# ANNALS OF SURGERY

VOL. LI. JANUARY, 1910 NO. 1

## ORIGINAL MEMOIRS.

### THE BLOOD IN SURGERY.*

A HISTORICAL AND CRITICAL STUDY.

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THERE are three commonly accepted methods of studying a problem—whether that problem be a political propaganda, a question of social science, a biological puzzle, a piece of medical research, or an undertaking in practical mechanics. These three methods we call severally, (1) the inductive method of the scientist; (2) the practical method of the technical craftsman, and (3) the literary method of the student. Take, for example, the steam-engine as a problem to be investigated: the *scientist*—the properly trained physicist, studies the force-production of coal and the expansive power of steam acting upon a complicated mechanism of steel for the accomplishment of work; on the other hand, the *technical craftsman*—the trained mechanic, is concerned with the construction of the apparatus, the firing of its boilers, and the setting it in motion; while by the literary method the *student* of steam power as applied to the development of civilization

* The Annual Discourse before the Massachusetts Medical Society, June 16, 1909.

looks to remote causes, and to effects immediate and remote. The last named—the student—reviews the observations and hypotheses of the ancients; the vagaries of the mediæval alchemists; the crude, practical endeavors of the early moderns, and so he comes down to the accomplishments of Watts and the Stevensons, and grasps the significance of those prophets of modern industry; while he summarizes and assigns to their proper perspectives the vast individual factors in the complex of modern life as affected by steam power; foreseeing perhaps —or attempting to foresee—the bearing of it all upon the mechanic arts of the future and their influence upon the history of the race.

These three methods of study are applicable as well to medical problems, and the three classes of workmen find their labor in appropriate fields: The scientist investigates in his laboratory questions of biology—of physiology, anatomy and chemistry as concerned with the problem in hand. The technical craftsman, or practical clinician, as we call him, carries to the sick-bed the findings of the laboratory, and demonstrates their significance in the vital field of therapeutics. And finally, by the literary method, the student of medicine as a whole—of medicine in its wide bearing upon human happiness and progress, adds his quota also to the elucidation of the problem. It is his function to trace out and to collaborate the story of men and of measures: on the one hand to show, in the broad sense, the immense influence which the progress of medicine has had upon the progress of civilization, medicine's present significance and its probable future; and, on the other hand, and in a narrower sense perhaps, to trace the growth of our knowledge of special diseases. In this way best, I believe, may one reach a proper conception of the attainments of our predecessors; of the place at which we are arrived; of the value of special research; of the futility of certain lines of endeavor; and of the rate and probable outcome of to-day's progress.

This third method of studying problems in medicine is a method deserving more consideration than we have always

given it. We are prone to consign it to the dust-bin of medical history—of history in the nonphilosophic sense; but the study of medical history, properly pursued, means something more than the resurrecting of remote happenings—the dry bones of an emotionless past. Past and present are interwoven closely in such studies. The most successful clinician or investigator of to-day will be the first to appreciate the bearing of past facts upon present problems; while the intelligent recorder of past events must be versed and facile in the conduct of modern research and in the interpretation of clinical facts.

To be specific, in the following paper I propose—somewhat haltingly, I fear—to consider the subject of the Blood in Surgery from our third point of view—the point of view of the student of literature. In these days most of us who investigate this matter are busied, some with laboratory studies on the effects of hemorrhage and on the results of transfusion, and some in applying directly to patients the measures proved useful by laboratory experimentation. Shall not we here properly and timely, therefore, review the development of studies in the blood as we see them to-day?

The problem of the blood in surgery presents certain features, which I shall recall to you; and I shall discuss these features from the historical standpoint as well as from the critical standpoint of the present. We shall consider the *circulation, hemorrhage,* and *transfusion,* while various cognate matters incidentally must be developed.

Let us turn first to a discussion of knowledge of the circulation, as it became clear gradually to physiologists. No subject in the history of medicine is more vital or illuminating. In a former writing, on Aneurism, I said some little on this matter, but in that writing I was concerned with a field more narrow than that we are now considering.

To the ancients the problem of the circulation was truly a problem, though time and again some prophet arose who thought he had solved it. It is interesting to recall the fact that the great Hippocrates early in the Third Century B. C.

described the heart as a great muscular engine, even though it was not clear to him what function the heart served. Yet, five hundred years later, Galen taught his Roman students that the heart is *not* a muscle. Galen led physiological thought for fifteen hundred years, with the result that his misconceptions regarding the heart turned away to false conclusions hundreds of his successors. This fact is especially surprising when we remember that Aristotle, the great natural philosopher of Greece, soon after Hippocrates, about 340 B. C., had stated that the heart is the central organ of the circulation and is the mover of the blood.

In the light of history we cannot but marvel at the centuries of ignorance and misconception which followed the two assertions of Hippocrates and of Aristotle—their assertions that the heart is a muscular organ, and that it moves the blood. Unhappily for the progress of physiology, however, Aristotle believed that arteries and veins serve the same purpose [1] and bear blood equally to the extremities. Erroneous as was this idea the matter was made worse by Praxagoras, who wrote a generation later, and distinguished sharply between the functions of these two forms of blood-vessels, but distinguished wrongly.

Praxagoras observed that the arteries pulsate, while the veins lie apparently motionless. Thereupon, instead of recognizing the obvious fact that the movements of the arteries are due to the heart's impulse behind them, he asserted that the arteries beat because they are empty of blood, and are moved by a mysterious pneuma, to which he gave the name "vital spirits"—a pneuma much resembling air in character. We all know of this old error, but we must remember that it was an error quickly exploded. To be sure the conception of these air-tubes led to the adoption of the name *artery,* but the trachea also was dubbed artery, long before the name artery was applied to any vessel concerned with the circulation.

