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BLOOD STANDARDS AND FAILED FLUIDS: CLINIC, LAB, AND TRANSFUSION SOLUTIONS IN LONDON, 1868–1916

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> It seems obvious that blood itself is the most appropriate fluid to replace blood, and there is no doubt as to its efficacy. On the other hand, to my surprise, it has not shown itself, experimentally, to be so much superior to certain artificial solutions, such as gum arabic, as I expected.[1]
>
> William Bayliss

In 1818, the English obstetrician and physiologist James Blundell began his campaign to add transfused human blood to the array of options available to medical practitioners for the treatment of deadly collapse following haemorrhage.[2] Ever since that time, doctors, it seems, have been working to accomplish a feat hitherto completed successfully only by Medea herself: concoct an effective blood substitute. Blood itself has substantiated this quest: if it is possible for a fluid to be double-edged, blood is that fluid. On the one hand, it has the power to bring those near death from blood loss back to life — in a fashion often described as miraculous.[3] On the other, it necessitates a reliance on donors and carries potential dangers ranging from coagulation to disease transmission. The exact nature of the "most pressing" difficulty posed by the movement of blood between (human) bodies has varied at different times and in different places. Indeed, both the primary impetus to replace blood and the kinds of suggestions made for that replacement have been shaped by a nexus of concerns ranging from institutional and intellectual to downright material.

In our own time, a social demand for absolute purity has collided with the emergence of an array of deadly blood-borne diseases in a fashion that has threatened the future of blood transfusion itself.[4] One such disease is most probably a product of the kind of tampering with nature that would not have fooled Mary Shelley: dead body parts served to sustain a kind of cannibalized (or, carnivorized) existence in English cows. The "Frankenstein" thereby created was dubbed bovine spongiform encephalopathy [BSE]. This so-called "Mad Cow Disease" came to popular attention when it was realized that humans, too, could contract a variant of it. The prions that apparently cause variant Creutzfield-Jakob Disease [vCJD] incubate in the human body for an undetermined amount of time. Then, for undetermined reasons, they attack the brain, giving it a sponge-like appearance. Those suffering from active vCJD lose their memories, their personalities, control of their bodies, and, ultimately, their lives.[5] Moreover, no effective test has been developed to determine whether the blood of particular individuals might carry agents of the disease.[6] Consequently, several countries, including the United States

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and Canada, banned anyone who lived in England for longer than a specified period between 1980 and 1996 from donating blood.[7] Concerns deepened when the first successful transmission of BSE by blood transfusion (in sheep) was reported;[8] they expanded with the discovery of BSE in cattle, and vCJD in humans, in several European countries. Restrictions on blood donors multiplied. This new threat to the safety and availability of the blood supply has made the search for effective blood substitutes an international priority.

In nineteenth-century England, however, it was not disease, but the complexities of blood transfusion itself, that motivated doctors to seek alternatives. Blood clotted, either in the transfusion apparatus or, more unfortunately, in the patients themselves. After trying a variety of instrumental solutions to clots,[9] doctors concerned with transfusion — in England, obstetricians — began to look, literally, for alternative solutions. They found saline. By the time, some three decades later, that saline was dismissed as ineffective, obstetricians were no longer involved in the search for new substitutes. Now, it was a gum acacia solution that was proposed to the medical practitioners most interested in transfusion: surgeons facing that epidemic of trauma known as the Great War.

On the surface, then, we witness a move from blood to saline to gum acacia, taking place roughly between 1868 and 1916.[10] If we look beneath this fluid surface, however, we find a modest treasure: a case study of the rise of laboratory medicine, conveniently poised at an historical juncture much disputed by sociologists and historians of medicine. How, specifically, did English medical practitioners see the laboratory as informing their medical practice?[11] In the case of early English efforts to find an artificial replacement for their blood standard, most of the discourse took place in London — at University College and the teaching hospitals. Yet, the shifting undercurrent connecting 1868 and 1916, saline and gum, universities and hospitals, medicine and science, was formed by physiology.[12]

THE CASE FOR BLOOD: 1818–1880

In teaching his midwifery students at Guy's Hospital, James Blundell quipped that he preferred transfusion with human blood donors because "a calf or sheep ... had not been taught to walk promptly up the stairs" to a patient's bedroom.[13] In fact, Blundell based his advocacy of human donors for human transfusions on his own animal experiments as well as on the latest scientific studies on blood.[14] His advice was unequivocal: "in performing the operation of transfusion on the human body, ... human blood should alone be employed."[15] For the next fifty years, British transfusion practitioners generally followed Blundell's teaching.[16] Not only did they use human blood, but they also, with Blundell, mostly limited their transfusing efforts to women "exhausted" by post partum haemorrhage and quickly "sinking" into a severe collapse that would otherwise most certainly have ended in death. In other words, for much of the nineteenth century, English transfusion was in the hands of that odd group of medical specialists known as obstetricians. So close was this relationship between blood and birthing that the very first volume of the

Transactions of the Obstetrical Society of London included a substantial review of transfusion, provided by Blundell's former colleague, Charles Waller.[17]

During the last third of the nineteenth century, transfusion's neatly circumscribed existence was challenged. Transfusion with defibrinated blood had been imported from France in the 1820s; but the blood used was still human blood.[18] Human blood, however, was a problematic substance. Donated blood frequently clotted — sometimes in instruments, and sometimes in patients; the procurement and use of donors created a host of complications. Indeed, blood clots and donor difficulties were the two problems most frequently cited by those who actively sought transfusion alternatives.[19] From outside the British Isles came a variety of suggestions for dealing with these difficulties. German physicians became enamoured of transfusing lamb's blood into humans in the early 1870s.[20] In the United States, it was "warm milk, fresh from the cow" that "was injected into the ... vein".[21] In keeping with the bovine theme, anaemic Cincinnati women began frequenting the local abattoir at tea-time, to "drink blood fresh from the slitten throats of bullocks".[22]

English transfusion advocates were on the whole reluctant to employ such fluids, some preferring initially to alter human blood.[23] Exactly fifty years after Blundell's first human transfusion, the obstetrician John Braxton Hicks suggested to the "Midwifery" section of the British Medical Association's Annual Meeting that a "saline" solution be added to blood before it was transfused.[24] The salt, "phosphate of soda", was "well known to be tolerated by the system" and would act as a safe anticoagulant.[25] It was a suggestion that had moved directly from the laboratory to the clinic. Hicks, Obstetric Physician and Lecturer on Obstetrics at Guy's Hospital, had discussed his concerns about blood clots with his hospital colleague F. W. Pavy.[26] Pavy, then Assistant Physician and Lecturer on Physiology, filled this latter position with a passion lacking in most so-called "lecturers in physiology" then appointed to the London teaching hospitals. Unlike these men, who were generally reluctant junior physicians who taught a glorified comparative anatomy, Pavy had gone to Paris to study physiology in Claude Bernard's laboratory and returned to London a veritable prophet for the value of experimental medicine.[27] In the physiology laboratory, anticoagulants such as phosphate of soda were frequently used in animal experiments. With both clinical and laboratory experience, Pavy was well positioned to advise Hicks. Hicks then took his own experimental turn, performing transfusions with blood thus modified on animals, before using it on patients.[28] While this blood modification was never broadly embraced by London's transfusion practitioners, it appears to have gained some popularity in Edinburgh.[29]

