been thereby saved. Two of these successful experiments were made in the Crosby Street Hospital, under the charge of Dr. Rhineland, where, I believe, 13 cases had been tried. In the first successful one, 40 ounces were injected of a solution composed of soda carbonate 1 dram, soda muriate 2 drams, dissolved in 6 pints of water. The patient was a female in a collapsed state. In the other successful case, a female, in like hopeless condition, had a similar injection to the extent of 105 ounces. The largest quantity of the saline injection that has been yet introduced by Dr. Depeyne, by whom the two fortunate experiments were made, was 332 ounces! The injection was made of the temperature of bloodwarmth, or rather higher, and introduced into the median cephalic vein. From the examples which I have seen of this practice I should deem it justifiably only in the extreme instances of collapse, when every other prospect of cure was lost. In such for-

lorn conditions the saline injections are fully justifiable."

Dr. A. Sidney Doane, in commenting upon the above, quotes the observation made to Dr. Francis by Dr. Vache, of New York, to the effect that "this remedy became a powerful auxiliary to a speedy recovery, provided the sudden and violent reaction induced be energetically met by corresponding anti-phlogistic means." Later on, in the following epidemics—those of '49, '54, '66, and of '73—it was but rarely if ever employed. Dr. Robert Dunglison did not look upon this treatment with favor. In his notes to the article on cholera in his edition of the "Cyclopedia of Practical Medicine" of Forbes, Tweedie, and Conolly, he states that this method, having failed to remove the pathologic causes that gave occasion to the profuse separation of the water and saline portions from the rest of the blood, it had not realized or answered the pre-conceived expectations.

That the practice had never largely found much favor in the United States has been mainly due to the teaching of our professors; George B. Wood, in his "Practice," observes that "the happiest effects seemed for a time to result from this remedy: the pulse returning, the surface assuming its natural color and fulness, and the patient reviving into the appearance of convalescence; but the evacuations recurred, and collapse ensued, followed by a speedy death. The general result of experience as to this plan of treatment has been that, though in a very few instances recovery has taken place under it, from a state of collapse, yet these instances have scarcely exceeded the proportion in which nature unaided has effected cures under similar apparently desperate circumstances."

As we have seen, the practice was generally disapproved, either tacitly or openly, and it is to this fact that, even in the epidemic of 1873, although the history of the many cases develops some that might have been assisted by the operation, we have no records of experiences. In 1873 there was an attempted but incomplete case of milk-transfusion which will be related further on.

During the epidemic of 1831-32 we hear but little of blood-transfusion proper for cholera ; the following cases are the only ones of which the writer had found a record.

The *Lancet* of November 10, 1832, prints the report of 3 cases of transfusion of blood in treatment of malignant cholera, the report being made editorially for the purpose of enlightening its many readers who were proposing that method of treatment, as he prints the account of these fatal cases in support of his previous disapproval of the method.

The first case was operated upon by Professor Dieffenbach in the cholera hospital in Berlin, on October 15, 1831 : Frederick Müller, a strong young man, taken ill 7 hours previously ; eyes were half open and sunk in orbit, tongue and face cold, respiration short ; hands and feet purple, and pulse gone, but he was still conscious. Professor Dieffenbach opened the right jugular vein which had been exposed for an inch ; a quill tube was introduced into the dying man by means of a small syringe. The patient immediately became insensible ; his eyelids opened and shut rapidly several times, and 5 minutes after the injection he was seized with a strong convulsion of the muscles of the neck, which threw the head backwards ; the convulsions spread to the rest of the body, and he died 6 minutes after the operation.

Case 2 occurred on the same day. M. Weber, a widow, aged 65, had been sick only a few hours, but presented the same symptoms as Müller. Professor Dieffenbach here opened the median vein, and injected an ounce of blood furnished by a student ; this producing no effect, the same quantity was injected a few moments later. The respiration immediately became hurried, the eyes agitated, but to questions answered that she was not in any pain. The Professor then opened the jugular vein to introduce a larger quantity of blood, and after opening the vein, and introducing the quill-tube; he first cleared the way for the blood by injecting a scruple of water, followed by 8 ounces of blood. The patient experienced no improvement, passed the day tranquilly, but died about 6 hours after the operation.

The third case was that of an elderly man, aged 61, who was operated upon the following day. He was in the same physical condition as the two preceding cases. Eight hours after the inception of the attack it was decided to attempt blood-transfusion. The experiences of the two preceding cases suggested that "it was thought proper to ascertain whether the circulation was actually going on or not. Esteeming this question one of great importance in pathologic physiology, Professor Dieffenbach, having taken every precaution necessary to arrest hemorrhage, did not hesitate to expose the brachial artery for an inch in the lower third of its course. The exposed artery showed no appearance of pulsation; it was opened longitudinally half an inch, and, to our extreme surprise, the artery did not contain a drop of blood. It merely enclosed a small, red clot; the living membrane of the artery was smooth and pale.

"During this operation the patient was perfectly sensible; he conversed with us about it, and answered clearly every question addressed to him. The deeper tissues were as cold as the surface of the body. After this examination, transfusion of blood was immediately employed. The median vein was opened, and $2\frac{1}{2}$ ounces were thrown in 3 successive times. The patient obtained no relief; he did not complain of any pain, except a slight uneasiness at the place where the artery was exposed. After the third injection the pulse reappeared at the axillary artery, and beat 60 to the minute. This lasted only for 5 minutes, no drop of blood escaped from the opening made in the artery. While transfusion was taking place, the iris contracted slightly, and the countenance became more cheerful, but the disease was not checked; the patient died 2 hours after the operation."

The transfusion of blood was, however, again and more profitably employed in the epidemic of 1873 (*Medical Times and Gazette*, October 18, 1873) by Dr. Stadthagen, physician to the Shed Hospital of Moabit, Berlin. In this instance, a woman, aged 29 years, was brought to the hospital with her two children, her husband having just died of cholera. Admitted at 10 A.M., August 26, she was at the time in commenc-

ing collapse. This continued to increase until 8 P.M., when she was cyanotic, and neither pulse nor second heart-sound could be detected. She had passed no urine for 15 hours. The case was considered hopeless and a fit subject for trial of blood-transfusion, so 180 grams of defibrinated blood was injected into the median basilic vein, without any obstacle, or the patient perceiving what was being done. The pulse gradually reappeared, and some bodily heat that began to distribute itself over the surface. The vomiting and stools which had not ceased continued, but both in gradually diminishing frequency. The reaction and recovery were slow, the anuria existing for 72 hours in all, and it being 10 days before a solid stool passed the bowel. The woman was discharged cured on September 7. In another like case, and under analogous treatment, the pulse partially returned, and there was some general improvement after the blood-transfusion, but the patient succumbed 24 hours later on. The persistence of the anuria in the before-related case, which certainly jeopardized the patient's life from uremia, would have suggested the use of the saline infusion by the bowel, hypodermically or otherwise, both as a diluent and as a kidney-stimulant—effects which no defibrinated blood-transfusion could produce.

In the cholera epidemic of 1853 there again appeared a great variety of treatments. Dr. McPherson, an Indian army-surgeon, particularly recommending the cold-water douche for the surface. Dr. G. Owen Rees, F.R.S., in the *Lancet*, of October 1, of that year, revives the practice of salt-infusion in the veins. "As the cholera has again visited this country," he observes, "I venture to direct the attention of the profession to a point of considerable importance as respects the application of one of the remedies of the disease. With a view of recovering some of the worst cases, and when other remedial means had been unsuccessfully tried, practitioners have occasionally injected saline fluid into the veins. As this proceeding has been attended with great advantage in several recorded cases, and has produced in nearly all a temporary good effect, it has

appeared to me that had the injected fluids been composed in more strict accordance with the chemical and physical constitution of the blood than was the case, we might have derived advantages from the injections very far exceeding those we have on record."

Dr. Rees then calls attention to the analysis, made by Vogel and by Wittstock, of the stools of cholera-patients, which, aside from intestinal mucus and traces of albumin, contained the ordinary salts of the blood, with soda carbonate somewhat in excess, while the analysis of the cholera-blood shows these salts to be deficient, all of which carries us back to the opinion of Drs. O'Shaughnessy and Latta, that the evident indications in cholera are to supply the lost water and the departed salts. For this purpose, Dr. Rees recommended that physicians should carry with them a package ready mixed for use, composed of sodium chlorid, 3 ounces; soda phosphate, 1 ounce; soda carbonate, $1\frac{1}{2}$ ounces; soda sulfate, $\frac{1}{2}$ ounce. Some of this salt-mixture was to be gradually added to some distilled water, at an ordinary temperature, until the urinometer gave it a specific gravity of 1030. When this was obtained it was to be warmed to 98° F., when the solution was ready for use for intravenous injection. Dr. Rees had found that infusions of various specific gravities produced different results upon the blood, referring the reader for further information to his and Dr. Samuel Lane's paper on the subject as published in the thirteenth number of "Guy's Hospital Reports."

Aynott J. J. Chitty, in the epidemic of 1847, while serving with the Thirty-seventh regiment, foot, in the Indian army, relied wholly upon vast injections, per rectum, of a decoction of catechu—2 washstand-basinfuls being given continuously, after the injecting of a smaller amount, until abdominal distention obliged the injector to desist, or where, as in more than one instance, it forced the straits of the ileum and appeared at the mouth—which, in his hands, had the happiest effects. In one case, by the aid of an ordinary embalming syringe, he infused through the malleolar vein, a warm infusion consisting of soda

sesquicarbonate and water into a soldier who was already in articulo mortis. "In a few seconds the pulse returned at the wrist, the respiration became accelerated, warmth was restored to the surface of the body, and animation became so far perfected that the soldier rose up in bed and spoke, and instantly an excessive vomit took place and he fell back and died."

"I was not allowed to repeat the experiment," continued Dr. Chitty,² "but I have since thought that had the injection been adopted earlier in the period of his existence; had it been done a little more slowly, continuously, and not so excessively—for I injected nearly a gallon,—the result might have been successful, and a valuable lesson gained. I am, however, so impressed with the force of that experiment, that on convenient opportunity, and friends permitting, I would not, as a *dernier ressort*, hesitate to repeat it."

While the experiments of 1831-32, made upon the blood of those exposed to and affected by cholera, demonstrated to the experimenters that no blood-change took place in the unaffected, they totally overlooked the comparative condition of the latter class, as experiments in the same direction have since demonstrated that the old experimenters were not altogether correct in their conclusions, as the prior condition of the blood exercises a palpable degree of influence.

Dr. William Robertson,³ of Edinburgh, found by the examination of various specimens of the blood, and especially the blood of cholera-patients in various stages of the disease, that anemic subjects are more prone than others to attacks of cholera. Aside from any microscopic or chemic examinations, the apparently anemic or those in whom induced anemia was present—this group being largely made up of females, especially the pregnant, the nursing, or those suffering from exhausting uterine or vaginal discharges—were those from whom came the greatest number of the affected by cholera.