Galen was the medical philsopher who set straight the ancient misconception of the arteries' contents. One is tempted always to dwell upon the life and accomplishments of

this extraordinary man—unquestionably the most distinguished medical scientist of the old world. But we must brush by him, noting merely that he died about the year 200 of our era. He studied and demonstrated physiological phenomena through animal experimentation. He proved beyond peradventure that both arteries and veins contain blood, and that the wounding of an artery or a vein may suffice to draw away all of the life stream. His knowledge of the nature of the circulation was at fault in many other regards, however; and as his views controlled medical beliefs for nearly sixty generations, and directed those beliefs into channels which now seem to us preposterous, it is worth our while briefly to glance at his teachings.

Galen and his successors were convinced that the system of veins springs from the liver, whence the venous blood draws its nutritive properties; and that the system of arteries springs from the heart. Those men recognized the fact that both veins and arteries mingle in the lungs, but the significance of that mingling they did not comprehend. Here is a fact, however, regarding these ancient men and their conceptions: The men seem never to have guessed, or even to have suspected the existence of that thing which we call the *circulation* of the blood. They named the arteries and veins—*blood-vessels,* the term which we still employ; but they used the word—*vessel*—to signify a blood container, a pitcher or a bowl as it were. The blood in these vessels—they thought—lies in them as water lies in a lake, and does not course through them as water flows in a river. One asks, naturally, how the blood, especially the blood of arteries, could be discharged in jets when the blood-vessel is wounded. Galen asserted that the arteries in themselves—in their own walls—contain a vital principle which causes them to dilate and contract. Strangely enough, he appears to have seen no special connection between the contractions of the heart and the throbbing of the arteries. He did realize, however, that there is probably some communication between the arteries and the veins; but he taught that this communication is mainly accom-

plished through the medium of minute openings in the ventricular septum of the heart, through which he imagined small portions of the blood-stream constantly to percolate. We know, indeed, that he used the word *anastomosis,* for Galen, as well as his predecessors in the Alexandrian School, believed that there is a communication between the terminal branches of both veins and arteries. Galen asserted this communication without being able to prove it; indeed, he demonstrated that this communication plays an important part in the bleeding to death of an animal and the exhausting of its veins, when an artery is opened; but in spite of the soundness of this conception he failed still to recognize the constant and inevitable round of the circulation.

So we have seen, as Fleurens [2] points out, that before Galen's time there were three principal errors in the conceptions of the circulation: the first, that the arteries contain air only; the second, that the ventricular septum is perforated; and finally, that the veins, as well as the arteries, carry blood to the extremities. Galen corrected the first error—the air error—but his false notions of the perforated septum and centrifugal function of the veins remained an accepted doctrine until after the Revival of Learning.

Curiously interesting is the return to a discussion of the circulation in the early years of the Renaissance. One of the great followers of Galen was Mundinus of Luzzi, who taught anatomy at Bologna in 1315. He reiterated Galen's story of the circulation and fixed it firmly in men's minds for more than three hundred years. In some sense he was our earliest modern comparative anatomist. Among other teachings he delivered himself of the following luminous statement: Man is to be distinguished from animals in that man has no tail, "because being naturally erect he rests himself by the sitting posture, and a tail would interfere with his sitting down." *Hec sufficiant de anatomia totius.*

We must recall also the shrewd Da Carpi who lived two hundred years after Mundinus, and followed closely his teachings. Da Carpi also taught anatomy at Bologna and dis-

tinguished himself by the astonishing discovery that men sometimes have been born with the heart covered with hair. On this account such men are braver than other peoples. In spite of this striking discovery, however, Da Carpi still clung tenaciously to the teachings of Galen.

Mundinus and Da Carpi were early prophets of the Italian schools, but a greater than they was to arise while Da Carpi was still living. This was Andreas Vesalius, the famous surgical anatomist, a Belgian by birth, who was called to the Chair of Anatomy at Padua in his twenty-third year. Vesalius is one of the most brilliant and attractive of our early heroes—the first great modern who refused to accept without demonstration the teachings of Galen. His work was done mainly in the anatomical theatre, and was concerned but indirectly with physiological problems. Vesalius came early to doubt those apocryphal percolations of the ventricular septum—"I still do not see how even the smallest quantity of blood can be transfused through the substance of the septum from the right ventricle to the left."

This great writer offered no explanation of the transference of blood from veins to arteries, but evidently he was impressed with the unreality of the accepted teachings and with the need of further study of the circulation. It is reasonable to suppose that his early retirement from teaching and his premature death postponed for a century the true explanation of the circulation.

Harvey, the distinguished English physiologist of the Seventeenth Century, is the man to whom we look as the discoverer of the circulation of the blood; and yet Harvey had that astonishing predecessor, Servetus, of whom too we hear too little. Servetus asserted the arteriovenous anastomosis in the lungs. He was a fiery soul—a bumptious opponent, a polemical disputant, always at odds with the authorities, whether civil, medical or theological. He was a Spaniard, born in 1510, four years before Vesalius; and Calvin burned him up at Geneva, when he was forty-three years old. Those were thorough-going days, and in this way the burning came

about. Though a physiologist, an anatomist, and a rebel against the Galenic teachings, Servetus was animated chiefly by a hatred of churchly dogma, whether of the old or the new school. He used his own recently discovered physiological facts to overturn religious conceptions, and he wrote a book called "The Restitution of Christianity"—preaching a return to the primitive faith and life. He found that the Scriptures say the soul is in the blood, and that it gets into the blood through the air; but, to do this, the blood must circulate through the lungs, which indeed it does, says he. The venous blood does not percolate through the ventricular septum, "but by a grand device, the refined blood is driven from the right ventricle of the heart in a long course through the lungs. By the lungs it is prepared, assuming a bright color, and from the *vena arteriosa* it is transferred to the *arteria venosa.*"

This was not the sum of his sinning, but at any rate the hard-fisted old Swiss reformer seized him when he found him in Geneva; and burned him up, with his books. Two copies only of the "Restitutio" have survived, so far as I know—one in the National Library in Paris, the other in the Imperial Royal Library in Vienna.