In short, during the 1870s, fluid options combined with a growing number of apparatus to muddy any previous clarity that might have existed about the practice of transfusion.[30] The Fellows of the Obstetrical Society of London [OSL], under the presidency of Braxton Hicks himself, responded to this growing confusion by forming a special committee to study the operation more systematically.[31] The *Lancet* commended the obstetricians for their efforts to investigate these "questions

of great scientific and medical importance". The OSL transfusion committee was to conduct this inquiry by compiling evidence about the outcome, applications, and methods, of transfusion. This evidence, however, was to be obtained first (second, and third) by gathering clinical anecdotes. To this end, *Lancet* readers who had performed transfusions were encouraged to send the details of these operations to the OSL committee. Only if this information proved insufficient would the committee "institute further experiments for the purpose of determining how far transfusion may be relied upon as a means of saving life".[32] Clinical notes would serve as the inquiry's foundation; experimentation provided a potential, if secondary, means of expanding this clinical knowledge.

In 1875, the new President of the OSL, William Priestley, announced that "the report is, I understand, nearly ready". He continued, in the clinical spirit of the original proposal, that "when it is presented it may be desirable to set apart an evening for its discussion, so that the opinions and experience of Fellows may be elicited on the general question of Transfusion and its value in actual practice".[33] Yet, as early as 1874, the committee's Honorary Secretary, Henry Madge, recognized that case histories alone could not answer all the questions they had raised about transfusion. How long, for example, did it take the blood to coagulate once drawn? Where did the blood go once transfused? What, microscopically, did defibrination do to the blood? "To place [transfusion] on a sound scientific basis", he asserted, "we must know more ... about the physiology and pathology of the blood".[34] This was no mere rhetorical embrace of scientific prestige. The committee recognized that these questions could be answered only by experiments "which naturally could not be performed by them". It was only in 1877, after meeting on a dozen occasions, that the transfusion committee formally proposed that the OSL commission a proper physiological review of transfusion. The Council provided funds to hire E. A. Schaefer, then at University College, for the job. Schaefer presented his report in 1879.[35]

This move of obstetricians towards laboratory analysis came at an important transitional moment, when British physiology was emerging from decades of near-dormancy. Indeed, the "stagnancy" of British physiology during the mid-nineteenth century has drawn much historical comment, occurring as it did during the very decades when Ludwig, Bernard, and Virchow were using chemistry, vivisection, and microscopy to endow laboratory-based medicine with an almost sacred status.[36] There were those in Britain who, like Pavy, made pilgrimages to the great European laboratories to learn from the masters; they returned home, however, to find few opportunities for expanding upon their experimental studies. The veritable "midwife" of a more disciplined physiology in Britain was William Sharpey.[37] Though himself essentially a comparative anatomist, Sharpey sustained a deep interest in the unfolding of Continental physiology. From the 1860s, he began importing that experimental model, adapting it to the contours of British medical education and making physiologists out of hand-selected clinicians.[38] His success in these endeavours is evident, not only in the rise of his own laboratory at University

College [UC] to international prominence, but also in the rising attention animal experimentation was being given by England's anti-vivisectionists. More, it seems, in response to the latter than to the former, the Physiological Society was instituted in 1876. One of its founding members was Edward A. Schaefer — who was also, as we have seen, an active member of UC's physiology laboratory.[39]

Thus, while it may seem perfectly logical that members of the OSL committee would turn to a physiologist to answer questions they had raised but "naturally" could not themselves answer, it was not. Several historians have argued that, despite the rise of English physiology, most English doctors tended to pay homage to laboratory science in word only. When it came to their clinical practices, they shunned its categories, tests, and assumptions. They also shunned instruments.[40] In the élite obstetricians guiding the OSL, however, we find a collection of men who defy simple categorization. Most — including their like-minded successors — had taken M.D.s at one of London's colleges (the majority at UC). A few had even studied experimental medicine in Europe. They held appointments at both the big teaching hospitals and, increasingly, at specialty hospitals for the care of women. And they actively turned to physiologists for guidance on at least this one, instrument-oriented, facet of their medical practice. Following Schaefer's report, W. S. Playfair, then President of the OSL, argued that, previously, transfusion work in England was "merely empirical or theoretical"; now, "the profession has some reliable data to act upon".[41]

At this point, any suggestions as to why these obstetricians evinced an openness to physiology must be provisional. Many of these men would certainly have been familiar with the close relations between obstetrics and physiology that their own history demonstrated: James Blundell, who lectured on physiology as well as midwifery, conducted an array of animal experiments before attempting human transfusion. More immediately, however, the case of John Braxton Hicks and his phosphate of soda might provide some insight. Hicks was an obstetric physician to one of the eminent London teaching hospitals, where physicians and surgeons dominated. During the nineteenth century, these hospital physicians and surgeons gradually consolidated their power as the consulting medical élite.[42] General practice — where most obstetricians started their careers, and many remained — was relegated to a lower tier. And, in this medical system, specialists of almost any sort were contemptuously dismissed as "quacks". "Élite" obstetricians were thus doubly marginalized, as were men like Pavy. Clinicians who held hospital appointments but harboured genuine experimental aspirations found themselves fighting for laboratory space among colleagues who saw little practical value in their designs.[43] It seems plausible that outsiders such as Hicks and Pavy would develop some mutual sympathy. Whatever the cause(s), this obstetrical openness to physiology — at least in the case of transfusion — would persist through the 1880s.

In the OSL report itself, Schaefer's task was to examine the fluids, techniques, and effects of transfusion, specifically as they related to "such cases as these we

are considering — cases in which speedy death is threatening in consequence of excessive loss of blood".[44] A specialist in histology, Schaefer opened his report with the results of his microscopic investigations. How did red and white blood cells react to the array of fluids doctors were now infusing into human bodies? He tested saline solution, cow's milk, and blood from domestic animals. While none of these infusions was harmless, blood from other species was by far the most harmful. In this work, Schaefer confirmed the influential findings Leonard Landois had quite recently published about the dangers of inter-species reactions to transfused blood.[45] Having eliminated the need to test such blood further, Schaefer subjected milk to *in vivo* experimentation. Using "fresh (*i.e.* not sour) London milk", he discovered an immediate danger: its bacterial content. Boiling the milk first averted this particular danger. Yet, even without its bacteria, milk was a poor transfusion fluid. While it did produce "a slight temporary rise in the blood pressure", this rise "very speedily disappeared". Occasionally, it even dropped below its original value. In other words, "there was never any permanently beneficial effect" from transfused milk.[46]