² *Lancet*, September 24, 1853, and *Braithwaite's Retrospect*, Vol. 28, 1853.

³ *Monthly Journal of Medical Science*, September, 1853.

Dr. Robertson, in common with Dr. James Begbie and Dr. Christinson, all of whom followed up a series of researches into the pathologic changes occurring in the course of a cholera attack, looks upon the re-establishment of the kidney function as being of the first importance after the patient has passed through the algid state in safety. It is here where the many die, the death being due to uremia ending in coma.

On looking backwards at the conditions fully recognized at the time, and the deadly coldness of the algid stage, the loss of water and of the salts of the blood, and the subsequent uremic complications, it does seem as if the full value of the warm saline solution—no matter how or by what method introduced into the general system—should have received a more considerate recognition, as it furnishes lost warmth, lost volumes to the circulation, lost salts to the blood, and last, but not the least, the much-needed diluent or menstruum for the urea salts and a natural stimulus to the kidney. Following these indications will seem to be the most rational form of treatment, considering our otherwise well-known helplessness in treating this disease.

I have elsewhere alluded to the employment of milk-transfusion in cholera patients. This practice was first suggested by Dr. H. Searle,⁴ of London, during the prevalence of the epidemic of 1832, when blood-transfusion and saline infusion were being very prominently discussed. The original conception was to substitute the use of milk-serum for that of the solution suggested by O'Shaughnessy, as the former was believed to contain the salts required by the blood in a far more natural state than when prepared artificially as an infusion. The serum was prepared by taking a quart of milk and beating it, to which was added 8 grains of rennet; as soon as the curd had ceased to separate, it was strained and heated to the proper temperature for a transfusion. As a further clarifier it was suggested to beat up the white of an egg with a wineglassful of serum, to which was added a few grains of tartaric acid; this was then mixed with the whole and boiled and strained, all

⁴ *Lancet*, August 10, 1832.

caseous matter being thus removed from the serum. The method was, however, only tried on one hopeless case, but even here, although in the end a failure, it seemed from the account given by Dr. Searle to have, for the time being, granted considerable relief.

Dr. Hodder, of Toronto, Canada, had, some 14 years previously, proposed to his friend, Dr. James Bovell, the propriety and probable success of blood-transfusion in cholera, but the latter had pointed out that few persons could be found who in the course of an epidemic would part with their blood, and that even if one should be found who was willing, would it not be questionable whether the blood of this person might not itself be suffering from some infection. To these objections Dr. Bovell might have added the almost sure coagulation that would follow any blood thrown into the veins of an algid patient, which only would accelerate the undesired end. Under these objections, and impressed with the need of a transfusion in these cases, but still clinging to the idea of supplying the patient with something as near to the nature of blood as possible, Dr. Hodder bethought of the experiences of Donne, who had successfully injected milk into the veins of rabbits, dogs, and birds, and of the opinion held by Wagner and Gulliver that the white corpuscles of the milk were capable of being transformed into red corpuscles, decided, when an opportunity offered, on attempting a milk-transfusion upon the human subject.

When the cholera appeared in Canada, an old detached shed on the hospital ground, formerly used for contagious and infectious diseases, was converted into a temporary cholera hospital, and Drs. Hodder and Bovell waited an opportunity to put their intended experiment into practice. The first few cases of cholera brought to the hospital were past all help, but on the second day of the appearance of the cases, the case upon whom the experiment was tried and which turned out successfully, was brought in at about noon, while Dr. Hodder was in the hospital. The following graphic account from the pen of Dr. Hodder describes the occurrence:⁵

⁵ *Practitioner*, January, 1873.

"A stout-built farmer, who had come to Toronto on business, was admitted. He was in a state of collapse, cold, pulseless, blue, and shrivelled; the secretion of the urine was arrested; there was purging and vomiting of rice-water fluid; in fact, he seemed dying. I immediately got everything ready, and then sent a message requesting consultation with any of the medical officers who might be in the hospital, when four gentlemen came, and I asked them the following questions: 'Do you consider this a genuine case of epidemic Asiatic cholera?' 'Certainly, and a very marked one.' 'Do you think anything can be done to save him?' 'Nothing, he is dying.' 'Would any medical treatment be likely to be of any use?' 'None.' 'Then he must die?' 'Yes.' 'Then, gentlemen,' I said, 'I am about to try the experiment of transfusing milk into his veins.' 'If you do, you will kill him,' was the reply. Thereupon, I invited them to be present at the operation, but three out of the four left the building; the fourth remained, but would not assist. Everything being ready, I ordered a cow to be driven up to the shed and while she was being milked into a bowl (the temperature of which was raised to about 100° F,) through gauze, I opened a vein in the arm and inserted a tube, and then filled my syringe (also previously warmed), and injected slowly therewith. No perceptible change, either for better or for worse, took place; after waiting two or three minutes, I again filled the syringe, and injected 7 ounces more. The effect was magical; in a few minutes the patient expressed himself as feeling better; the vomiting and purging ceased, the pulse returned at the wrist, the surface of the body became warm; in fact, the man rallied and speedily recovered without a bad symptom."

Another case, that of a woman, greatly resembled one of Dr. Latta's cases, in that she was a very intemperate person, being an habitual drunkard, was also admitted in a state of collapse. Fourteen ounces of milk was transfused, and in a few minutes put a stop to the vomiting and other symptoms. But towards evening a second collapse occurred, when a second transfusion of 14 more ounces of milk was performed. This patient went through the secondary fever and eventually recovered.

The third and last case operated upon in this milk-transfusion series was in *articulo mortis* at the moment of the operation; he rallied, nevertheless, for a time, but died before a second transfusion could be attempted. After this last case, Drs. Hodder and Bovell applied to the Corporation for a good cow and better facilities for carrying on this treatment; and on this being refused, they promptly resigned from their position on the hospital staff.

Milk has, however, been condemned by some authorities as a transfusorial remedy, on account of its tendency to form coagula. In the above cases it seems to have accomplished all that could have been expected of a saline infusion.

In the epidemic that visited the United States in 1873,⁶ there is a report of an attempted milk-transfusion essayed by Drs. F. C. Wilson and William Berry, of Louisville, on a colored woman at Lancaster, Ky. The woman was pulseless when the operation was begun; after 6 or 7 ounces of milk had been injected into the vein at the arm, her pulse became moderately strong, and her voice, which had been reduced to a husky whisper, was so far restored as to be audible in an adjoining room; she gained in strength, so that she was able to raise herself and turn in bed. This movement displaced the tube in the arm, and it was determined to let her rest for the time. In half an hour she was sinking rapidly, and died before the apparatus could all be readjusted.

Aside from these cholera cases, I find the record of several other transfusions in which milk figures as the fluid used. Some of these being in Europe and some in New York—one being employed to recover the patient from a collapse due to long-wasting uterine hemorrhages and the shock of an extensive operation, and in the other cases for the relief of exsanguinated patients suffering from uterine hemorrhages. In most instances the results were gratifying, although it would seem as if no special indications existed for resorting to this doubtful and more difficult and complicated transfusion, when a salt-infusion would have accomplished as much, as well as the latter is easier of procurement and management and not in the least dangerous. Prof. T. Gaillard Thomas was a strong advocate of the method, his reasons being the strong qualitative analytic analogy that exists between the chyle, which is thrown directly into the flowing current of blood and cow's milk, the two fluids being nearly identical. In cholera, however, there is only an urgent need: first, water; and, secondly, salts, and the saline solution fills all demands admirably.

⁶ Cholera Epidemic of 1873, in United States Government Printing Office, Washington, D. C., page 490.

In the summer of 1863, Dr. Thomas E. Wise⁷ proposed preparing for or anticipating the coming algid stage of cholera, by resorting to what he termed an hemostatic treatment or an autotransfusion. This consisted in applying field-tourniquets to one or more extremities, so as to retard the flow of blood in the veins, or by their application to the femoral arteries, cause the bulk of the blood to occupy a narrower circle. Dr. Wise had formerly employed this measure of arterial compression to restore cases of profuse uterine hemorrhage, the diminished vascular circle, and increase of blood-supply or volume in the proper parts tending to stimulate the sinking heart, and thus retaining and reanimating the system in its vital centers.

"In the collapsed stage of cholera, when, in many cases, the physician first sees the patient," observes Dr. Wise, "the system is so much prostrated that the most powerful remedies fail to take effect; the application of the tourniquet affords the only chance of cure. This most powerful remedy immediately removes the powerful cramps, and produces the same equalizing effect as blood-letting without the debility caused by this evacuation. It likewise increases the volume of blood, which stimulates the heart to increased action, removes morbid congestions, and changing the morbid distribution of the blood from the secreting surface of the alimentary channel, sets up a new and salutary action in their place. It thus affords the most ready and most powerful means of rousing the system. By this means the purging and vomiting are stopped, the pulse becomes stronger, the heat and strength of the system are quickly restored, and time is allowed for medicines to act.

"The tourniquet may be applied to two or to the four extremities, according to the effect intended to be produced. It may be kept on for hours, or even for a day or two. In one case I kept the tourniquet applied for three days, as the exhaustion was very great, with the best effects, only relaxing one or more as it appeared. When reaction has taken place, by relaxing cautiously one or more of the tourniquets, so as to allow the blood to flow to the extremities, it afforded a ready means of relief. In a pretty extensive experience I have not seen any bad effects produced by the application of tourniquets. The effect, however, varies according to the stage and severity of the disease. When the patient is stronger, or when reaction has taken place, the pressure of the tourniquet is complained of, and much caution is required to prevent the patient loosening them. If it be done too abruptly, the blood spreads over the extremities, and the patient rapidly sinks."

⁷ *Dublin Quarterly Journal*, August, 1863.

In the above we have an autotransfusion, which is frequently recommended and used to recover patients from accidental hemorrhages, and can be employed either by itself or as an aid to the injection of the saline infusion. The method has its merits as an auxiliary measure, and from the account given by Dr. Wise it is not without its measure in affording a certain amount of relief to the much-suffering patient.

At the Chester meeting of the British Medical Association, in 1866,⁸ Dr. B. W. Richardson exhibited an instrument for the transfusion of liquids into the veins, the liquids intended to be transfused being a solution of albumen subjected for a long time to a degree of heat below the point of coagulation. Dr. Richardson's plan had been tried successfully in many cholera patients. According to the doctor, the application of this measure was intended to sustain the patient.

"As to albumen," observes Dr. Richardson, "it was either poisoning or nutritious. When raw, it did not mingle with the blood; and it had the same effect as scarlatina on the kidneys. A donkey, upon which he had tried it, died with the same symptoms as in albuminuria. But since then he had found that, by subjecting it for a long time to heat beneath the point of coagulation, none of those symptoms were produced. He believed that the digestion in the stomach was, to albumen, simply exposure to a certain degree of heat. The subject was so profoundly grand in its relations to both physiology and pathology that he hoped a very great advance in that direction would be made during the year."