Various other commentators on the circulation lived in the time of Vesalius, but none, not even Vesalius himself, seems to have recognized the work or the existence of Servetus. Rialdo Columbus of Padua indeed reasserted, or rather, independently discovered the pulmonary circulation, and denied vigorously the common belief in an open ventricular septum—while Cæsalpinus of Pisa, towards the end of the Sixteenth Century, again described the complete flow of blood through the lungs, and devised the word *circulation.*

Although the three writers I have named last—Servetus, Columbus, and Cæsalpinus—asserted the fact of the pulmonary circulation, they asserted it from inferential reasoning, and not from demonstration; and mark this especially, that no one of them, save Cæsalpinus, had a word to say about the *general* circulation. Now Cæsalpinus in 1583 made this remarkable

statement: Blood is conveyed to the heart by the veins; receives there its perfection, and this perfection being acquired, it is carried by the arteries to all parts of the body.[3] It is hard to see how this can be any other than a clear assertion that there is a *general* circulation. Unfortunately Cæsalpinus' contemporaries do not seem to have grasped the significance of his surprising assertion, if we accept the account of Fleurens, who brilliantly defended him some fifty years ago. Our own Dalton, writing in 1884, makes this astonishing comment on the work of Cæsalpinus: "It must be evident that there is nothing in this passage which would imply in Cæsalpinus a knowledge of the general circulation." This is an old controversy, important only, perhaps, to the medical historian. For myself, I cannot but believe that Cæsalpinus knew of what he wrote, and that we should take literally his writing.

We note one other name before coming down to Harvey himself. Fabricius ab Aquapendente in 1574 took note of the valves of the veins, but failed to perceive their significance in assisting the flow of venous blood towards the heart. He supposed they serve the purpose of little dams, constructed to oppose the too violent rush of venous blood from the heart to the extremities.

Then came Harvey, whose name marks the second period of interest in the history of the circulation. Three years ago Osler delivered the Harveian Oration on the "Growth of Truth," an oration so well known to us all that it is needless here to rehearse the orator's collected facts of Harvey's life and career. Suffice it only to remind you that Harvey was in Italy at the end of the Sixteenth Century, when the medical atmosphere of the Italian universities was charged with the new interest in physiological studies, and that he was an actual pupil of Fabricius, the discoverer of the vein valves. As Fleurens says, when Harvey appeared, everything relative to the circulation of the blood had been indicated or suspected; nothing had been established.

In the year 1616—fourteen years after his return home—

Harvey was made lecturer on anatomy at the College of Physicians in London; and in 1628, twelve years later, he published the first edition of his great work—even to-day a wonderful volume, though it is but a little book. Dalton writes of it: "This volume, a small quarto of seventy-two pages, undoubtedly contains a greater amount of important material in small compass than any other medical work ever published." Here we recall the facts merely that he took up *seriatim* the organs concerned with the circulation. He discussed the structure and action of the heart; the successive contractions of the auricles and ventricles; the passage of venous blood from the right auricle to the right ventricle and to the lungs; the passage of blood through the pulmonary vein to the left auricle, to the left ventricle, and to the aorta. He observed the valves, membranes and *ostiola* which are found at the entrance to each of the passages. He traced the blood through the arteries, and showed that the arterial pulsation depends upon the pulsation of the heart. Then he passed to the veins, and from a study of their valves drew the important deduction that venous blood can flow only *towards* the heart. He opened arteries in animals and perceived the rapid exhaustion of their blood, and the death from hemorrhage, from which he argued that blood circulates throughout the body with great rapidity.

One important step in the circulation, however, was not clear to him—the movement of the blood from the arteries to the veins through the capillary network, in both the general and the pulmonary circulation. He was convinced that in some way the blood does pass, and he conceived of a transudation through the parenchyma of organs,—a transudation, not through anatomical vessels, but through the structure of the tissues themselves. In this conception doubtless he followed the reasoning of Servetus, of Columbus, and of Cæsalpinus.

It remained for Anthony van Leeuwenhoek in 1688 to complete the story begun by Harvey. Here is Leeuwenhoek's graphic description of his first sight of terminal anastomosis. He studied with his crude microscope the organs of tadpoles,

and was able to observe the flow of blood through their terminal arteries and capillaries. In a letter to the Royal Society of London, he exclaims with enthusiasm: "Having seen this many times to my great satisfaction, I would not keep the knowledge to myself, but I showed it to five distinguished gentlemen, who told me that they had never seen anything deserving so much to be seen. . . . We could not possibly have distinguished it, but as the blood consisted of a very clear liquid mixed with larger and smaller globules . . . so the observation of the circulation was the more distinct." Van Leeuwenhoek spoke the last great word in the story of the circulation.

With the establishment of an understanding of the circulation, there came about gradually a readjustment of the old conceptions of blood-vessel diseases and injuries and of their treatment; while the significance of hemorrhage, grave as that significance always had been, became still more appalling. I fancy that the poets and prophets of old time made more mention of the blood than did many of the philosophers and physiologists even. Vainly one searches the writings of Hippocrates for any word upon hemorrhage from wounds, and Celsus, who wrote in the year 50 A. D., says merely that one must apply lint dressings and must tie vessels which are obviously bleeding.

Since the complete round of the circulation was not appreciated in ancient times, the possibility of the body's emptying itself of blood was not apprehended. The fear of the old surgeons seems to have been merely that blood-vessels immediately adjoining the wound would become emptied. Doubtless it was through this misconception and through recognition of the occasional value of bleeding that the widespread practice of venesection[4] arose, which held bound conventional physicians for centuries, even after the actual discovery of the circulation.