Schaefer's work on saline, and on a saline/human blood combination, was of a wholly different nature. There is no evidence in his report or attached tables that he ever conducted experimental studies of their effects in animals. Instead, he appears to have dismissed them because they did not fit into his conceptions of haemorrhage, blood, and the body's responses to trauma. Raising the possibility of saline transfusions, he argued that "a little consideration will show that they can be of no benefit in such cases". No experiments followed. Instead, he reviewed what physiology had already revealed about the nature of the body. It was not the "diminution in the *quantity* of the circulating fluid", he claimed with authority, that "produces the effects which we see". He based this conclusion on a "long-standing observation", that the blood and plasma became more dilute after haemorrhage. According to Schaefer, this fact indicated that the body reacted to blood loss by absorbing "into the vessels ... much of the fluid which occupies the interstices of the tissues".[47] Since this was so, he reasoned, the deadly symptoms that followed acute haemorrhage must arise from a "deficiency in *quality*, the diminution in number of the oxygen-carriers, the red blood-corpuscles". Obviously, as the "system is suffering from deficiency of haemoglobin", it was "useless to supply it with any fluid which does not contain this".[48] It is a revealing move. There is no question that Schaefer could have carried out saline analyses similar to those he conducted on milk, measuring blood pressure and watching for clinical effects. He did not. So certain was he, it seems, of his reasoning, he felt no need to conduct such studies.

Schaefer was similarly emphatic in his conclusion: "*in the case of man the fluid used for transfusion must always be human blood*."[49] Further animal experimentation supported his assertion. First, he "reduced" a dog "to an almost lifeless condition" by draining its blood, then transfused it with blood from another dog. "The effects of the transfusion were in every case most remarkable": even after only a small

amount of blood had been added, there was a "marked and permanent rise in the blood pressure" and a general amelioration of "the patient's" condition.[50] Further diminishing the significance that fluid loss in itself might have for the body, Schaefer explained that this recovery was "not so much ... [due to] the amount of the new blood as ... [to] its action in directly stimulating" the arteries to contract and the heart to beat more forcefully.[51] Working sixty years after James Blundell, and using the latest scientific instruments and physiological ideas, Schaefer had come to the same practical conclusions as had Blundell himself. Human blood was the best fluid to transfuse into women near death after haemorrhage. Both based this conclusion, in great part, on a qualitative understanding of the blood coupled with animal experiments. And both encouraged obstetricians (or accoucheurs) to use blood in such cases. Yet, as it turns out, this was the end of an era.

LAB, CLINIC, AND SALINE

Both clinically and physiologically, the long-standing privilege of blood over the body's other fluids (and tissues) was being challenged. From both perspectives, saline was becoming an increasingly attractive substitute for blood.

In fact, it was in the treatment of cholera that saline was given its most substantial therapeutic connection to that condition we would now call haemorrhagic, hypovolemic shock. Like acute blood loss, cholera was thought to result in a state of profound collapse, or "exhaustion", that often ended in the patient's death.[52] Whereas blood caught on by mid-century for treatment of blood loss, it was saline that seemed more promising for treating cholera. Though the future-famous ovariotomist Spencer Wells attempted a saline infusion for cholera in 1848, it was W. J. Little, Physician to the London Hospital, who was saline's most persistent early investigator in England. In 1832, 1848, and 1866, Little — who had taken his M.D. in Berlin, where he studied under Mueller and worked with Schwann and Henle — dutifully tried an assorted combinations of salts, distilled water, and alcohol, in his efforts to revive exhausted cholera patients.[53] Occasionally, as we have seen, some interest arose in the possibility of using intravenous saline, generally in combination with blood, to counter the collapse that followed upon blood loss. Yet, it was only in the 1880s that saline began to challenge the sacred space that had, to then, been filled by blood.

In 1883, a new treatise on transfusion was published. *Transfusion: Its history, indications and modes of application* was written by Charles Egerton Jennings, recently a House Physician and Resident Accoucheur at the London Hospital, and Fellow of the OSL. A relative newcomer to transfusion, Jennings was struck as much by the difficulties as by the benefits of the operative procedure.[54] He drew upon this disjunction in his book's introduction, playing with the concept of "operating theatre" by describing transfusion as "elaborately performed in hospital practice".[55] First, he set the happy scene: "students, with smiling faces, are rapidly leaving the theatre of one of our metropolitan hospitals." They were, of course, smiling because they had just witnessed "the most brilliant operator of the day"

performing immediate transfusion with "a very beautiful instrument ... complex and ingenious", and thereby saving a poor "fellow-creature" (meaning, most certainly, a woman) "from the effects of severe haemorrhage". Of course, there were those *unfortunate* complications. A mechanic had to adjust a malfunctioning part on the transfusion apparatus. Then, the blood donor, "a powerful and heavy young man, swooned". In came two porters, who "carried him on a stretcher" to a separate room, where he was attended by "energetic dressers".[56] It was a large cast indeed. What would happen, Jennings mused, if one of those smiling witnesses found himself "in a lone house in the country, face to face with an alarming case of post-partum haemorrhage"?[57]

In the preface to the book's first edition, Jennings gave few hints as to the answer he would propose to his rhetorical question. His goal, he claimed, was simply to point out the cases in which blood was and was not beneficial, to underscore the "fallacies and dangers attendant on the operation", and to suggest "*the means of obviating them*".[58] It was only near the end of his introductory chapter that Jennings revealed his ideal for the elimination of the dangers and difficulties of traditional transfusion: "as a rule blood-transfusion should be dispensed with, and an artificial substitute found."[59] He was more forthcoming about this suggestion in the book's second edition. Appearing later that same year, it opened, "in this edition I have endeavoured to draw a very marked distinction between the indications for the intravenous injection of saline fluid, and for the transfusion of blood". Jennings even changed its title: *On transfusion of blood and saline fluids*.[60] Moreover, this revised edition sported a "Special Preface", penned by none other than Spencer Wells, who proclaimed that it would be "a distinct step in the advancement of Medical Science by Research" if it could be proven that "saline fluids may be safely substituted for transfused blood".[61]

Despite this overt shift in emphasis between the two editions, the texts themselves are virtually identical. In both, Jennings's point was to underscore the complications of blood and (in his clinical judgement) the relative effectiveness — and simplicity — of saline solution.[62] Certainly, Jennings came to his position partly through clinical considerations. For the uninitiated, transfusion was indeed a complex and dangerous operative procedure. Further, donors were not always available: indeed, he himself first turned to saline by "compulsion", not "election": it was a Sunday afternoon, his patient was dying from haemorrhage, and no donors could be found.[63] That he turned to saline solution, supplemented by alcohol, was no coincidence: he was working in the very hospital where Little had performed his salino-alcohol infusions. He even cited Little's work.