There is much to contend with when claiming any case of recovery from cholera, as the apparently most hopeless case will often surprise their friends, relatives and physicians by making the most unexpected recoveries. I have heard of some cases in European epidemics returning home from the graveyard with their grave-clothes as their only garments, where in the haste and scurry and great press of burials in an epidemic they often carted away the collapsed patient for dead. This is not so strange when we consider

⁸ *British Medical Journal*, August 25, 1866.

the extreme and protracted lethargic conditions that precede real death in so many cholera cases. In the epidemic in 1885, in Japan, Dr. Nakamura recovered a case who had been without a perceptible pulse for 48 hours. Elliotson, in his "Principles and Practice of Medicine," observes that in an Indian epidemic the temperature of the body after death was higher than in life, and that twitchings of various muscles was a frequent occurrence. He mentions one case wherein this twitching and twisting begun 15 minutes after the patient expired, the movement beginning in the fingers of the left hand, gradually affecting the arms; then the pectoral muscles were affected, and later on the cramping or knotting reappeared in the calf of the legs. In another case the toes first began to move in various directions, the muscular actions moved on upwards, the hands pronating and supinating and the fingers extending rigidly; at last the muscles of the face moved and the head was observed to shake. . . . "the total duration of these appearing appearances was half an hour."

It will not be uninteresting, after this review of the history of saline injections in the treatment of cholera to take a short review of the evolutionary processes that have taken place in this regard in the last few years. Cantani, of Italy, employed enteroclysis, which by antiperistalsis-motion will force the ileocecal valve, flooding the whole intestinal tract with a solution of tannin. Two quarts of water at a temperature of 100° to 104° F., with from 1 to 5 drams of tannin and a little laudanum and acacia powder were injected into the bowel. Generally one injection was sufficient, and the death-rate by this treatment was remarkably small—34 only out of 117 cases. The above Cantani treatment, it will be observed, was but a more specific amplification of the treatment employed by Dr. Chitty, mentioned in a former paragraph, where the latter obtained four and three-quarter recoveries to one death. Dr. Cantani explains, however, that as to which Dr. Chitty left us in the dark, that tannin possesses the most active germicidal properties on cholera germs. Like Dr. Chitty, he found that the earlier the treatment was begun the better were the results.

Dr. W. W. Johnson, of Washington, in 1865, suggested the use of a saline subcutaneous injection of the strength of 3% sodium carbonate and 4% sodium chlorid at a temperature of from 100° to 104° F. This method was employed in 1884 by its advocate, Michael, in Hamburg, and at the same period by Samuel, of Königsberg.

"*Hypodermoclysis*," observes Dr. Johnson, "gives startling results in arousing the patient in the algid state. Its advantages over intravenous injections consist not alone in avoiding the danger of opening or manipulating veins, but also in absorption being more uniform and natural. In 187 severe cases thus treated the mortality was 39%. Enteroclysis is used for the premonitory diarrhea in the first stage; hypodermoclysis in the algid and typhoid stage. When treatment is begun, with the disease already advanced, both are used!"

Dr. Johnson also gives a resume of the treatment adopted in the hospitals of Chili, which consisted, as the disease advanced, first of enteroclysis and warm mustard baths at 102° to 104° F., the latter being administered for 10 or 15 minutes, but avoided as harmful in the algid state; with the advent of the second stage the enteroclysis were repeated every 3 or 4 hours. In the algid state, either camphor and caffen subcutaneously, with the subcutaneous injections of the saline solution, which was, in this stage, considered the most important part of the treatment. This solution consisted of 1 dram of sodium chlorid; 45 grains of sodium hyposulfit to the quart of water. This was injected in doses of from 1 to 6½ ounces, according to the state of the pulse.

When the subcutaneous injections in the loose areolar abdominal tissues failed to produce the desired reaction, a resort was then had to peritoneoclysis; by this method absorption was found to be more rapid, reaction lasted 4 hours, and perspiration appeared. A normal temperature and an absent radial pulse were considered indications for this latter form of injection, which saved some lives while it prolonged others. No evil results followed this new procedure in which only from 1 to 3 ounces of the solution were used.

In the above-mentioned intraperitoneal injection employed in the hospitals of Chili, we only have a revival of an old method, one first introduced to the notice of the profession at the time of the epidemic of cholera of 1853-54, by Dr. B. W. Richardson, who then fully established the principle that through the peritoneal cavity the body of an animal can safely be fed with water, and that fatal symptoms from injections do not occur until as much water as is equal to a fifth of the weight of the animal is injected; when more than this is thrown into the peritoneal cavity of a healthy animal, the blood becomes unduly thin and a death from coma results. At that time, this intraperitoneal injection was practised upon a cholera patient who made a good recovery. This method of injecting, as well as the hereafter-mentioned method of cystoclysis, is given by Lesage, of Paris, for the purpose of stimulating the urinary tract, and through this the kidneys, were both the results of the labors of Richardson, he having found that an empty or contracted bladder readily absorbs any water injected into it. From his experiments at the time he decided that absorption was more active from the bladder or the peritoneal cavity than from the cellular tissue. This rational and practical experiment was fully in line with those formerly instituted by Dr. Blundell in the second decade of our century, and greatly assisted in adding to our knowledge of peritoneal tolerance. In 1884, two British physicians, Dr. Purdy and Dr. Cooney, unacquainted with the above facts concerning the relations of Dr. Richardson to the subject, published this new method of injection and claimed to have discovered something new; but they were simply following unawares in the wake of the latter.

Dujardin-Beaumetz⁹ reports that Heyse, of Hamburg, concludes from his researches on cholera made in the last Hamburg epidemic that the only remedy which appeared to have a happy effect on the disease was intravenous injections. "The sterilized liquid was brought to the barracks in large balloons from which the irrigator was filled. To avoid infection the

⁹ *Ann. Universal Med. Sciences* for 1893.

tubes of the apparatus were filled with gauze filters." Heyse employed a solution composed of 90 grains of sea-salt per 1000, to which he at times added a little over a dram of alcohol to the quart. In repeating the infusion he chose a new member. He has administered as many as 7 and 8 intravenous injections to one patient. The only other medicine he employed was calomel. The amount of the injection used by Heyse is not stated.

The same authority tells us that Lesage, of Paris, employs first a warm bath— 164° F.—for 20 minutes or half an hour, a little mustard being sprinkled into the bath a few minutes before the patient is taken out. If reaction does not establish itself he then transfuses 1 quart of artificial serum at the temperature of 104° F. This is, if found necessary, repeated more than once. He irrigates the stomach and provokes a kidney-action by filling the bladder with a warm borated solution.

Galliard, of Paris, also uses the intravenous injections of an artificial serum, but his is composed of $1\frac{1}{4}$ dram of sodium chlorid, and $2\frac{1}{2}$ drams of sodium sulfate to the quart of distilled water. Of this he injects 2 quarts to an average-sized adult, taking a quarter of an hour for its infusion. Algid collapse and absence of radial pulse, are, with Dr. Galliard, indications for a transfusion. He uses the infusion at a temperature of 136.4° F., or 58° C., probably calculating that the slowness of the injection permits its reaching the veins at a proper temperature.

Dujardin-Beaumetz also cites Siredy, of Paris, as another transfusionist—the word transfusionist is here used as employed by our author—who considers this method as the best means of fighting grave cases of cholera. In addition to the intravenous injection of the infusion, he also uses its introduction by the hypodermic method, some of these injections being thrust into the thigh and into the gluteal regions—5 to 10 ounces of the infusion being so injected at a time, and this being repeated 4 or 5 times in the 24 hours if found necessary. I should prefer the subcutaneous or the bladder, or intraperitoneal injections by all means, as these deep muscular injections may be followed by some disaster.

Cantani is this year reported as having obtained 60% of cures by the subcutaneous injections of the saline solution, which he considers a superior method of administration to the intravenous, claiming that the artificial serum is more quickly diffused in the former method. This serum is composed of sodium chlorid, 1 dram; sodium carbonate, 45 grains; sterilized water, heated to 104° F., 1 quart.

Neuman (same authority) uses salt-infusion subcutaneously in the flanks; from 3 to 10 ounces are thus administered to children, and from a quart to a quart and a half to adults. Massage causes its absorption as fast as it is pushed in.

Hayem, whose studies, experiments, and experience in hematology strongly entitles his opinions to our consideration, is a strong supporter of the administration of the saline solution by intravenous injection in the algid state of the disease. He advises the employment of a solution composed of 1 part of soda carbonate, 5 parts of sodium chlorid, 25 parts of soda sulfate, and 1,000 parts of distilled water. The latter of the solid or saline ingredients—soda sulfate—has a twofold action in this stage of cholera; instead of acting, as is supposed, as a laxative, it is in reality constipating, and, according to Hayem, the use of this solution by transfusion into the veins or tissues will not only tend to arrest the process of transudation of fluids into the intestines, but will even in some cases tend to promote the reabsorption by the tissues of the fluids that have already escaped from the bloodvessels. When more than a quart is injected he advises that the proportion of soda sulfate be reduced. When, owing to the indistensibility of the cellular tissues, or to the collapse of the vessels, intravenous injections are inadvisable or impracticable, he advises that the attempt to restore the normal fluidity of the blood be made by intraperitoneal injections. In either case he advises that the solution should not exceed the natural temperature of the normal blood. The soda sulfate is looked upon by Hayem as an excellent preservative of the integrity of the red globules of the blood, possessing a special effect upon this part of the blood.

Dr. Charles H. Wendt,¹⁰ who quotes from Hayem in the above details, does not place much reliance upon the procedure, following all former American authorities in looking upon the results as not sufficiently permanent to be encouraging.

In the course of a lecture on the treatment of epidemic cholera, delivered in the therapeutic lectures of the Faculté de Médecine de Paris, in July of 1884, after going over at length the best then-known means of combating the disease in its earlier stages, Hayem, on reaching the description of the stage of collapse, or the algid stage, gives us a most classic description of the subject. "In the majority of the cases," he here observes, "it is the blood which now plays the principal role, but we must not overlook the action of the choleraic poison which probably is still exercising its morbid influence on the heart and nerve centers. The intestinal transudations, enormous in quantity and rapid in action, has here drained greatly from the total bulk or volume of the blood, despoiling it of its salty and watery particles; the albumen, as we now understand, is left in the vessels. Is it necessary to insist upon the multiplied consequences that such a state of the blood details?"

"Some authorities have attempted to throw doubts upon the importance that this state of the blood exerts in the production of the algidity or of this choleraic asphyxia, citing in support of their theories cases in which the disease ran a 'foudroyante' course, and where the algid stage has come on very quickly (Hayem here refers to such cases as Sir William Gull, and others call up in support of their opposition to accepting the views of Wittstock, O'Shaughnessy, and of Schmidt, owing to the fact that the algid stage supervened in some of the cases without a seeming amount of the vomiting and purging, but where they took no account of the excessive urinary action nor of the rapid transudation). Such authorities have, however, failed to tell us that the blood of these 'foudroyante' cases has also lost its fluidity, and that in fact there existed in these cases

¹⁰ "Asiatic Cholera." Wendt. 1885

the pathognomonic blood-thickening peculiar to the algid stage.