The truth about the circulation of the blood had become acknowledged by all men at the beginning of the Eighteenth Century; but vital as was the truth, generations passed before

surgical practice became modified. Indeed, the work of John Hunter in demonstrating collateral anastomosis about an occluded artery, was needed to bring home to surgeons the significance of a constant blood-stream.

The history of the *treatment of hemorrhage* up to recent times can be summed up in three words, pressure, cautery, and the ligature; yet one cannot study old writings without perceiving that these methods commonly were not satisfactory. The use of pressure went through many phases—packing, tenting, handpressure, bandaging, acupressure; though strangely enough the tourniquet, the popular pressure instrument of to-day for controlling serious hemorrhage, was not satisfactorily developed until the time of Petit in the middle of the Eighteenth Century.

The old surgeons liked to employ pressure as a hæmostatic. They found, that pressure continued long enough, checked nearly all forms of hemorrhage; and that hemorrhage checked by pressure rarely broke out secondarily. The old surgeons did not understand the reason for this absence of secondary hemorrhage after the use of pressure, though we now know that the reason as contrasted with ligature treatment lies in the frequent elimination from the wound of sepsis-causing foreign bodies. A striking and original pressure method was that advocated in 1869 by J. Y. Simpson in Great Britain—the acupressure method. Simpson realized the disadvantage of ligatures, which in his time were left with long ends protruding from the wounds, that they might be pulled off when the artery had sloughed, and he devised the acupressure pin, an instrument resembling a hatpin, which was passed in from the outside of the wound, and was made to compress the vessel for two or three days, or until the artery was completely blocked by natural processes. He then removed the pin, and in consequence left the wound free from external irritants. The familiar Wyeth pin used in hip and shoulder amputations is the acupressure pin of Simpson.

The cautery (the actual cautery) was needed to supplement the uses of pressure; and the story of the cautery

wanders down through the history of surgery. If there were time, it would be interesting to quote Paré and his opinion of this barbarous hæmostatic. Paré could not stop its use, and the cautery continued to torture patients, to destroy valuable tissues, ineffectually to check hemorrhage, to create horrible sloughing, and to comfort the surgeon's conscience for generations after Paré's time. Indeed, the use of the cautery in its various forms was regarded as a fine art down nearly to our own day.

The ligature is one of the ancient devices of surgery. The Alexandrians used it before the Christian Era. Celsus commended it. Galen established its value for the control of vessels wounded in continuity; and finally Paré, in the middle of the Sixteenth Century, reintroduced it on the battle-field as *the* hæmostatic in amputations. The ligature was an improvement over the cautery and the equally barbarous boiling oil; but even so, the ligature was a constant source of danger, and an incentive to secondary hemorrhage until after the introduction of the principles of Lister.

J. F. D. Jones, an English surgeon of 1810, states: "The records of our profession afford us few and detached observations on the suppression of hemorrhage, if we contrast the knowledge we possess with the importance of the subject." A hundred years ago Jones produced a valuable book on this matter—a book dealing with the dangers of hemorrhage, its treatment by drugs, the operation of the ligature, and the nature of the healing of arteries; and his treatise contains fifteen remarkable plates which demonstrate the character of arterial wound-healing. Jones discourses at interesting length on the studies of other men upon hemorrhage and the nature of hemorrhage; and with commendable accuracy describes the knowledge of hemorrhage and its treatment as such knowledge existed in his time.

Such, as I have sketched them, were some of the measures used to combat active hemorrhage; but one finds also surgeons in all times endeavoring to correct the exhausting ill-effects of hemorrhage after the flow of blood had ceased—the employ-

ment of after-treatment, as we call it. Indeed, such stimulating and upbuilding measures always have been familiar, rational and effective, so far as history or legend carry us. Rest and nourishment, repose and stimulation—those for centuries were the means employed to bring back to health patients exhausted by hemorrhage. Freedom from apprehension, as well as freedom from pain, has always been recognized as supremely important. So we find Hippocrates and Celsus, Vesalius and Harvey, Paré and Wiseman prescribing supporting food, and enjoining soothing medicines. Andrew Blake a century ago wrote, "but opium is necessary . . . with the view of quieting tumult and where the pain is excessive."

Though such were the measures commonly used to check hemorrhage and to re-invigorate the body, wise surgeons and physiologists were appearing here and there, in ancient times even—wise men who looked for still more prompt and effective measures for restoring the lost strength and the lost blood. Since loss of blood was seen to be the immediate and obvious cause of the loss of strength, we expect to find surgeons seeking to put back *fresh blood* into the exhausted tissues,—and indeed, we do so find them.

All men know that our recent successful employment of *transfusion* is a revival and an improvement of a former practice; but few men realize that the conception, if not the practice, of transfusion is nearly as old as medical literature. In the development of much modern surgical progress we are going over the old ground and following the old steps in somewhat the same order as the ancients went and followed before us.

Modern surgery took up first the investigation and treatment of *gross and obvious lesions*—compound fracture; abscesses, and inflammations from infection—such as appendicitis; and tumors, innocent and malignant, such as ovarian cysts, uterine myomata and breast cancers. Then surgery expanded to concern itself with *derangements of organs*—ureteral obstruction, gall-bladder hypertrophy and pyloric

stenosis. Next, in a burst of energy, it advanced upon the *more intimate seats of life;* it took up impaired nervous structures, brain tumors, and peripheral nerve lesions; and finally, inspired and strengthened by recent teachings in physiology, it has succeeded actually in repairing damage to the heart, in mending diseased nerves, in joining severed blood-vessels, and in replacing amputated organs and limbs. In the midst of all this enterprise there has been involved inevitably the question of *conserving the blood-stream;* and while we are concerning ourselves with questions of blood-vessel surgery, we are not forgetting the *Blood.*

The surgery of ancient times developed along lines parallel to the lines I have just sketched, and it reached many important conclusions and outposts. The thought, if not the practice of *transfusion,* was familiar to men of Virgil's time.