Yet, it was more than perceived clinical necessity that brought Jennings to champion saline solutions. As a young member of the OSL, he was familiar, not only with the passionate transfusion debates, but also with Schaefer's report on transfusion. Moreover, he had received his medical training at a time when physiology, though far from an established discipline, had found significant institutional niches in London. He was familiar with its findings, and its methods.

Indeed, in his book, Jennings often seems to have followed Schaefer's model, citing the most recent findings of Continental physiologists and even subjecting chemicals he suspected of damaging the blood to microscopic analysis.[64] But most revealing of his physiological inclinations was his position on animal experimentation. Microscopic analysis, he argued, was quite helpful; however, the "special changes" which "occur in the vascular system" as a result of intravenous infusion "might most probably be elucidated by vivisection". Yet, in this desire to seek knowledge "for the future benefit of our race" through animal experimentation, he and his fellow physiologically-inclined Englishmen were "seriously hindered ... by the arbitrary trammel of a restrictive and oppressive legislation".[65] When P. H. Pye-Smith — another London physician-physiologist — allowed Jennings to conduct animal experiments in his laboratory at Guy's that autumn, Jennings thanked his host in his resultant *Lancet* article in a manner that again drew attention to London's laboratory limitations. Guy's, he pointed out, was "one of the few places licensed for experiments on animals in the United Kingdom".[66]

How, then, did Jennings, who admired Schaefer's work, come to a conclusion about saline's efficacy that directly contradicted Schaefer's? On one level, Jennings's shift resulted from a different conceptualization of blood and body. Whereas Schaefer believed the body could easily compensate for mere fluid loss but was hindered by its incapacity to replace haemoglobin in a timely fashion, Jennings was sceptical that the body could so easily compensate for such a diminution in the circulating fluid. Further, while he did, with Schaefer, believe the blood to have a nutritive function, he denied that reduction of this function caused the frightening collapse that followed severe haemorrhage. This condition was, he believed, principally caused by fluid loss itself. It was the "*dynamic* rather than the nutritive value of transfusion" that was most important in reversing this state.[67] Reversing causal priorities, Jennings could then reverse Schaefer's conclusions: in "*most* of the instances where transfusion is called for, I unhesitatingly advise the intra-venous injection of [saline] fluid as being certain in its action, comparatively free from danger, and not requiring any special skill" in its performance.[68] In this shift, I would argue, Jennings was being guided by both clinical and physiological considerations. The clinical considerations are certainly the most evident in the text itself: but the clinical difficulties of transfusing human blood had persisted over the decades and into Jennings's present. Earlier, however, English obstetricians responded to these complications by designing new instruments for "simplifying" the procedure. Jennings responded by denying the central importance of blood itself: a position only possible within an emerging physiological conception of the body that finally demoted blood to a mere, if fluid, tissue.

Throughout Western history, the blood had managed to maintain its privileged status. From Greek humoralism through Christian symbolism and past Harveian circulation, there was something special about the blood. Even after the Enlightened debates about the chemistry of respiration, metabolism, and animal heat, when Lazare Spallanzani argued that respiration took place in the tissues and not, as was

so long held, in the blood, the blood managed to retain its hold over physiological and chemical imaginations.[69] As Charles Culotta has shown, despite Carl Ludwig's physico-chemical biases and Claude Bernard's experimental reductionism, both influential physiologists long resisted any interpretation of respiration that would strip blood of its active participation in the process, and instead confer control upon the tissues.[70] It was only in the 1870s, following upon Edouard Pflueger's experiments directly challenging the previous view, that the idea of tissue oxidation began to be generally accepted. Pflueger's focus on tissues, argues Culotta, was guided more by his philosophical neo-vitalism than his experimental evidence. In this, Pflueger was rejecting the materialism that Ludwig and his generation had held dear.[71] Ironically, it was this shift of 'vital' function from blood to tissue that opened the way to a less privileged, and more mechanical, view of blood itself. Perhaps it *was* simply a fluid tissue that brought materials to, and took waste away from, the body's more solid tissues. This conception of blood as mechanical transport system was most probably strengthened by the growing physiological tendency to quantify the circulatory system, with improved devices for measuring and recording the blood's pressure and volume.

In London of the early 1880s, this de-vitalized blood concept was evident, of all places, in the physiological laboratory of University College — in experiments being conducted by yet another clinician-physiologist, Sidney Ringer.[72] Ringer, then Physician to University College Hospital, was also a serious researcher with a particular interest in pharmacology. Of specific concern to Ringer was understanding precisely how drugs affected the body. There was, however, no lab at the hospital, and so the respective directors of the UC physiology laboratory — John Burdon Sanderson, then, from 1883, Schaefer himself — made a place for him in their own facility.[73] It was here that Ringer began to conduct studies of the effects produced by a variety of substances on the isolated, or 'detached', heart. Following the lead of the Continental physiologists, Ringer kept his animals' detached hearts beating by perfusing them with a saline solution. He found, however, that the sodium chloride in the solution disrupted the heart's normal beat. Upon further investigation, he discovered that the addition of potassium and chloride not only counteracted this effect, but also extended the length of time the detached heart could be kept beating. "Ringer's Solution", then, relied on a combination of salts in solution to approximate the normal functions of the blood itself.[74]

In short, just as blood was being reduced in physiological concept to a flowing transport system, and in laboratory practice to a specific saline solution, Charles Egerton Jennings was arguing that a saline solution comprised of assorted salts in distilled water was a fit blood substitute for cases of acute haemorrhage.[75] At about the same time, Continental doctors were also replacing blood with saline solutions for transfusion.[76] Encouraged by Spencer Wells, Jennings went to Ghent in the autumn of 1884, where he became even more convinced that saline suitably replaced blood lost in acute haemorrhage.[77] His work had also attracted the attention of several of London's physiologically-oriented élite, including Pye-Smith, B. W.

Richardson — and Ringer and Schaefer. In 1888, the third edition of his transfusion treatise was published. Though Jennings preserved the title from the second edition, he could well have reversed the order, making it "saline and blood". His confidence in saline infusion was complete.[78] Still, even in this latter edition, Jennings continued to argue that blood did have a "nutritive *quality*".[79]

Yet, even this final vestige of vitalism did not hold for long. Simple volume replacement, with the aim of raising and sustaining the blood pressure, became the focus of infusions. At Guy's from around 1885, Peter Horrocks had been working with his colleague L. C. Wooldridge on the effects that large quantities of infused saline solution had on the body.[80] Wooldridge, with Horrocks, had taken his M.D. in London and trained at Guy's; like Hicks and Pavy before them, Horrocks was an obstetric physician and Wooldridge, Lecturer in Physiology.[81] Their collaboration is suggestive of the role obstetrical interests continued to play in blood's replacement by saline. Unfortunately, Wooldridge died suddenly in 1889, before the pair could publish their findings. [82] That same year, a young Cambridge physiologist named William Hunter reported on the extensive studies he had conducted — studies which, he argued, demonstrated that the blood had no nutritive function. Blood was a tissue. Like any other tissue, it suffered when the body starved.[83] In this work, he confirmed experimentally what a convergence of lab and clinic had already decided: that medicine had come "to the last stage in the development of transfusion, viz., the intravenous infusion of simple saline solution".[84] It seemed a natural product of the progressive evolution that was being effected by medical science.