"We have here, as a result of the diminution of volume, a corresponding diminution of vascular pressure, with the blood circulating slower and slower as it thickens, at last becoming almost stagnant and surcharged with carbonic oxid, and in the end acid, as has been shown by the experiences of M. Strauss. Now we have the patient cyanosed, cold to iciness, with suppressed secretions and retention of all excrementitious matter within the blood and system, as well as of the choleraic person which, acting directly on the whole organism, produces a state of hypothermia, especially of the heart.

"The ideas of Dieffenbach of 1832, that the transfusion of new blood could assist in this stage of cholera, were neither practical nor rational. There is here no need of blood, as its corpuscles and other solids, except the salts, are all present, even to the albumen; what it here requires is a diluent, and neither blood nor stimulation to the blood-making functions. The blood is here really in most need of water. The corpuscles are not only present, but present in excess of the normal in the cubic millimeter of blood; what it therefore needs, instead of blood, is an increase of the natural diluent to bring these down to their normal distribution, and this can best be accomplished by intravenous injections of water, the saline solution being the preferable method."

Hayem credits Jachnichen, of Moscow, with employing intravenous injections in the treatment of cholera when the epidemic first appeared in Russia in 1830; according to this authority, Magendie and Latta employed them in the same year; the first, in Paris, and the latter in Edinburgh. M. Dujardin-Beaumetz, who investigated the subject in the epidemic of 1873 accounts for the poor results obtained by the use of the saline injections at that epidemic, to the fact that it was mostly employed in the altogether hopeless cases, where, nevertheless, it proved successful in a number of cases. He also calls attention to the fact that, as a rule, the successful cases are those that represent a persistent and undiscouraged employ-

ment of means to their relief. Hayem calls our attention to the successful cases of Latta and Weatherill, where these physicians employed full and repeated injections.

Hayem advises a 5:1000 solution of table salt, warmed and then filtered through a triple thickness of Berzelius paper. When the vomiting and purging are persistent he advised the addition of 2 or 5—according to the demands of the case—centigrams of the chlorhydrate of morphia. The soda sulfate—already mentioned for its good effects on the blood—had been shown by M. Rabuteau to be constipating instead of laxative.

Hayem instituted some experiments to solve this point, and for the purpose took a dog weighing 20 pounds and administered a transfusion of chlorid and sodium sulfate to the quantity of 835 grams, thus producing into the vascular system of the dog the enormous dose of 20 grams of soda sulfate. The animal supported the transfusion well, only vomiting once; like after any transfusion the animal experienced some slight fever, but from the day of the operation on the 5th of July to the 10th, he remained constipated. The urines were clear, not albuminous, but exceedingly rich in sulfates. From the results of this and other analogous experiments Hayem formulated the saline solution containing 25 per thousand of soda sulfate, whose formula is in another paragraph. When, aside from any thickening of the blood, there also may exist as a cause for the collapse a feeble heart, he advises the additional subcutaneous injections of ether.

Manchot publishes the results of the experience obtained in the Neue Allgemeine Krankenhaus at Hamburg, of which a short resume is given by J. P. Crozer Griffith, M.D., in the *Annual Univ. Med. Sciences* for 1894. The new remedy, the anticholerin of Klebs, of Zurich, gave only a mortality of 67.7%, while saline infusion is credited with a mortality of 84.5%. The anticholerin of Klebs was injected subcutaneously. The report states that enteroclysis, hypodermatoclysis, venous infusion, etc., each has its place, and is not to be omitted under the circumstances to which it is appropriate.

It is not clear how a remedial measure which is inapplicable to the early stages of the disease, and by many not recommended to be used even in the algid state of collapse until reaction absolutely refuses to appear, can be tabulated as a distinct form of treatment and its results contrasted with a remedy like anticholerin—a remedy somewhat on the antitoxin order, both in its preparation and action—which can be depended upon in the early stages, but which, in the algid stage, must in many cases be as helpless and as out of place as the saline intravenous injection would be in the opening stage of the malady. I cannot, from these premises, perceive upon what basis Manchot tabulates his figures for statistical comparison.

The saline infusion, whether administered in the muscular tissue, or in the loose areolar tissues of the flanks, or of the abdomen, intravenously, or into the peritoneal cavity, can only be used at a certain stage of the disease; and when its use is required, it can only be looked upon as the last charging squadrons that have been held in reserve to put to final flight the disordered and beaten enemy and to decide the battle.

The questions raised by Manchot's statistics are very much akin to the much-disputed question as to whether Waterloo was a victory for Wellington or Blücher, or as to whether, at any time, the battle was with Napoleon? It is useless to undertake, from the inception to the end of an attack of cholera, the purely anticholerin or the purely saline infusion treatment of these separate cholera patients, as they are not separately applicable to like stages or conditions, although both used in cholera cases; one has an abortive effect in one stage, where the other only would aggravate; and one has a resuscitating effect in another stage where the other would, in most cases, be hopelessly inert.

In looking over the literature of the subject, as it touches transfusion and infusion, it is very evident that there exists a needless amount of confusion—if not in the actual understanding of the matter, as regards its proper sphere in cholera, at least, in the de-

ductive descriptions and allusions to the subject, as at best saline infusion can only enter as a part of a system of treatment, and even then when urgently called for; but it can at no time be logically termed or be treated as a separate treatment throughout the course of the disease.

Kleb's anticholerin is injected in doses of 1 cc.; 6 or 7 separate doses are given on the first day; on the second day it is given 5 or 6 times; and 3 times on the third day; on the fourth day, only once or twice. "The frequency of the injection was governed by the depression of the temperature, upon which anticholerin exercised a favorable influence, being usually followed by a febrile reaction." As Condie and Bell observed in reference to Dr. Anderson, of Rochester, England, when commenting on his meager details and unroofed conclusions, we are left considerably in the dark by the reporters as to how the treatments were really applied to the cholera patients in the Neue Allgemeine Krankenhaus at Hamburg, or as to what was the real ratio of deaths or failures of the anticholerin treatment, as we are not told whether the cases handed over for infusion or transfusion—which were credited with the deaths—were not also the cases upon which the anticholerin was helpless; nor are we told if those charged to the anticholerin were not subjected to other treatment.

It is unreasonable to believe that a series of patients were set aside for the exclusive anticholerin treatment, and rigorously restricted to that one remedy, regardless of that which, in the later stages of the disease, and under varying circumstances, may have suggested some other more appropriate therapeutic measures. Anticholerin is an antitoxin, but it cannot supply water when this alone is the crying need, or when this is needed to stimulate the kidneys to carry off the urea. Some such cases must have occurred in the series wherein anticholerin treatment is credited with a certain specific mortality. There here exists something illogical in action or of words and relation. It is hardly supposable that one series of patients in this Hamburg hospital were left severely alone throughout the premonitory, invading, and in the

violent stages of the cholera when the saline solution would have been eminently inappropriate to be reserved for this treatment alone in the algid or collapsed stage—the only stages where saline infusion can have any play or office—while it is as illogical to believe that another series of patients, a series whose diseases failed being checked by the exclusive use of the anticholerin, were, in every instance, and that, regardless of conditions, pointing clearly to the need of other remedies, allowed to die without any further attempted relief, and that for the sake of formulating useless comparative statistics. There is, it is well understood, a certain broad degree of incertitude with everything that concerns recoveries from cholera, but some statistical relations only make confusion more confounded.

Augyan, of Budapest, is quoted by Griffith,¹¹ upon the results of anticholerin, who reports its employment in 19 cases of cholera of unusually severe type, 9 of the patients dying—a mortality of 52%. In this series of cases it was found that the remedy exerted a most beneficial influence upon the course of the disease. “In some cases slight transient febrile reaction appeared. Most of the symptoms soon changed for the better, diarrhea and vomiting ceasing on the first or at least on the second day. Cyanosis, which would sometimes yield to hypodermoclysis, frequently, however, to recur, disappeared permanently after the employment of anticholerin. The secretion of urine was resumed under the influence of the treatment, and soon attained respectable proportions; while in the algid cases not treated with anticholerin the anuria would persist for 3 or 4 days. Although the number of cases was too small to lead to a final conclusion, the general impression was a favorable one.”

From the above we are led to believe that in this series of cases it was the cholera toxins that exercised throughout an intense influence on the body, something against which saline infusion is not directly active, as it can here only act as an assistant depurator, while there are here no doubts but that the anticholerin exerts on these toxins a direct modifying influence.

¹¹ *An. Universal Medical Sciences*, 1894.

From personal experience and acquired knowledge in the effects of a strong infusion of black coffee, in all uremic affections or stages of disease, wherein a uremic complication plays an important part (and deleterious part), such for instance, in the closing stages of yellow fever, bilious fevers of various types, cholera, etc., I should, on general principles, approve of the suggestion of Bubelir, of Moscow, who administered it in doses of several tumblerfuls daily. I should consider this remedy as a powerful aid to the subcutaneous saline injections and the tannin enteroclysis of Cantani.

Lokoloff, with a placid conviction and that exhibition of settled harmony that, like a May morning sun, warms the smiling landscape of Medicine, as if it were one of Theocritus's ancient sylvan bowers, looks even upon the saline subcutaneous injections as "utterly useless, and should be discarded from the therapy of Asiatic cholera, since they inflict a totally wanton torture on an already severely ill patient."

In the last epidemic, at the cholera hospital at Havre, if the patient failed to react from the algid stage, and caffen and ether hypodermics were unavailing, 2 quarts of an artificial serum were injected into the internal saphenous vein. One injection was generally sufficient to revive the patient, although one case had it repeated 5 times. After an interval of 11 hours, if necessary, another injection was administered.

Of 173 cures accomplished in this hospital 25 are attributed wholly to the influence of the infusion. Dr. Galliard mentions the curious fact that in the height of the epidemic, out of 62 male nurses employed, only one contracted the disease, and his recovery was due to the use of the saline infusion.

In the last epidemic at Hamburg, Hager reports that 967 cases were treated by the infusion method at the General Hospital of that city. From his experience he believes this to be the only scientific and practical method, and the only one of any value whatever in the algid stage. He employed both subcutaneous and intravenous injections of a solution of sodium chlorid warmed to 40° C. (104° F.), 1 to 3 liters (quarts) at a time. The results were most

striking in the algid stage. The chief value of the method depends on its power to tide many patients over this stage, but if patients passed into the typhoid stage, it appeared to have little influence. Of the 967 cases 291 recovered—*i. e.*, 30%, which is 10% more than the average number of recoveries as stated by Griesinger. In most of the cases one injection was sufficient. In 92 cases dying in the typhoid stage the treatment had brought the patients through the algid stage.