Oré,[5] the well-known French writer on transfusion, has discovered many references to the ancient use of blood-transference. He finds that it was employed among the early Egyptians; in the armies of the Roman Republic, and by the Jews of Bible times; while it is mentioned by Pliny, Celsus, Ovid, Libavius, Fabricius ab Aquapendente, Harvey, and sundry others.

Many of the older essayists on the history of transfusion speak of transfusion as though it had been performed commonly; but, indeed, there is no good evidence that it was ever systematically and intelligently performed until after the middle of the Seventeenth Century. There is one rather amusing and striking anecdote always related among the early cases of transfusion—the case of Pope Innocent VIII, who died in the year that Columbus discovered America. Writers, following the text of Sismondi, used solemnly to assert that the prelate, finding himself about to die, was persuaded by his Hebrew physician to consent to submit to the transfusion of blood, after the usage of certain practitioners, although they had never tried it "except on animals." Accordingly, three boys about ten years of age were bought, and their blood drawn. All three are said to have died at the

beginning of the operation, probably from air embolism. In spite of these heroic efforts to save the pontiff, he himself died a few days later.

If the story is true, this is the first well-recorded instance of transfusion. Unfortunately, however, the critics have denied the anecdote; especially has Casse [6] denied it, who has written an entertaining monograph to prove the improbability of that old-time transfusion. Whatever the rights and wrongs of the tale, the fact remains that the thought of transfusion, especially as between animals, was familiar to surgeons of the Renaissance.

On June 15, 1667, nearly two hundred years after the lamentable demise of the three Italian boys, Jean Denys in Paris tried transfusion in man for the first time in French history. Although the experiment seems to have succeeded, the community was roused to an extraordinary pitch of excitement, and opposing factions were formed—these praising and those abusing the novel undertaking. Finally, after a year, the civil authorities took the matter in hand and formally prohibited transfusion in human beings.

Almost at the same time, in 1668, during the reign of Charles II, the Englishmen Lower, King, and Wren, the Italians Riva and Manfredi, and the Germans Kaufmann and Purmann, succeeded in transfusing blood from man to man. All of these experimenters used an extremely crude and dangerous method. They drew venous blood from the donor, received it in a vessel, and then poured it through a tube or catheter into a vein of the patient. The inevitable accidents happened; clots and air were introduced into the circulation of the sick man; little benefit resulted, and an occasional death was reported. The operators became discouraged and the community alarmed. The procedure came into contempt. This outcome was a grievous disappointment to enthusiasts, for the thought of transfusing vigorous blood had aroused tremendous interest and hysterical hopes,—the sick were to be made well; the old were to be made young, and perpetual youth was to become the happy lot of all men.

Shattered hopes were not revived for many generations. Early in the Nineteenth Century, after nearly one hundred and fifty years, Blondell and Doubleday, the Englishmen, instituted again transfusion by a successful operation on a woman dying of postpartum hemorrhage. Recent interest in the procedure dates from that year, 1818, the beginning of the modern, or *third period* of transfusion history, as Oré calls it.

Blondell was indeed experimenting in a field practically untrod; but he reached conclusions of striking importance, if only they might always have been proven true—that the passage of blood through a syringe does not curtail the blood's functions; that small quantities of air in the veins do not especially endanger the life of the patient; that blood transference from artery to vein is hazardous; and that human blood transferred to a dog may kill the latter. Two years later, Prévost and Dumas, after a series of experiments, were able to assert that immediate transfusion through a tube may properly be made from the artery of one animal to the vein of another.

The third transfusion period lasted for more than half a century. It covered the years from those early experiments of Blondell's to the time of the firm establishment of aseptic surgery—that is, to about the year 1885. During this era a great deal of interest regarding transfusion was written and was said. Pect, in 1841; Soden, in 1852; and Higginson, in 1857, urged vigorously the value of transfusion, and discussed various methods of employing it. Especially Bischoff, in 1835, urged the value of defibrinating the blood drawn, and then injecting it by the indirect method, that is by collecting it in a vessel and then passing it through a tube into the patient —as contrasted with the direct method, the passing of blood from donor to recipient through a short intervening tube only. Many surgeons were convinced that Bischoff's practice of using defibrinated blood marked a revolution in surgical therapeutics, and his method was extensively tried throughout Europe.

Numerous ingenious apparatus were devised; one of the

best perhaps being the funnel of Higginson, which was so constructed as to keep the blood warm in a hot-water chamber—while Brown-Séquard, in America in 1857, carried the process further by oxygenating the blood before injecting it.

In 1871, De Belina, in Paris, gave a further impetus to the use of transfusion by important studies and clinical demonstrations, and wrote these words: "Not only do these cases show in an inevitable manner the value of transfusion in post-hemorrhagic anæmias, but also in asphyxia and eclampsia; and open a vast field to those future experimenters who shall profit by what has already been accomplished."

The discussion and enthusiastic work went on. Roussel of Geneva, in 1876, had become a recognized authority on transfusion. This earnest writer returned to the direct method and asserted that transfusing blood can mean only conducting without interruption and without contact with modifying agents, the living and unaltered blood, from one organism to another, so that it can produce all those vital effects which constitute the real rôle of the blood: and to this end a transfusing apparatus should be a direct anastomosis only from one vascular system to another. This illuminating statement gives us pause, and we think we have leaped at once to the latest modern method; but we find that Roussel did not look ahead so far. His direct anastomosis was through what he called an "artificial heart." To-day we should content ourselves with the more familiar name—Davidson syringe. He used what was in effect that familiar syringe, made of "pure unadulterated india-rubber," for which he claimed great virtues; and he pumped 200 Grams of blood from vein to vein in five minutes. Incidentally, we learn from Roussel's article, that the governments of Belgium, Austria, and Russia had already at that time (1876) furnished their army surgeons with a good transfuser, from which we are to suppose he means his own transfuser.