BLOODLESSNESS IN A BLACK BOX

For nearly 75 years, English transfusion practitioners had attempted to control blood by defibrinating it, diluting it, and modifying its instrumental route between bodies. They went to this trouble because, with Blundell and Schaefer, they believed that blood alone could reanimate patients near death after blood loss. At the beginning and near the end of this period of blood-faith, English obstetricians turned to physiology for guidance about the fitness and methods of the operation. In the end, they found they could tame blood only by denying its vitality and, therefore, its therapeutic value. Small quantities of transfused blood could be replaced by far larger quantities of infused saline, turning what had been a grand and risky operation performed by highly trained experts into a relatively safe procedure that could be easily mastered. During the 1890s, blood transfusion quietly dropped from British medical literature.

Thus greatly simplified, fluid replacement therapy came to enjoy a kind of extension never seen with blood. The timing was fortuitous: modern medicine and modern life were creating far more trauma than had ever generally been witnessed outside of war. Surgeons, with the unrestrained operative enthusiasm that characterized the early decades of post-Listerian abdominal surgery, spilled great quantities of blood; this was conveniently replaced with a few to several pints of saline solution. City life itself was creating its own special brand of trauma:

abundant crush wounds, fractures, lacerations, and gunshot wounds, all tended to bring about that tenuous state that was still called "collapse", and was stabilized with infused saline. Diabetic comas and diarrhoea, too, were combated with infusions.[85] Thus simplified, generalized, and justified, fluid replacement could be neatly placed into its own black box, where it could be taken out and used without much further thought.

Century's end, then, marked a break between English obstetricians and blood transfusion. While clinical and conceptual pressures helped bring about this break, professional interests played a part as well. The same rapid surgical expansion that let so much blood in theatre had attracted the attention of London's obstetrical élite, who sought to retain their rights to operate on "the diseases of women" and thereby partake in the profit and prestige surgery increasingly offered.[86] In other words, just as the operation of blood transfusion was being replaced by the procedure of saline infusion, many obstetricians were refashioning themselves as gynaecologists. And, it had been precisely this class of obstetricians — founders of the OSL, with hospital appointments and, often, physiological inclinations — that had been promoting, and guiding, blood transfusion throughout the century. Saline infusion posed few challenges and, thus, commanded little direct attention from men with grander aspirations.[87]

There were, however, many unanswered questions about saline infusion. The move in the 1890s towards mass saline infusion — thirteen pints, in one case — seems to have relied on the assumption that the body would take what it needed, then safely eliminate the excess water.[88] This was not, however, the only possible interpretation of the evidence. The American surgeon George Washington Crile, who in 1895 had spent a month studying physiology at UC, conducted a series of animal experiments on blood loss and fluid replacement upon his return to the States. He became convinced that infused saline left the system so rapidly and totally that it had no lasting value — and that only transfused blood would remain in the vessels.[89] Shortly thereafter, Crile led an American return to blood transfusion. No such champion came forth in England, where saline remained the preferred infusion fluid until the Great War.[90] English physiologists, however, were having second thoughts.

By this time, English physiology had gained international respectability and was fairly well integrated into pre-clinical medical education.[91] At the same time, it was becoming more detached from its clinical roots, as clinician-physiologists were increasingly replaced by full-time physiologists. UC, of course, had the most active and prestigious physiology laboratory in London; but King's College, too, was quite respectable. Even leaders at some of London's voluntary hospitals thought physiology important enough to solicit public funds to add such laboratories to their facilities. By century's end, however, these hospitals would find it increasingly difficult to keep their best physiologists from taking university appointments.

At Guy's, for example, Wooldridge and his co-lecturers were given a small laboratory in the 1880s.[92] When Wooldridge died in 1889, his place was well-filled

by the young Ernest Henry Starling, who just that year had qualified in medicine.[93] Starling had entered Guy's to study medicine in 1882; however, he soon discovered physiology, and Wooldridge. While the aspiring young physiologist did continue his medical studies, he also found himself, with Wooldridge's encouragement, learning a bit of physiology (and German) in Germany and assisting Wooldridge with his lectures back at Guy's. After 1889, Starling held Wooldridge's former position for a decade, doing his best to convert a part-time lectureship into a full-time research position by supplementing his salary with a series of scholarships.[94] He also managed to make fairly substantial progress for physiological teaching and research at Guy's, despite an array of institutional limitations. Most notably, he successfully led the campaign to expand and improve the hospital's laboratory facilities in the 1890s.[95] It was the Guy's lab, in both its original and enhanced incarnations, that Starling credited as the location of his influential studies on lymph formation and the microcirculation. However, this nod to Guy's was more professional courtesy than practical fact. Starling did much of his work at the UC lab, in the company of physiologists rather than clinicians. It was work, however, that flowed out of — and would later come to have an impact on — clinical concerns with fluid balance in the body.

When last we left our broader understanding of blood and tissues, Pflueger had made his neovitalistic break, giving active powers to cells and effectively demoting the blood to a transport system. In subsequent decades, the struggle between physico-chemical reductionism and neovitalism continued. It was in this context that late nineteenth-century debates about how the body made, balanced, and distributed its internal fluids would be conducted. How was lymph formed? How did fluids and substances move between the tissues and the blood vessels? Materialists of Ludwig's school gave physical answers; neovitalists, on the other hand, offered cellular interpretations. In 1891, Rudolf Heidenhain, an eminent physiologist in Breslau, suggested that lymph formation, as well as the movement of fluids between vessels and tissues, could not be fully explained in physico-chemical terms. He argued instead that cells took an active role in the process, secreting lymph, and even, in part, determining the fate of excess fluids introduced into tissues.[96]

Fluids had been of great interest to the physiologists of Guy's. Wooldridge, it will be remembered, was working on blood coagulation and the efficacy of saline infusions as blood substitutes in the 1880s. It is therefore unsurprising that Starling followed his mentor into this fluid debate, which led him to Breslau.[97] Here, Heidenhain persuaded his English visitor of his cellular interpretation's plausibility. Starling returned to London eager to confirm Heidenhain's work. However, when he performed experiments to this end, he found that his own results pointed away from physiology and towards physics. In paper after paper, he dismantled Heidenhain's interpretations.[98] In their place, Starling built up a sophisticated vision of fluid production and movement that, coincidentally, provided insight into the limitations of any simple saline solution as a blood substitute.[99]

At the heart of Starling's vision was a system of fluids and salts in vessels and tissues, all in a kind of physico-chemically adjusted balance.[100] This balance, he believed, was most simply explained by filtration, absorption, pressure differentials, and osmosis. Osmotic theory had been elaborated by chemists over the course of the nineteenth century to explain the movement of water and salts of unequal concentrations through membranes.[101] It was found that, gradually, water moved through the membrane towards the side of greater salt concentration, and salt, in turn, moved towards the side of lesser concentration. Using semi-permeable membranes, it was determined that the osmotic pressure on the membrane rose as the concentration imbalance between the two sides was increased.[102] Starling applied this chemical knowledge to the fluid balance between capillaries and tissues in the animal body.