In his comparisons between the advantage of the two forms of injection—the subcutaneous and the intravenous—Hager gives the former method his decided preference. The proportions of recoveries were 36.64% and 28.1% respectively. He found the intravenous method more difficult, not any more prompt in its effects, and possibly somewhat dangerous, when contrasted with the simplicity and safety of the subcutaneous method.

Augyan considers that the use of the infusion of salt-infusion reduced the mortality in some epidemics by 25%. Hagerstadt and Van Lingen, from their Russian experience of 1893, arrived at the conclusion that intravenous injections and hot baths furnish the only reliable measure for combating the dangers of the algid stage. Even when useless to save life they afford the patient a certain degree of relief from his sufferings.

Another authority, K. Dehio, in opposition to the expression of Hager, of Hamburg, prefers the intravenous injections to the subcutaneous method. To simplify its administration, he attempts the introduction of an aspirating needle directly through the skin into the vein. Its introduction into the vein is said to be announced by the trickling of blood from the needle. The latter is then connected by a rubber tube with the irrigator holding the warm solution. This treatment he tried in 18 selected well-developed cases of cholera asphyxia, with scarcely or not at all perceptible pulse. "In some of the cases there was temporary improvement, often with a surprising recovery from the symptoms of the algid stage. In only 3 cases, however, did ultimate recov-

ery take place." His conclusions were that the injection had the power of removing the cardiac weakness and feebleness of pulse only as far as these conditions were dependent on the state of the blood and the emptiness of the vessels.

In commenting upon the above operative method of Dehio, it will not be improper to criticise his technic. The method that he depends upon as a proof that the needle has entered the vein—the trickling of blood from the free end of the needle—is precisely one of the points that practised experimental physiologists experimenting on transfusion and infusion are most carefully persistent in their efforts to avoid, as they here dread the occurrence of coagula. In fact, it is advised that the needle be full of the fluid about to be injected when operating, so as to avoid the possibility of the slightest regurgitation of blood from the vein into the needle or tube. Dehio's plan must unavoidably force back into the vessels the needleful of blood filled during its insertion and essay as to the location of its point. This only tends to show the numerous risks and accidents which in many ways attend the subjects of transfusion and infusion, and how one operator may have a succession of unfavorable results.

We have now brought the history of transfusion and its many derivatives in their varied relation to cholera down to our own day, and the relation, aside from any practical applications that the many described methods and uses may suggest, is particularly interesting as exemplifying the importance of the history of all that concerns our art. Since the beginning of the century, 12 different epidemics of cholera have started from India, and many of these have reached Western Europe, and at least 6 have come to our own shores. In that time it has been interesting to watch the evolutionary processes that have developed about this subject in its relation to the treatment of cholera. We have also been somewhat interested in observing how old methods are, now and then, brought forward as new discoveries or innovations.

Let us take, for instance, the incident reported in

1853, in the *Lancet* of September 24 of that year: Dr. Chitty, then dwelling in England, detailed his experience at Colombo, in Ceylon, in 1847, while with H. M. 37th Regiment, which was severely stricken with cholera. He then inaugurated the intestinal flushings with a catechu decoction, which has since, through the peculiar evolutionary processes of medical progress, merged into the Cantani tannin method that has been so extensively and successfully used in the last epidemics. It is true that Dr. Chitty did not then know of the existence of the comma bacillus nor of the action of tannic solution on the former. Dr. Cantani may or may not have been influenced in his researches by the experience of Dr. Chitty, but he certainly deserves the credit of having pointed out the deadly relation of tannin to this bacillus, from which we further learned the reasons of the peculiar immunity enjoyed by tanners in tanyards from cholera attacks.

Throughout the long period that this paper spans—from 1831 to 1895—we have seen continued revivings of old methods, and some that were even not so very old, but that were not universally known or their existence had probably been forgotten or overlooked. To this order belongs the intraperitoneal injections so much lauded in Chili and in some parts of Europe, and by many believed to be a new innovation, as well as the cystic injections practised lately in Paris. These two therapeutic measures had both been introduced, as we have seen, many years before by Dr. B. W. Richardson. Not only had these methods been known and published but they had as well been discussed. At a meeting of the Medical Society of London, on Saturday, October 21, 1854, during a debate on Dr. Buchanan's paper on the "Injection of the Cellular Tissue in Cholera," Dr. Richardson had again called the attention of the Society to the superiority of intraperitoneal absorptive powers over those of the cellular tissues, absorption being much more rapid in the former. It was at that meeting that Dr. Richardson predicted that if a dropsical patient—meaning one that was afflicted with ascites—should ever become attacked with cholera, the drop-

sical symptoms would be relieved by the new disease on the one hand, and be relieved from the fatality of the choleraic attack on the other. He had, in fact, just seen a case of cardiac disease complicated with dropsy attacked by cholera, and where one disease had so well offset the other that, in the end, the patient had escaped from both.

It will be remembered that O'Shaughnessy had based his views and subsequent suggestions as to the saline injections in cholera upon the comparative physiology and pathology of the blood in health and in cholera. Wittstock, of Berlin, with greater advantage than those enjoyed by his London co-worker, carried his experiments upon a still greater range in the same direction. The results of these, as well as of the experiments of Marcet, Denys, and of Lecanu, of Paris, and of the various other experimenters, finally crystallized in the methods of Latta, which with many backings and fillings, have now, in variously modified shapes, or in their original conceptions, become, after a lapse of sixty years, with many, the established modes of practice for the algid stage of cholera.

Some seven or more epidemics have occupied the time from Latta to Hager, and yet, in the intervals between 1832 and 1894, the system first brought to notice by Latta was only sporadically employed.

From its inception the saline infusion treatment, as first adopted by Latta in the treatment of cholera, has been recognized as being based on such physiologic and pathologic grounds and comparisons as consigned and confined or restricted its sphere of employment or usefulness to the algid state of cholera. It was from the first designed to fill those certain functions and offices whose necessity does not occur until the algid state is fully reached. It never was even suggested as a prophylactic treatment, or one tending to relieve the violence of the onset in the struggle between the disease and the patient that precedes the final vanquishment of the latter and the ushering in of the stage of collapse. But it has been urged as being the proper remedy, when, to use the words of that eminent cholera authority, Charles

McNamara—whom we do not wish to misrepresent as suggesting the use of the saline injections, as he has not, but whom we simply quote as to his opinion regarding the uselessness of the ordinary remedies of the algid stage—the patient has reached that stage of collapse where there is little that can be done for the patient.

It is this stage when McNamara advises enemata of warm beef tea, and, if possible, to have the patient drink about half a pint of water every second hour, so as to add fluidity to his blood and assist in remedying the suppression of urine, that the advocates of the administration of saline infusion in some of its many modes of administration have urged its employment.

A. Ferrand¹² observes that while the saline infusions have not accomplished all that was desired, this consideration should not be neglected in our cholera therapeutics, as the successful experiences of Lorain, who employed intravenous injections of warm water, prove that the object for which the saline injection is administered—the furnishing to the blood its lost fluidity and volume—is certainly fulfilled.

In 1854, William W. Guil and William Balz, on the part of a committee appointed by the Royal College of Physicians, presented their voluminous report on cholera to that body. In this report, that which is particularly interesting, is the detailed researches on the blood of this disease made by Garrod, of London and Schmidt, of Dorpat. Schmidt, among his numerous experiments, took for comparison the blood of a cholera patient (female) who had been in perfect health up to the moment of the cholera attack, and the blood of another female in as perfect a state of health, and of like race, age, habits and bodily formation, and arrived at about the same conclusions as the experimenters of 1832; he furthermore concluded that the chemical alteration of the blood was the cause of the transudation of its watery and saline particles into the digestive tract, and that this loss in the constituency of the blood was in turn the loss of heat. His general conclusion led him in reality to

¹² *Revue de Therapeut. Med. Chir.*, 1873.

support the identical views formerly enunciated by Wittstock, O'Shaughnessy and others.

The British profession was not ready to accept anything that would prove but a partial explanation or the suggestions that would only lead to partial ideas of treatment. It wanted something definite. Even Dr. Gull, one of the chief framers of the report, was dissatisfied with the results of his labors and the explanations of Schmidt. There were, he said, many cases of collapse that did not depend upon the amount of the effusion, and as the loss of fluid could not, in these cases, be accounted as the cause, the results and deductions of Schmidt would not cover the question. Dr. Gull doubted whether death could be ascribed to the loss of fluid, however great, as he had seen some such collapsed and bloodless cases recover their elasticity and health, although he admitted that in part the proportionate degree of the loss of fluids often bore some relation to the degree of the attendant collapse. Sir William undoubtedly represented the trend of the views of the profession of the time, who, in their helplessness, were very much in this matter in the condition of the laity who want a specific or nothing.

To really understand the attitude of the profession at this period, we must analyze the conflicting emotion by which it was swayed. It stood somewhat in the position of a maid with an offer of marriage which she hardly considered all that was desirable, and yet was not wholly disposed to refuse. The grounds upon which to found clear and comprehensive etiologic ideas or to follow the pathologic processes are not clearer now than they were then. The discovery of Koch has only verified that which Hartshorne, Stillé, Flint, Woodworth and Leal, of the medical profession, as well as every advanced physician in the European profession, has long before anticipated. The disease was known to depend upon the bacillus which only awaited to be discovered, although much more was anticipated as a result of this discovery than actually resulted. It was in this expectation of the discovery of the yet unseen but known to exist, and in the anticipation that this discovery would revolu-

tionize our etiologic ideas and forms of treatment, that the profession felt so backward about committing itself to the acceptance of that which the expected lifting of the veil might at any moment prove to be a palpable error.

Since these expectations and uncertainties have been in a manner settled, and since we have realized all that was expected or possible from anticholerin treatment, we have been more at liberty to adopt some of the older views. It is plain, that prior to this, the profession was in a perplexity as to how best not to commit itself too definitely—especially as has been explained—to something that was not deemed sufficiently comprehensive or final. It was striving hard not to permit itself to be convinced by the labors of the experimentalists, physiologist and chemist, who in reality, but unknown to us, had gone so far as modern science can even now permit. This is plainly evident in the remarks of Sir William; and the same evident desire not to ignore palpable facts, but at the same time be inquiringly noncommittal is very apparent in the editorial review of the above mentioned report on cholera presented to the Royal College of Physicians by Sir William and Dr. Boly, which appeared volume 14 of the *British and Foreign Medico-Chirurgical Review* in 1854, in the course of which there appears the following critical queries:

“How, in the collapsed stage, are we to reverse the current which is pouring from the blood into the intestines? How are we to get the potash salts into the blood-globule, and the water into both cells and into cellular fluid? How, in fact, are we to replace in its wonted order, this extraordinary medley of substances, which in the healthy system are kept in such singular accuracy in their proper boundaries? To these questions chemistry is either dumb or returns a despairing answer. The steps in one direction are traced, but the return appears impossible to science, since the causes of the phenomena are totally unknown. We are driven back on our empiric knowledge, and what is termed a scientific treatment of cholera must yet be looked for.”