All the writers in what I have called the third period of transfusion seem to have had a sound understanding of the physiology of the procedure. They recognized not only the

value of fresh blood *per se,* but the importance of fluid in bulk supplied to the exhausted circulation. Few of them, however, if we except Roussel, transfused large quantities of blood. For example, P. T. Morton, of the Pennsylvania Hospital, in 1874, writes of eleven ounces of blood as the largest amount that he had ever transfused, and his experience was considerable; while he states that he has known two ounces to stimulate the heart and save life when that life was on the verge of extinction.

All the writers speak of the numerous conditions in which transfusion is of benefit—for exhausting hemorrhage, whether from wounds, from childbirth, or from gastric and intestinal ulcer; for asphyxia of the new-born; in illuminating gas-poisoning; in chronic anæmia, whether primary or secondary; in epilepsy; septicæmia; uræmic poisoning,—and in all these and similar cases they urge the performance of transfusion early—not waiting until the patient is at the point of death.

About thirty years ago, numerous experimenters began to advocate the employment of fluids other than human blood for infusion. So long ago as 1830,[7] Jœnichen of Moscow practiced and advocated intravenous saline infusions in cases of persons dying of asphyxia; while Roussel, in 1876, pointed out the propriety of employing the term *transfusion* to indicate blood-transference only—the term *infusion* to indicate the injection into the body of some substance other than blood. The suggestion of Jœnichen was adopted by numerous investigators: Schiff and Gaule demonstrated the value of saline infusions in cases of acute anæmia; Bischoff, the same who advocated the employment of defibrinated blood, made a brilliant success with the injection of saline solution, an agent which numerous other experimenters down to our own time have shown to be of life-saving value.

In the early days of the use of saline infusions, and later, nearly up to twenty years ago, certain enthusiastic surgeons asserted, and with great show of reason, that salt solution was far preferable to blood as a vehicle of cardiac stimulation. In some sense and for obvious reasons, these assertions were

true, for salt solution is readily obtained, and is safely employed. No physiologist, however, could admit any intrinsic superiority in salt solution over blood. Eighteen years ago, Matas expressed the situation correctly in saying that *mechanically* or *physically* saline infusions are the rivals or equivalents of blood infusions, while, *physiologically,* salt solutions never can rival or equal blood.

It is extremely interesting to read in this early writing of Matas (1891) these words also: "In speaking of blood as a medium for transfusion, we mean, of course, only pure, entire, living blood, and not the altered pathological material, known as defibrinated blood. We also mean blood of the same species, and not that derived from heterogeneous sources." This last statement, which suggests a knowledge of the hæmolyzing effect of blood of different species, had first been enunciated by Panum, writing in Virchow's *Archives,* and quoted in 1871 by De Belina, who makes this interesting statement: "The bloods of animals can revive animals of a different species, but only as a result of its passage. It decomposes at once, and if it has been injected in small amounts can be eliminated without causing disturbance; but if it has been injected in large amounts, it can cause death."

The convictions of Matas, expressed eighteen years ago, as I have quoted them, are the convictions to-day of surgeons the world over. We all use saline infusions in cases of hemorrhage, after the bleeding has been checked, as well as for various other accidents threatening life. At times we supplement the simple saline by fortifying it with adrenalin, but our principal proposition maintains: we need to support by the bulk of the injection the vital or central avenues of the circulation, the heart and the blood-vessels in the trunk and in the brain.

The whole subject of the value of saline infusions in the treatment of hemorrhage is too familiar to need repetition, especially in view of the elaborate work of Crile and Dolley, which they sum up in an admirable paper published three years ago.[8] Those writers refer briefly and almost casually

to two important facts regarding the use of saline infusions—two facts which indicate the limits of its value, and mark off sharply its physiological action from that of transfused blood: (1) In the case of an anæmic heart, there is always a possibility, or the probability even, that an intravenous infusion may precipitate an acute cardiac dilatation. When the pulse-wave is large, when the pulse-resistance is slight and the rhythm slow, we must use infusions with extreme caution. (2) The blood does not tolerate great dilution. Large amounts of salt solution pass quickly through the great blood-vessels, and accumulate in the lungs, the pleural cavity, and the abdomen, with the result that the patient not only loses the benefit of the salt solution in his circulation, but may chance to find himself seriously embarrassed by abnormal accumulations of fluid in the trunk cavities.

Thirty and more years ago, surgeons were not satisfied that saline solution was the best agent to accomplish the benefits of which we now know it capable. They experimented with many other agents and with apparent success—with weak solutions of albumin, of bicarbonate of soda, of glycerin, and of milk.* T. Gaillard Thomas especially, in 1878, reported a series of remarkably interesting results from the infusion of milk,[9] and stated—a fact often forgotten—that this novel agent was first employed on man for infusion so long ago as 1850 by Edward M. Hodder, of Toronto. Hodder had given as much as fourteen ounces of milk at a single injection; but Thomas convinced himself that eight ounces is the limit of safety. These experimenters and others found that absolutely fresh and sterile milk should be used, as decomposing milk quickly causes death. Thomas collected twelve cases of milk-injection, and wound up his paper with the following rather pathetic statement: "I should be false to my own convictions if I did not predict for 'Intravenous Lacteal Injection' a brilliant and useful future."

* The history of milk injection can be traced back to the year 1667, when Johannes de Muralto of Zurich practiced the injection of milk into the vessels of one of the lower animals. Statement by August Schachner in the American Medical Practitioner and News, October 31, 1896.

In spite of such rather freakish and bizarre experiments, the value of infusions of some sort continued to attract the confidence of the profession, but by 1890, the saline infusion had taken a front place as the one safe and available agent.