Specifically, over the course of the 1890s, Starling reinterpreted Heidenhain's ideas in physico-chemical terms. Within this model, lymph was not the product of cellular secretions, but instead the result of the physical filtration of fluids out of the blood vessels (through their presumably semi-permeable membranes) and into the tissues. Filtration occurred when the pressure in the capillaries rose above that in the tissues.[103] How, then, did fluids, once in the tissues, find their way into the blood vessels? The more biological explanation was that they moved through the lymphatic system, through the thoracic duct and into the blood. Preferring the simplest explanation, Starling looked for a more direct route and found it through the capillary walls themselves. In a series of experiments, Starling added saline solution to the tissues, to disrupt their equilibrium with the blood vessels. He found that, when the added solution had less salt than normally found in the blood (hypotonic), the blood vessels absorbed fluid from the tissues; when it had more salt (hypertonic), the tissues absorbed fluid from the blood vessels. Salt, too, gradually passed through the capillary membrane, until a new equilibrium was achieved. These findings were simply explained by his physical model of filtration and absorption.[104] This, of course, left open the question of how isotonic saline solutions could move between tissues and vessels. That such movement did occur, argued Starling, was evident in a well-established physiological phenomenon: after a body had been bled, the remaining blood rapidly increased in volume and became more dilute; water and salts were drawn from the tissues and — somehow — into the vessels. (This was, of course, the example that Schaefer had used nearly two decades earlier.) Further, Starling had repeated earlier experiments demonstrating that an isotonic salt solution "was taken up fairly rapidly ... from the pleura".[105] The phenomenon may have been demonstrated, but its explanation was still being debated.

It had been argued that the uptake of an isotonic solution could not be wholly explained by the process of filtration and absorption, as the solution, by definition, did not disrupt the normal salt balance. Instead, this uptake was interpreted as evidence of the "vital activity of the cells".[106] Starling, of course, disagreed. The capillary membrane was indeed part of the answer, but not in any vitalistic fashion.

It will be remembered that Starling believed lymph formed when capillary pressure increased, thereby causing fluid and salts to filter into the tissues. Water and salt were able to move in this manner because the capillary membrane was permeable to them. It was not, however, permeable to blood proteins. Thus, as fluid and salts filtered out, proteins remained in the vessels, creating a fairly substantial protein imbalance between lymph and blood. Starling then demonstrated that these proteins possessed a small, but significant, osmotic pressure. The normal balance created between vessels and tissues took this difference into account. When an isotonic solution was introduced into the tissues, it further diluted the protein concentration of the lymph. Despite this new pressure differential, the blood proteins could not pass into the tissues, as the capillary vessels were impermeable to them. Instead, their greater concentration effected the absorption of fluids out of the tissues and into the blood vessels, until a new balance was reached.[107]

At the same time that Starling was conducting these delicate experiments on the mechanisms by which the microcirculation maintained the body's fluid balance, medical practitioners were infusing large quantities of saline into collapsed patients. In one of his final publications out of Guy's, Starling uncovered physiological evidence strongly suggesting that the fluid replacement efforts his clinical colleagues were making might be misguided. His focus in these experiments shifted to the kidneys and the formation of another fluid produced by the body: urine. Was urine formed by the stimulated secretions of the glomular endothelium, or was it the result of a simple process of fluid filtration out of the glomular capillaries?[108] To study the process, Starling stimulated diuresis in his experimental animals by injecting a normal saline "of strong salt and sugar (dextrose) solutions"[109] into their jugular veins. He found that this excess fluid caused a rise in pressure in the glomular capillaries, which in turn effected a more rapid filtration of fluid out of the vessels. The more the capillary pressure increased, "the more rapidly would this process [of filtration] go on".[110] The body, in other words, quickly rid itself of the added saline solution.

The clinical implications of this work are evident. Starling, however, did not draw them. Further, I have found no evidence that he attempted to persuade his clinical colleagues at Guy's of the limitations inherent in their chosen infusion fluid. Indeed, during the 1890s, Starling, with English physiology in general, seems to have been moving from direct clinical interaction to more clinically-isolated laboratory research. Shortly after Wooldridge's death, Starling had started using UC's facilities, preferring, it seems, the collegiality of the collective to the silence of his lab.[111] It was here that he met the man who would be his greatest partner in research (and future brother-in-law), William Maddock Bayliss.[112] Bayliss assisted Starling with many of his experiments on fluid balance. And so, despite his success in expanding the conceptual and institutional place of physiology at Guy's, Starling accepted the position of UC's Jodrell Professor of Physiology, and director of the laboratory, when Schaefer left the position for Edinburgh in 1899.

This series of moves provides some insight into why Starling did not press

the clinical consequences of his laboratory investigations. Yet, any conclusions that this silence gives unqualified evidence of physiology's split from clinical concerns would be inappropriate. For, at this time, Starling's attention was diverted to more pressing, and potentially influential, concerns. Administratively, he became increasingly drawn into the work of reforming medical education.[113] Scientifically, he turned, with Bayliss, to the closer study of ... secretions. The pair discovered secretin in 1902 and, for the next few years, Starling investigated the chemicals he would come to baptize as "hormones". Despite the apparent irony of this turn, it was taken in a physico-chemical manner consistent with his earlier work. Significantly, Starling saw hormones as real, persuasive evidence of physiology's medical relevance. When presented with the opportunity to speak before the Royal College of Physicians in 1905, he chose to make this hormone argument the subject of his talk.[114] Clinically, saline infusion remained safely in its black box, where it stayed — in Britain, anyway — for another decade.

PANDORA'S BOX?