Just why the British, German, and French profes-

sions should, with the labors and suggestions of Wittstock, Schmidt, O'Shaughnessy and of Latta, as well as those of Richardson, then being made, discussed and published, have chosen to wander about aimlessly in the wilderness of speculation and of futurity, with the truth rubbing briskly under their very noses—truths first exposed in 1832 but not fully recognized until 1894—is past comprehending. It greatly reminds us of Galen pricking an artery and seeing the blood spurt with each cardiac impulse, and of the long list of noted men who, from Podalirius down, had applied the fillet to the upper arm to swell the veins for venesection; of Pare applying the ligature and his predecessors the hot pitch to a bleeding surface; the whole scheme of the circulation passing continually, with all of its suggestions, under their scientific noses asking to be discovered without their seeing or even suspecting its existence.

In all the conflicting reports regarding treatment we must believe that when the blood is not ruined beyond the possibility of recuperation, that one of the crying needs of the system is then for water, and that many undoubtedly die just through this one want. Prof. Mitchell's case, in which the patient accidentally supplied himself with water, being one that would have been fatal in earnest but for the opportune big pitcher. Prof. Austin Flint mentions that his first cholera patient, after the failure or discontinued measures, was permitted to drink all the water that he wanted, under the impression that the case was hopeless, but which made a rapid recovery through this remedy. In the hopelessness in the collapsed stage and the later experiences it would seem as if the supplying of this want by some of the many means suggested is not only safe but useful.