Saline infusions, however, have not always been given in one and the same manner. For example, Johnson-Alloway employed successfully in a case of desperate collapse from hemorrhage, the infusion of salt solution into the peritoneal cavity—injecting three quarts at a temperature of 110°, through a glass drainage tube, when he found that this fluid was taken up rapidly by the exhausted circulation; while Dawbarn in 1892, and H. A. Kelly in 1894, advocated the injection of saline infusion directly into an artery. Dawbarn devised the technic of inserting a hypodermic needle into the femoral artery, and sending the infusion through the needle by the force of a Davidson syringe—the fluid at a temperature of not less than 120° F. This writer maintained at the time that two quarts at least should be injected. Kelly infused a litre of salt solution *centrally* into the radial artery of his patient, forcing the fluid towards the heart through a cannula introduced into the artery. Both of these experimenters were satisfied of the value of arterial infusion, claiming for it a quicker action than when the solution was injected in the ordinary way into a vein.

H. T. Hanks, of New York, writing in 1898, remarks: "Just how this simple salt solution acts in arteries may not be fully understood, but it is certain that the heart responds at once to the presence of the fluid. The cardiac and arterial ganglia are stimulated, whether the fluid is stimulating or not. . . . The additional fluid in the arteries certainly pushes on the half-stagnated capillary circulation, clearing out what would in a short time become semi-poisonous in itself. . . . The flushing out of the smallest blood-vessels by this diluted fluid is a virtue in itself."

Dawbarn makes this further note: "I need hardly add here that *blood-transfusion,* either mediate or immediate, has now been dropped by almost all surgeons. When a person

has bled to death, more than half the blood still remains in the body; and if this is properly increased in bulk by any innocent fluid, this added bulk is all that the heart needs to make it resume work." But note Schachner of Louisville, who stated in 1896 that transfusion of blood proper, though regarded by different writers as both safe and unsafe, can no doubt in the hands of a careful operator be made free from danger. He remarks, however: "From the history of transfusion it is apparent that formerly its range of application was far more extensive than its merits justified." Schachner says further, that the publication in 1891 of E. Schwartz, "On the Value of Salt Infusion in Cases of Acute Anemia," established the modern confidence in salt infusion.

We see then as a result of our researches that about the beginning of the present century surgical opinion had crystallized into the belief that blood infusions are hazardous, and that salt infusions are satisfactory and life-saving, because what is wanted is an increased intravascular pressure; that in some cases of alarming hemorrhage, infusion should be supplemented by transfusion with defibrinated blood; that the indications for infusion include any pathological state attended with a feeble pulse, and with shock; that the improvement of the circulation after infusion is due in part also to the stimulating influence which the hot salt solution has upon the heart, while at the same time "auto-infusion," a forcing of the blood by bandages from the patients extremities toward his centres, is an extremely useful manœuvre.

Every surgeon of a few years' experience recollects that such conceptions were held to be sound and such practices satisfactory a very few years ago; and he knows that in most emergencies such measures still suffice.

Within the past ten years, with the additional light thrown upon the nature of shock and on the effects of hemorrhage—our conception of a paralyzed or of an exhausted vasomotor centre—we have come to see that something more than the mere presence of salt solution in the blood-vessels sometimes is necessary to restore a depleted circulation; while the obser-

vation that excessive amounts of saline solution in the vessels may paralyze an enfeebled heart, or may be exuded into the cavities of the trunk, has brought about successful attempts to return to a more rational employment of the long-neglected blood transfusions.

It is a fortunate and interesting fact that with this swing of the pendulum, with this turning back towards an endeavor to utilize the blood itself, a flood of new light has been shed recently upon the surgery of the blood-vessels. Our knowledge of the healing of veins and arteries has been broadened, while at the same time we have learned the entirely novel fact that blood-vessels under proper conditions themselves may be repaired and anastomosed, so as to continue their normal functions. Taking advantage of this new knowledge, we have been enabled to make good the half-completed undertaking of Roussel the Swiss investigator, who asserted more than thirty years ago, that true transfusion means the passage of sound or unaltered blood from the arterial system of the donor to the venous system of the donee.

We are now approaching so vast, so intricate and so fascinating a theme that one may not properly in a brief paper do more than suggest the lines upon which studies of the blood in surgery are developing. Less than two years ago, Stephen H. Watts of the Johns Hopkins Hospital collected in a luminous monograph a statement of accomplishments in blood-vessel surgery up to that time. Since then further progress has been made—progress strikingly picturesque if not more practically important. The list of laborers in this field is already great. Watts gave us a bibliography of eighty-three numbers, and this bibliography to-day could be doubled. We in this country look especially to Abbe, J. B. Murphy, Carrel, Guthrie, Matas, Dorrance, and Crile for information on these matters. Indeed, there are many others, while the list of European investigators is a long one.

The first and most striking fact in *blood-vessel healing* soundly demonstrated by these investigators, is the fact of the ready adhesion of intima to intima, directly reversing the prin-

ciple upon which the *intestinal tube* is sutured—serosa to serosa. For some time it seemed as though the necessity of applying intima to intima in small friable blood-vessels would oppose a serious obstacle to the progress of vascular surgery; but thanks to the sound demonstrations of Carrel and of Guthrie, we have now been furnished with a simple and reliable technic, which answers practical purposes. We have learned further that for the handling of blood-vessels special training is required, and the employment of special agents—constant and proper lubricants, constant and unfailing warmth and moisture, and delicately and accurately applied needles and suture materials.

The surgeon who hastily and confidently undertakes any considerable work on the blood-vessels finds to his chagrin that the operation is anything but easy. We talk lightly of arteriovenous anastomosis and of transfusion by the method of Carrel or of Crile, but the novice at such work will find himself floundering in clumsy perplexity, and will exhaust hours of strength and patience unless he has equipped himself for the task through painstaking and faithful experiments on animals in the research laboratory.