In the British *Official history* of the Great War, the author of the chapter on "wound shock" commented that, "in the treatment of the Somme casualties in the summer and autumn of 1916 intravenous infusion of normal saline was carried out on a large scale, but it was found most disappointing".[115] The author of this chapter was Ernest Cowell, a young UC medical graduate with a strong interest in physiology. As a Casualty Clearing Station surgeon for the British First Army, Cowell had witnessed the inadequacies of intravenous saline for the treatment of war trauma first-hand.[116] The following year, C. Gordon Watson, Consulting Surgeon to the Second Army, was more blunt. The apparent benefits of infused saline, he argued, were "too often transitory — a flash in the pan — followed by greater collapse than before".[117] A saline substitute was urgently needed. While Canadian surgeons in France were attempting to persuade their British colleagues of the benefits of blood, physiologists in London were working on more bloodless solutions.[118]

It was Bayliss, not Starling, who adapted physiological discoveries to this clinical need.[119] In the years leading up to the war, several younger physiologists had been investigating the implications of Starling's diuresis work for the retention of fluid in the blood vessels. Starling had shown that intravenous saline solution was rapidly filtered out of the blood vessels. He had also shown that the presence of proteins in the vessels effected the absorption of fluids from the tissues and into the vessels. F. P. Knowlton, then at Cambridge, reasoned that, if Starling was correct, the addition of "some substance allied to protein and which exercises approximately the same osmotic pressure as the blood proteins" should "produce less diuresis".[120] Accordingly, he added three different substances of varying osmotic pressures — gelatine, gum acacia, and soluble starch — to saline solution, and measured their relative effects on diuresis. He found that gum and gelatine, when added to a hypertonic sodium chloride solution, were "effective in inhibiting the diuresis produced by normal saline solution".[121] Knowlton did not, however, make any

specific connections between his research and its potential clinical applications. In 1916, Bayliss did.

Bayliss, like several other of Britain's best physiologists, remained at home during the Great War, participating in special committees designed to use laboratory research to lessen the clinical horrors of war.[122] He came to the treatment of haemorrhage, however, before any committee had been officially formed to study the problem.[123] By the summer of 1916, just as British surgeons in France were being confronted with the failures of saline, Bayliss had devised his saline substitute. It was, in fact, a saline enhancement, assembled along the lines suggested by recent physiological research and explicitly in accordance with immediate clinical need.[124]

The danger posed by haemorrhage, Bayliss explained in this initial article on the subject, was that the related drop in blood pressure further hindered the circulation of the remaining blood. "What is needed is to increase the volume of blood, without constricting arterioles." In most cases, this volume was supplied by "the intravenous injection of saline solutions", though "sometimes" it was provided "by transfusion of blood". Revealingly, Bayliss mentioned blood transfusion only once, dismissing it even more abruptly than Schaefer had dismissed saline in 1879. He returned quickly to his point. Noting that saline solutions had been found "unsatisfactory" in the treatment of haemorrhage, Bayliss argued that a "more efficient fluid" was needed.[125] An understanding of saline's limitations would provide a clue as to how this efficient fluid might be made.

It was now accepted (as Crile had argued much earlier) that saline solution could effect only a temporary rise in the blood pressure: shortly after it was introduced, the fluid left the blood vessels and the pressure fell. To explain saline's limitations, Bayliss underscored two ways in which water differed from blood. First, frankly, blood was thicker than water. More scientifically, it had been demonstrated by several eminent Continental physiologists of the earlier nineteenth century that blood flowed through vessels at a rate "inversely proportional to the viscosity and directly proportional to the driving pressure". Consequently, when the viscosity of the blood decreased, so too did the blood's driving pressure.[126] By decreasing the blood's viscosity, an infusion of saline would ultimately result in a lowered blood pressure. Were this the only problem with saline, one could simply add a substance that would increase its viscosity. Starling's work itself had indicated that viscosity was not the only problem. There was still that second crucial way in which saline differed from blood: it had no osmotic pressure. Infused saline thus not only heightened capillary pressure, it diluted the protein concentration of the remaining blood. This protein dilution further disrupted the normal balance between the hydrostatic pressure in the capillaries and the osmotic pressure on the tissue fluids, lessening the osmotic pressure and, consequently, decreasing the amount of fluid the vessels could absorb from the tissues.[127] But, as more recent researchers had shown, there were substances that would safely increase the osmotic pressure of the injected saline: specifically, gelatine and gum acacia.[128] Ultimately, Bayliss

chose gum, finding that "a solution of 6 to 7 per cent. [gum acacia] in 0.9 per cent. sodium chloride has the viscosity of blood and the osmotic pressure of its colloids".[129]

To Bayliss, gum acacia solution was the ideal fluid for the battlefield replacement of blood shed. Also called gum arabic, it was derived from the Egyptian acacia tree and reduced for medical use into "nearly colourless lumps".[130] These could be prepared in advance, easily stored, and simply reconstituted as the need arose — thereby removing the whole process of fluid replacement from those complications presented by a reliance on blood and blood donors. Moreover, it was designed in accordance with the latest physiological theories. It *had* to work. Until his death in 1924, Bayliss remained convinced that it did: he had found the perfect fluid substitute for blood. The surgeons he had hoped to convince, however, remained unpersuaded.[131] After the war, just as the nation abandoned substitutes and returned to the gold standard, English surgeons abandoned substitutes and turned to blood.

CONCLUSION

Closer study of the fluids chosen by English medical practitioners to replace blood between 1868 and 1916 has brought attention to a set of interrelationships about which many questions remain.

Saline emerged as the preferred blood substitute in late Victorian England out of clinical difficulties posed by the blood, in combination with changing physiological conceptions of the blood; these were articulated within specific institutions and in the hands of a group of men looking to the laboratory for clinical guidance. All these interactions took place at a time when English physiology was itself fluid: though no longer "stagnant", it was not yet fixed within disciplinary boundaries. Further, it was a time when many élite London clinicians were not at all certain that the laboratory had anything to tell them about medical practice. Within this context, élite obstetricians and physiologically-oriented clinicians came together, in part through shared institutions and inclinations, and held up saline solution as an effective blood substitute. Later, in the 1890s, the gradual fall of saline from obstetrical focus and from physiological favour underscores the professional changes both groups were then undergoing. Élite obstetricians were moving towards gynaecological surgery; physiologically-inclined clinicians were moving away from the clinic and towards the laboratory. Connections between the groups grew thinner.

Finally, gum acacia was promoted by the physiologist William Bayliss as a response to the pressing need for replacing, simply and efficiently, the blood spilled on the battlefield. It was a solution that mostly serves to highlight the distance that existed between the laboratories in London and the fields in France. Accepted by physiologists, gum acacia was rejected by surgeons. Yet, one cannot simply generalize from this case of resistance that a wide gulf had been created between physiological experimentation and clinical application in relatively short order.

The relations between English physiology on the one hand, and English surgery on the other, still need closer study.

An advantage to the historical study of failed fluids is that there are no obvious — and tempting — islands of 'progress' on which to rest one's narrative. One must chart a course suggested by the motives, concerns, and values of the historical actors themselves. This process sometimes leads one on elaborate journeys that do not entirely map onto predicted courses — even if the final destination remains the same.