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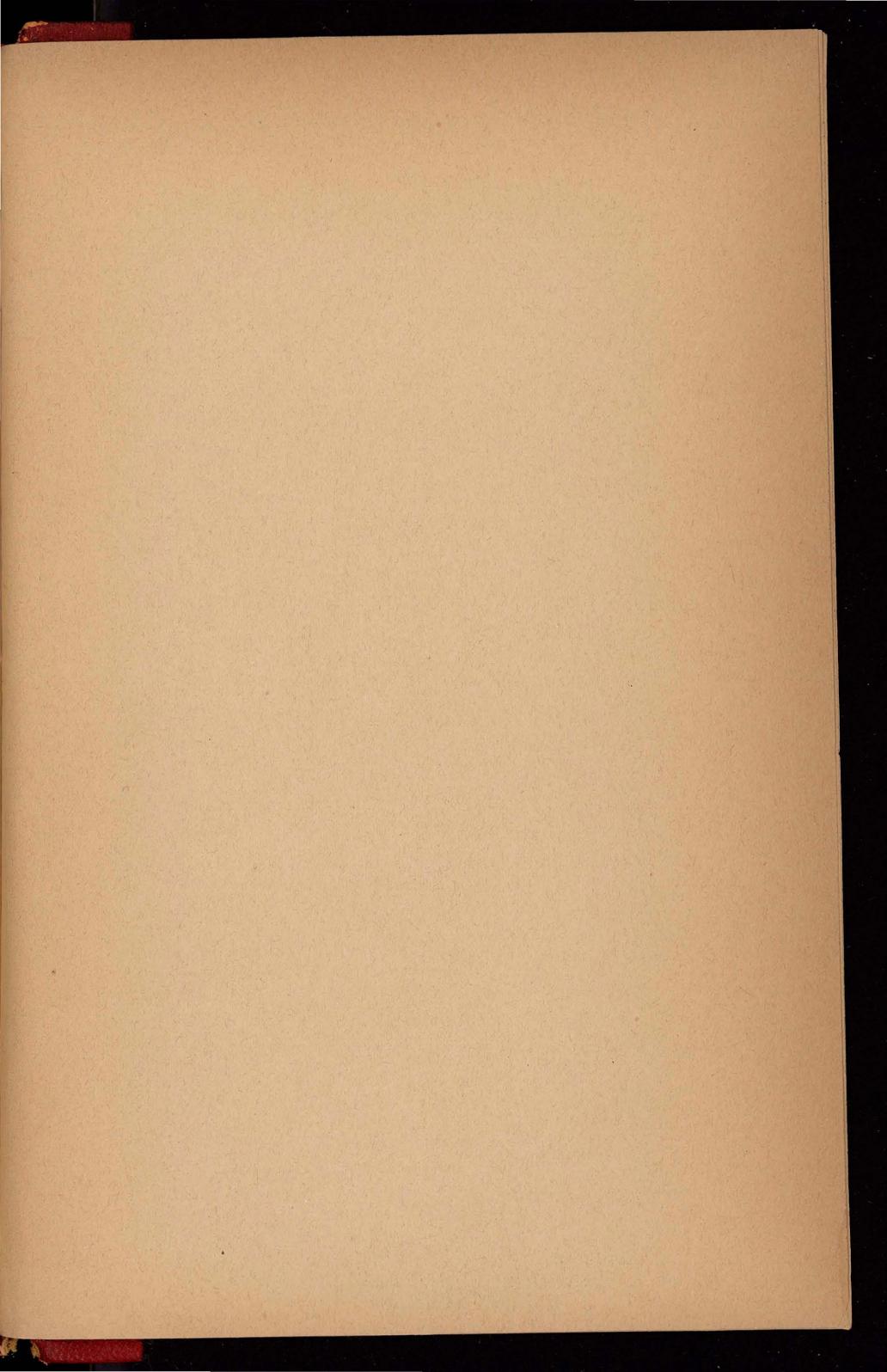
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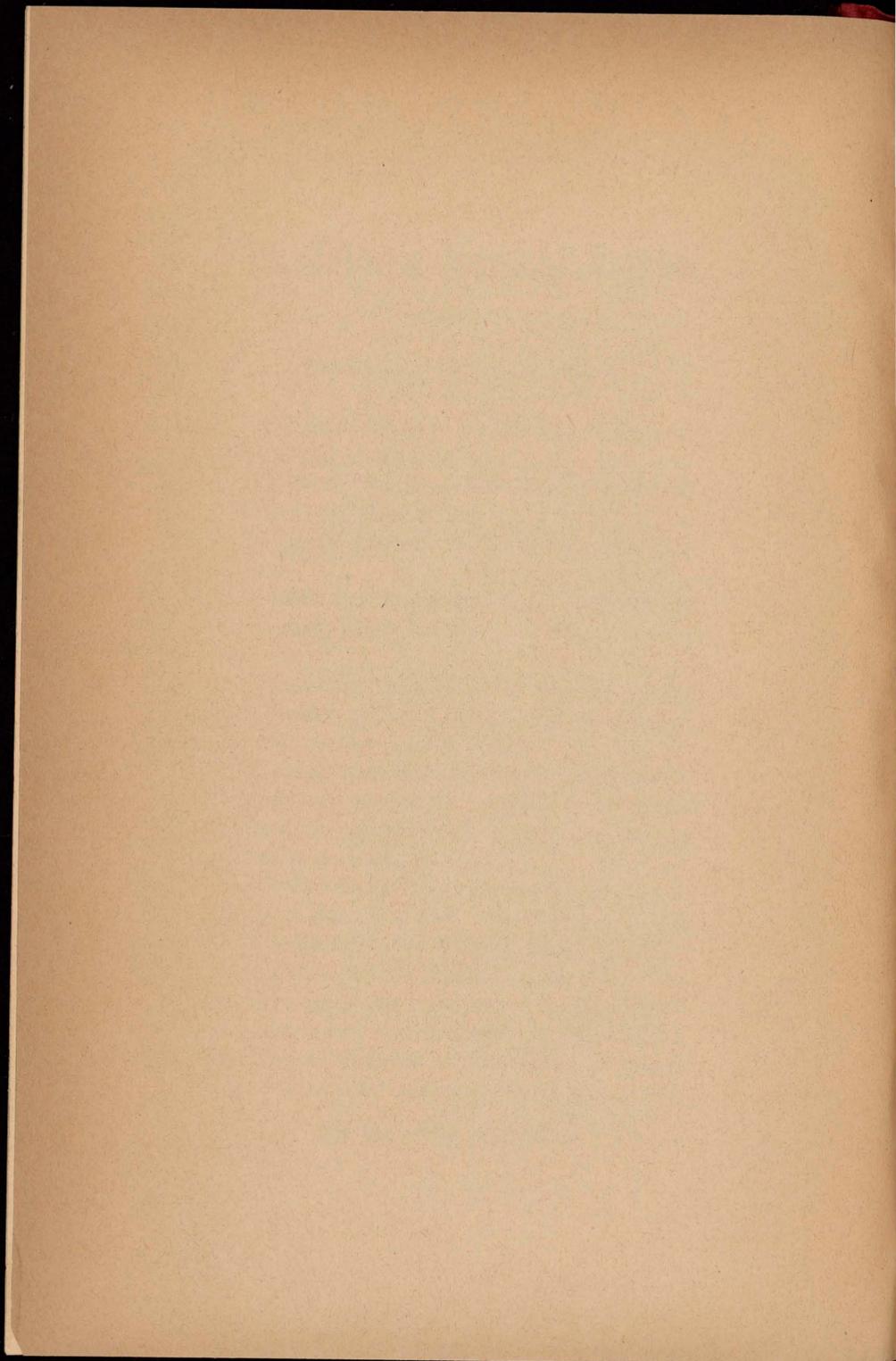
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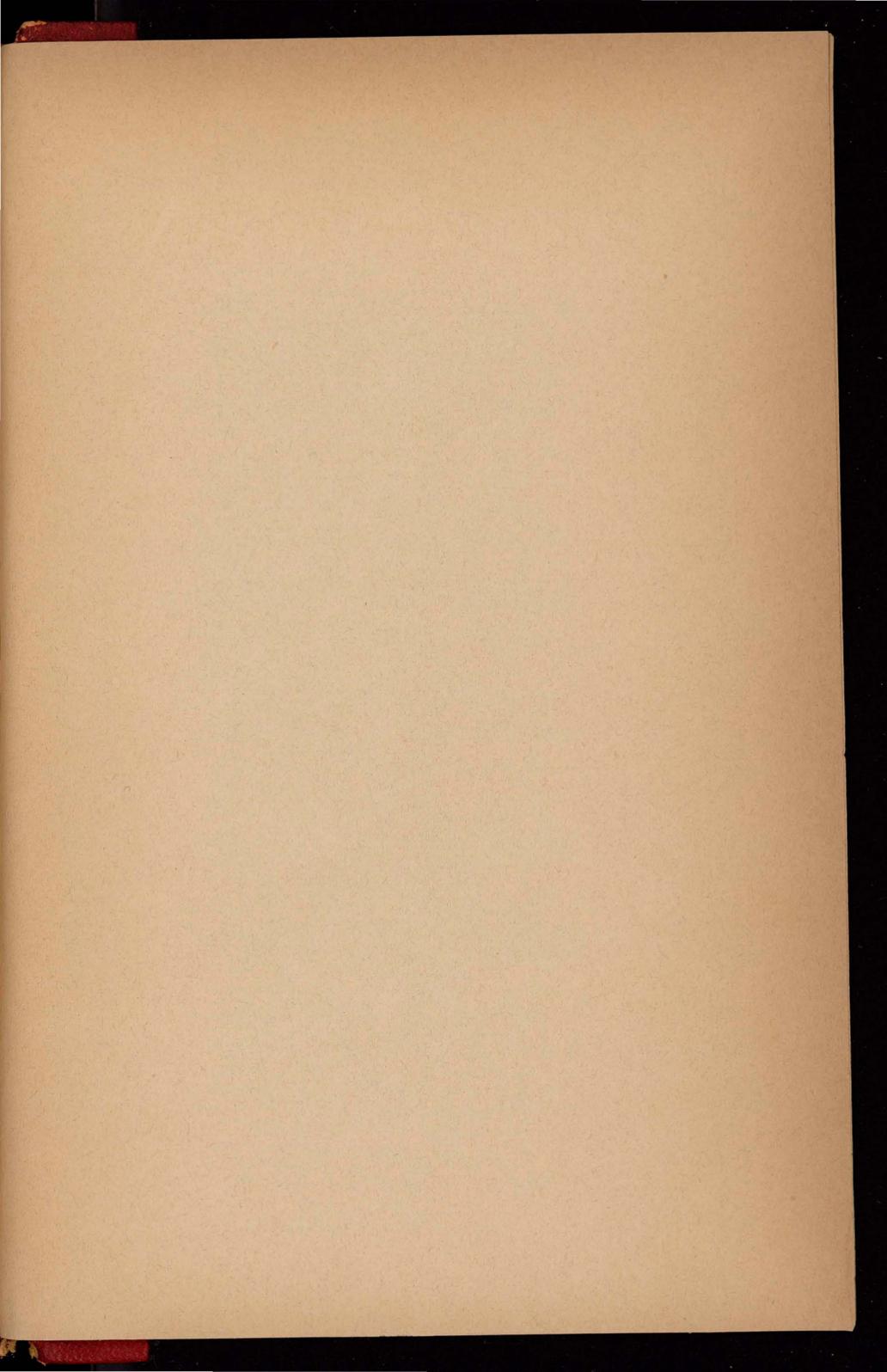
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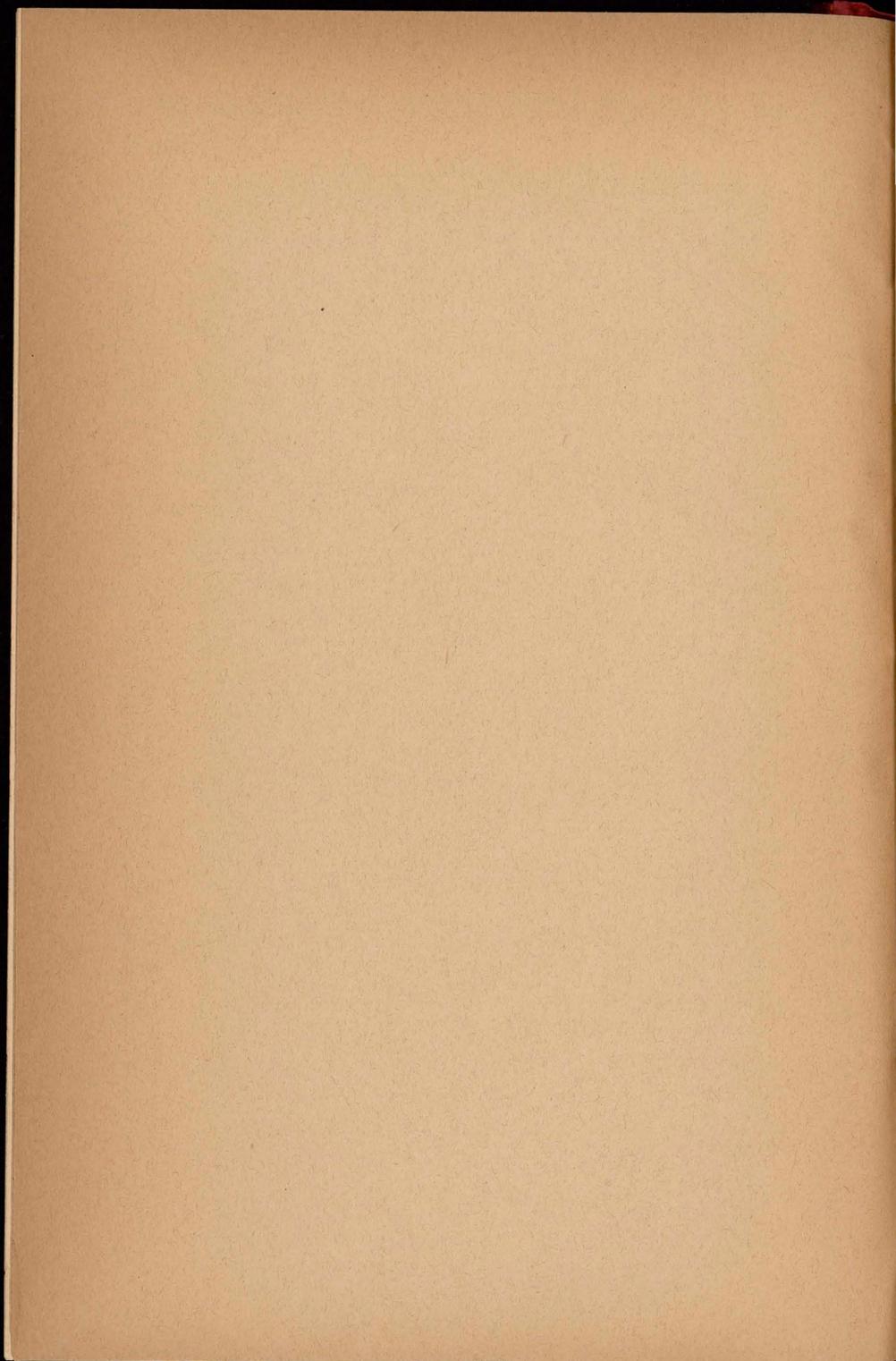
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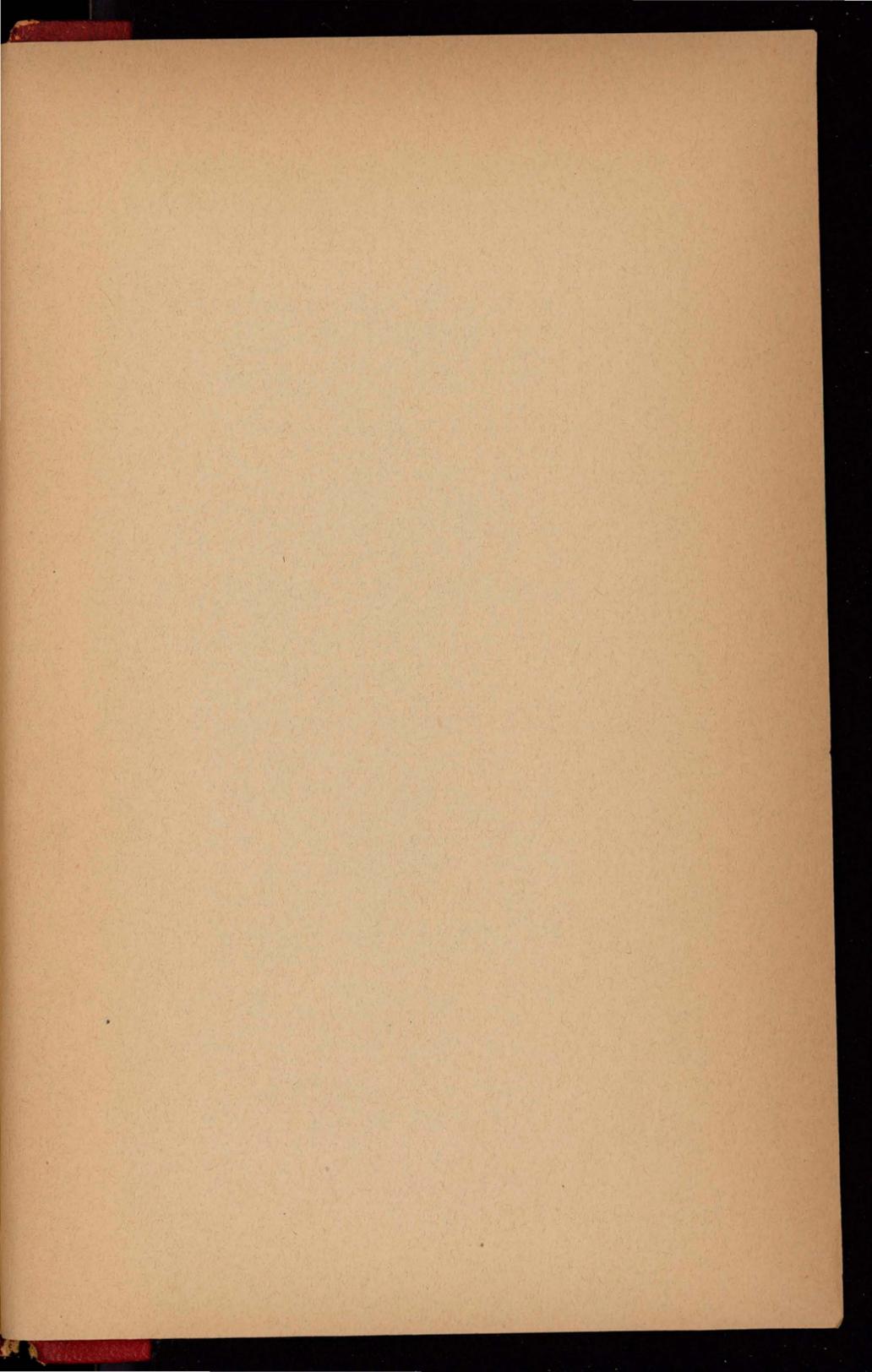
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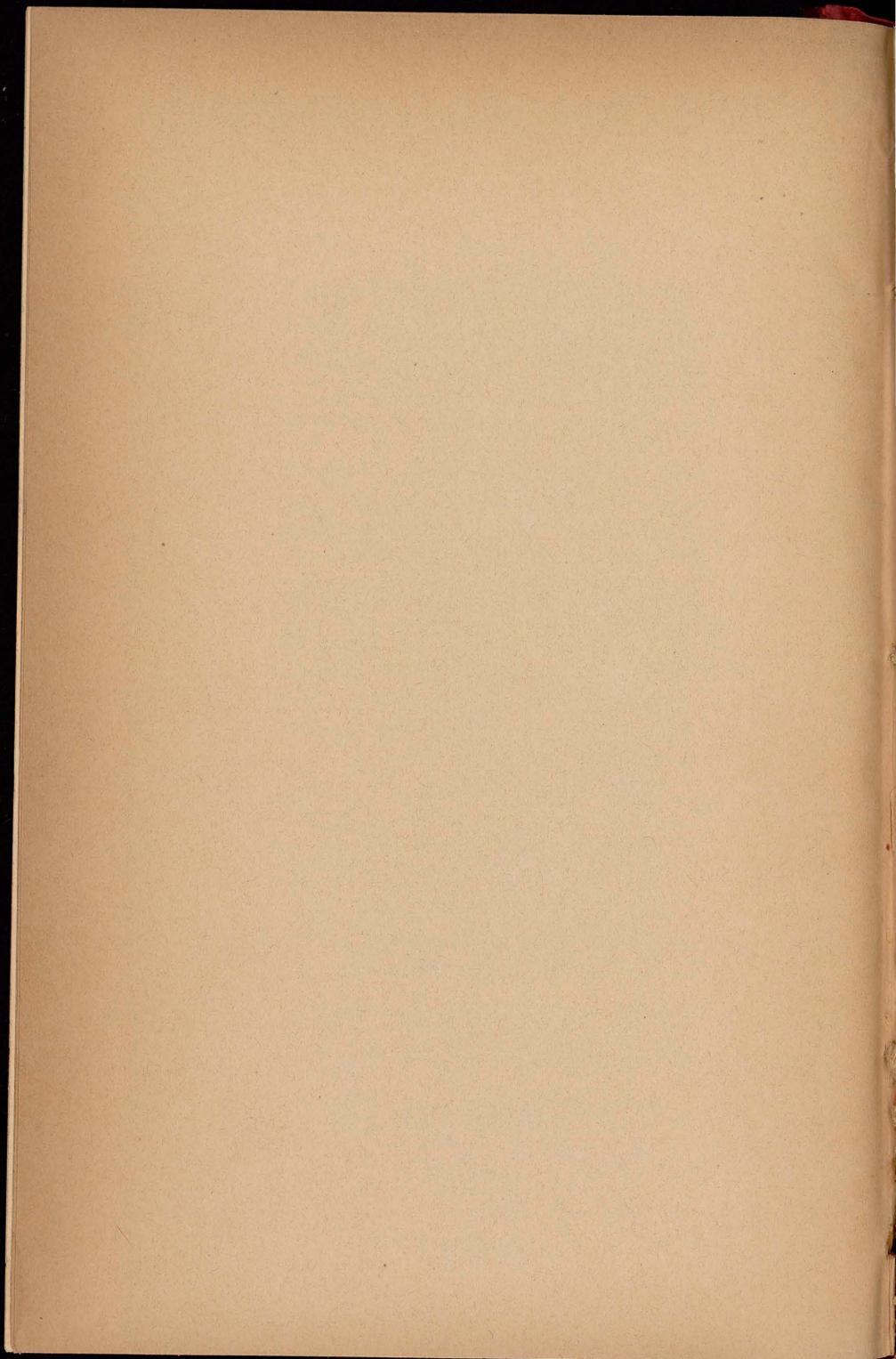