For years Crile has taken the keen interest of a surgical physiologist in the nature and treatment of shock in hemorrhage. It was to be expected, therefore, that the development of blood-vessel surgery should suggest to him as to others the feasibility of practicing blood transfusion by utilizing our recently acquired knowledge of blood-vessel surgery. In July, 1906, he published one of his most extensive articles on the treatment of shock and hemorrhage through the use of *saline* infusions. In November of the same year he published his first article on the "Direct Transfusion of Blood in the Treatment of Hemorrhage."[10] On April 20, 1907, he demonstrated on a patient before the Society of Clinical Surgery his method of transfusing blood.

Already at that time others had become interested in this important work, and now some hundreds of cases have been collected. It is needless here to suggest the types of cases

which are benefitted by this operation further than to state that the transference of blood from donor to patient is not limited by any means to that class of cases which are commonly called surgical. The treatment will benefit a great variety of persons who suffer from a diminished quantity of blood, or from an inferior quality of blood. One sees, of course, the value of refilling a circulation exhausted by hemorrhage, but frequent observations teach us that something more than the mere bulk of the blood benefits the patient.

Many observers, from Alexander Schmidt and Kohler to the investigators of our own time, especially Weil, Richet, and Leary, have pointed out that certain properties in serum, whether of animals or man, exercise a coagulating influence on the blood in cases of chronic hemorrhage. These observers have not been able to show, however, that the sera employed invariably act beneficially. On the other hand, small amounts of whole human blood transfused to a patient who suffers from repeated hemorrhages are sometimes found to shorten his coagulation time as well as to check the habit of bleeding.

Last spring I had a patient who illustrated the above fact: A girl of twelve who had passed through her first three menstrual periods with alarming bleeding at each, at the time of her second period, on the advice of Leary, was given 15 c.c. of rabbit serum by hypodermic injection. Leary noticed that blood oozed afterwards from the needle punctures for half an hour. Two days later the injection of serum was repeated, but was followed by no oozing from the needle punctures. Her next menstrual period was of the same character, and was treated successfully with guinea-pig serum. With the next, or fourth period, in May, 1908, she bled until nearly exsanguinated, when I was called to see her. She was in an alarming condition—waxy, nearly pulseless, prostrated, after ten days of continual bleeding. I transfused to her from a vigorous young man, her cousin, about six ounces of blood. Her bleeding ceased immediately, and within three weeks she was well; but the notable fact in the case

is that since May, 1908, more than twelve months ago, she has had the normal catamenia of a girl of her age.

Internists as well as surgeons are beginning to appreciate that the transference of blood is becoming an important therapeutic measure—but a measure whose ultimate value is not yet determined. The technic of blood transference is still somewhat debated—whether to use the direct suture of Carrel, or some mechanical device such as that of Crile, of Ottenberg, or of Levin.

At the same time that the therapeutic employment of transfusion is revived, doubts of its universal applicability are raised through modern knowledge of the nature of the blood and the blood content. *Iso-agglutination* and *hæmolysis* are terms which express conditions with which we must reckon,

By *iso-agglutination* we mean the clumping of the blood corpuscles of one person by the serum of another, and this phenomenon may have an important bearing on blood transfusion, for iso-agglutination suggests, as Hektoen pointed out two years ago,[11] that under special conditions homologous transfusion might prove dangerous by leading to erythrocytic agglutination within the vessels to which blood was transfused. Hektoen suggests that this possible danger can be avoided by the selection of a donor whose corpuscles are not agglutinated by the serum of the recipient; and whose serum in turn does not agglutinate the corpuscles of the latter.

The condition *hæmolysis* raises quite another question—a question the subject of much careful study during the past five years, and admirably summarized by Richard Weil in the *Journal of Medical Research* for October, 1908. Hæmolysis depends upon the fact that a red blood corpuscle is covered by a delicate membrane which is easily susceptible to change or destruction; and that when the membrane is so destroyed the important contents of the corpuscle, notably the hæmoglobin, escape. This destructive process is known as hæmolysis, and agents causing hæmolysis are termed hæmolysins. Among the organic hæmolysins are the blood and tissue juices of alien

species, and notably the blood and tissue juices of the same species when subject to certain pathological conditions. For example, in pernicious anæmia, in certain fevers, sometimes in chronic suppuration, and in certain cases of malignant tumors, there is such a change in the blood serum of the patient that his abnormal serum will hæmolyze the red corpuscles of a normal individual of the same species.

This phenomenon and the technic of the corresponding investigations are outside further discussion in this paper. but the significance is apparent, as well as the importance of determining hæmolysis in cases subject to transfusion. Moreover, the fact of hæmolysis may become, as we know, a suggestive factor in determining obscure diagnosis. Says Crile:[12] "Our conclusion is that hæmolysis occurs in a number of diseases. It occurs in great frequency in cancer and tuberculosis. The reaction in tuberculosis is the reverse of that for cancer." *

In view of the struggles of our predecessors to establish, make available, and popularize blood transfusion, and in view of their ardor and their recurring failures, the recently ascertained facts regarding the nature of the constituents of the blood are extremely illuminating. Denys, Lower, Kaufmann and their contemporaries failed successively to establish transfusion because they could not control clotting and air embolism. Blondell, Dumas, and their contemporaries in the last century failed to realize the danger of employing the blood of alien species; while Bischoff started the practice of defibrination, which for years led away his successors on a false trail. Brown-Séquard and his associates do not seem to have guessed even the intricate processes which mixed bloods may precipitate. The problem of transfusion is still by way of solution; the indications and the straight road are not always obvious. Our ancestors looked to transfusion for rejuvenescence and

* Wyman Whittemore, working in the laboratory of the Massachusetts General Hospital, writes (Boston Med. and Surg. Jour., Jan. 21, 1909): "From these results, at the present time, hæmolysis is of no value in the diagnosis of carcinoma."

perpetual youth; we, in a more modest generation, may look to transfusion for the re-establishment of health in certain cases which hitherto we have often deemed hopeless.

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