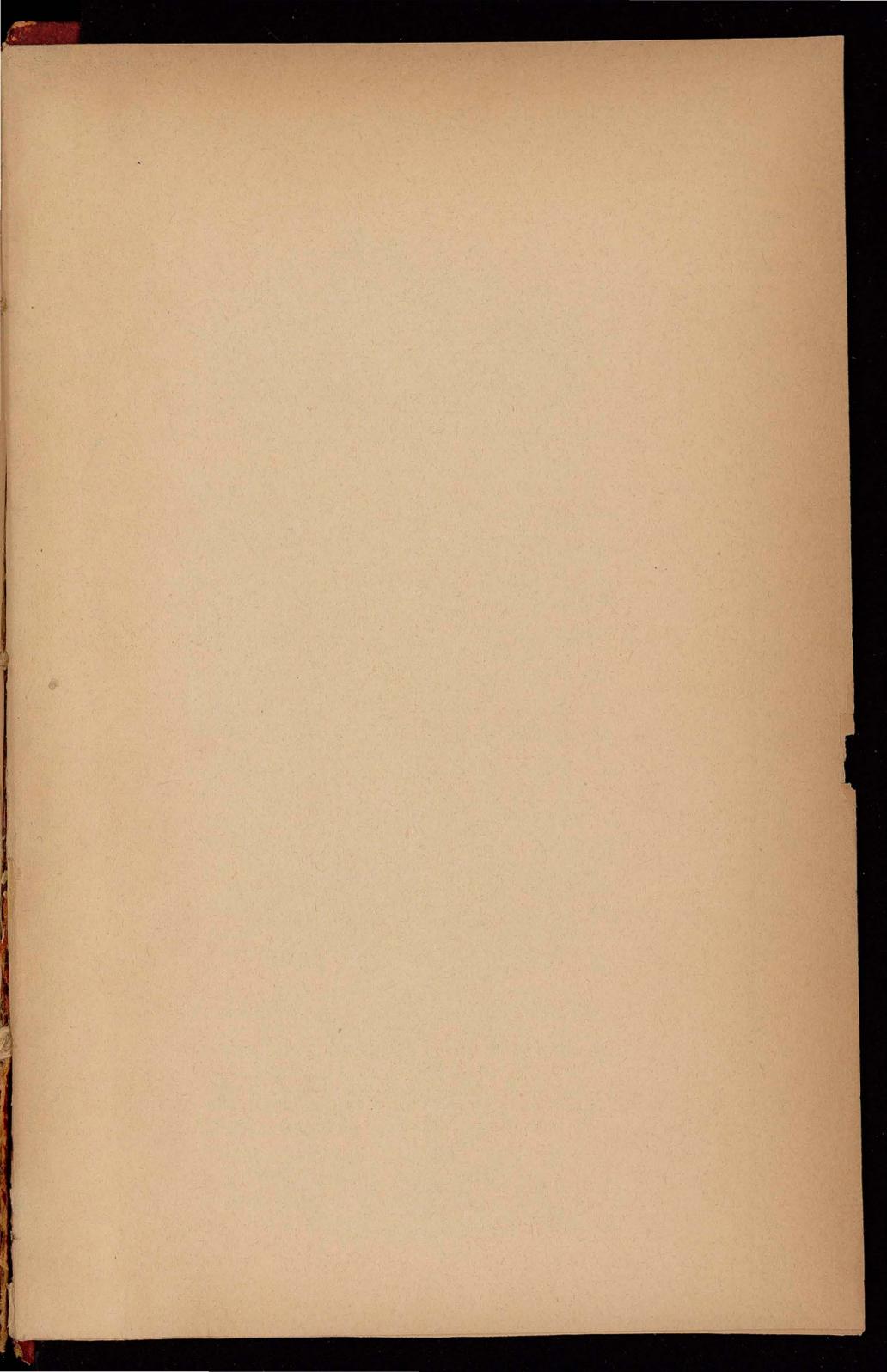




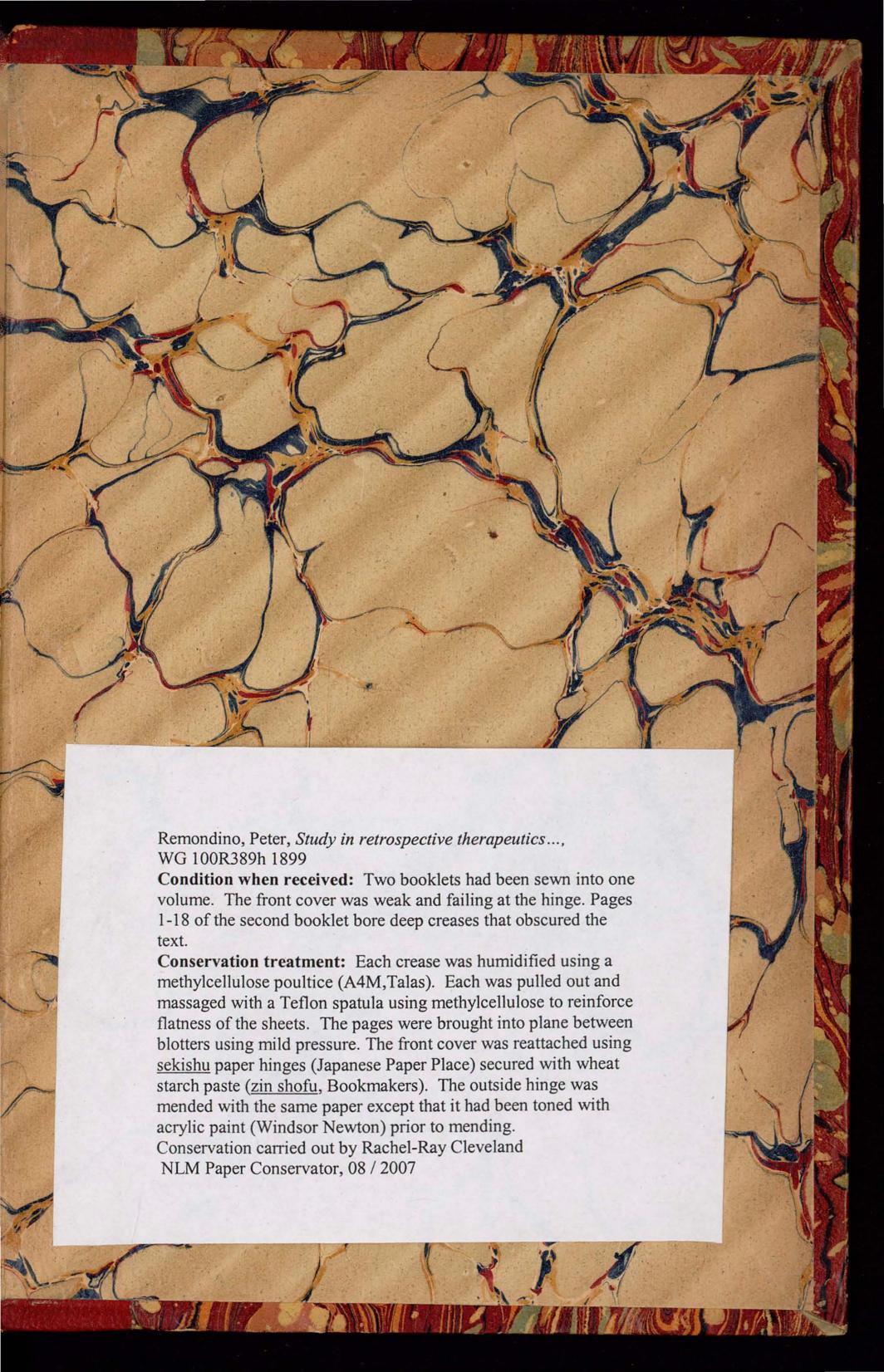










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