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1. William Bayliss, *Intravenous injection in wound shock* (London, 1918), 20.
2. James Blundell, "Experiments on the transfusion of blood by the syringe", *Medico-chirurgical transactions*, ix (1818), 56–92. Blundell reported his first human trial (it failed) on 22 December 1818, and this was published as "Some account of a case of obstinate vomiting, in which an attempt was made to prolong life by the injection of blood into the veins", *Medico-chirurgical transactions*, x (1819), 296–311. It seems relatively clear that Blundell's "collapse" corresponds with what would now be called haemorrhagic, hypovolemic shock.
3. George Washington Crile, the American physiological surgeon who re-introduced blood transfusion to medical practice in the early twentieth century, described the results of his first successful transfusion as "a midnight resurrection". Grace Crile (ed.), *George Crile: An autobiography* (2 vols, Philadelphia, 1947), i, 166. (I have commented on this strange intersection of biography and autobiography in my paper, "Taking credit: The Canadian Army Medical Corps and the British conversion to blood transfusion in W.W.I.", *Journal of the history of medicine and allied sciences*, in press.) Accounts of the effects of blood on the collapsed patient using terms such as "miraculous", "re-animated" and "resurrection" are pervasive in the literature.
4. The classic analysis of the placement and power of ideas of purity remains Mary Douglas, *Purity and danger: An analysis of the concepts of pollution and taboo* (London, 1966, 1984).
5. In Britain, an official government inquiry into BSE and vCJD was set up in January 1998. The full text of its sixteen-volume report may be downloaded from the official web site, "The BSE Inquiry Report", http://bse.org.uk (accessed 7 February 2001).
6. Dorothy Bonn, "Future uncertain for reliable vCJD screening tests", *Lancet*, ccclvi (2000), 228.
7. In the United States, for example, the ban extended to anyone who had lived in England and Wales for more than six months.
8. F. Houston, J. D. Foster, Angela Chong, N. Hunter, and C. J. Bostock, "Transmission of BSE by blood transfusion in sheep", *Lancet*, ccclvi (2000), 999–1000.

9. In this paper, I extend, and occasionally modify, an earlier study of nineteenth-century transfusion methods. Kim Pelis, "Blood clots: The nineteenth-century debate over the substance and means of transfusion in Britain", *Annals of science*, liv (1997), 331–60.
10. These dates, like most, are somewhat arbitrary. 1868 marked not only the fiftieth anniversary of James Blundell's first human transfusion; it was also the year that a chemical addition to transfused blood was first formally proposed in England. 1916, on the other hand, was the year William Bayliss introduced his gum acacia solution as a blood substitute. During the course of the Great War, the discussion about blood loss and blood substitutes became quite complex: this story plays an important part in my forthcoming monograph on the history of transfusion and trauma treatment to the First World War.
11. Historians seem to have focused principally on general claims of late nineteenth-century clinical resistance to the laboratory, and reasons (from "truth" to professional advantage to broad social resonance) for its eventual integration into medicine in the first half of the twentieth century. A good review of these positions (with articulation of their own interpretation) is found in Steve Sturdy and Roger Cooter, "Science, scientific management, and the transformation of medicine in Britain *c*. 1870–1950", *History of science*, xxxvi (1998), 421–66. Case studies of the twentieth-century integration of clinic and laboratory may be found in Christopher Lawrence, "Moderns and ancients: The 'new cardiology' in Britain, 1880–1930", *Medical history*, supplement 5 (1985), 1–33; and in Sturdy, "War as experiment: Physiology, innovation and administration in Britain, 1914–1918: The case of chemical warfare", in Roger Cooter, Mark Harrison and Steve Sturdy (eds), *War, medicine and modernity* (Stroud, 1998), 65–84. I am interested in cases on the other side of that nineteenth/twentieth century divide. Lawrence qualifies his presentation of clinical resistance to science in practice (if not always in rhetoric) by pointing out that his resistant élite tended to have top positions at London's prestigious voluntary hospitals. There were others — specialists, for example — who were more open to the tools of science. Lawrence, "Incommunicable knowledge: Science, technology and the clinical art in Britain, 1850–1914", *Journal of contemporary history*, xx (1985), 503–20. It is men closer to the latter category who are the focus of the first part of the present paper.
12. As will become evident, I do not use 'physiology' in any absolute, essential sense; thus, the "shifting" undercurrent. I am suggesting that the very changes in the persons, institutions, and ideas then attached to 'physiology' both permitted a blood substitute to be sought and guided the composition of the substitute proposed.
13. Charles Severn (ed.), *James Blundell's "Lectures on the principles and practice of midwifery"* (London, 1839), 249.
14. Blundell was particularly impressed by the recent investigations of Charles Turner Thackrah, who had turned his prize-winning dissertation into a treatise in 1819. C. Turner Thackrah, *An inquiry into the nature and properties of the blood, as existent in health and disease* (London, 1819).
15. James Blundell, "Some remarks on the operation of transfusion", from *Researches physiological and pathological: Instituted principally with a view to the improvement of medical and surgical practice* (London, 1824), 92. The book's title itself testifies to Blundell's beliefs about the relations of science and medicine.
16. It was Blundell who introduced human-to-human blood transfusion into medical *practice*. The idea was being discussed, however, well before 1818. In 1805, for example, one of John Haighton's midwifery students reported Haighton as lecturing that, in cases of severe haemorrhage, "something must be done to stop the struggle. If left to yourself you would convey 30 or 40 oz. of blood into the system by the process of transfusion, but this could seldom be done in sufficient time, and if it could the prejudice is such as to prevent you". "Unidentified student's notes [ca. 1805]", taken in John Haighton, *A syllabus of the lectures on midwifery delivered*

at Guy's Hospital (London, 1799), 131. Manuscript at the Wellcome Archives. Haighton was Blundell's uncle and predecessor at Guy's.

17. Charles Waller, "On transfusion of blood, its history, and application in cases of severe haemorrhage", *Transactions of the Obstetrical Society of London*, i (1859), 61–72. By this time Blundell, still very much alive, had severed all connections to medical institutions, enjoying instead a lucrative private practice.
18. See Pelis, *op. cit.* (ref. 9), 340–1, for more on defibrination.
19. Despite overwhelming evidence to the contrary, the myth that ignorance of blood typing and fear of disease transmission led to the fall of transfusion in the nineteenth century persists. Doctors did sometimes note reactions that would now be classified as haemolytic; then, however, they were generally thought to be the product of small clots in the transfused blood. The possibility of syphilis transmission was occasionally noted but, at least in England, did not in any observed way drive the early search for blood alternatives. This may have been a product of the most common identities of English patient and donor: the birthing mother and her husband. If the husband had syphilis, it most probably would have been transmitted already by means other than transfusion. The next two donor sets, too — doctors and coachmen — may have been assumed trustworthy in reporting their state of health.
20. The *Lancet* published a number of articles on international efforts to replace human blood; the *British medical journal*, on the other hand, essentially ignored the phenomenon. See "Transfusion with lamb's blood", *Lancet*, 1874, i, 777; "A transfusor in trouble", *Lancet*, 1875, i, 37. In Britain, transfusion with lamb's blood was attempted at the German Hospital. "Transfusion", *Lancet*, 1874, ii, 462. A participant in the operation, Dr C. Farber, the hospital's Resident Medical Officer, wrote a letter to the journal following its notice of this transfusion. Farber commented that "in Germany direct transfusion from the lamb is coming into fashion just now, and has already proved a most powerful remedy in very different diseases". C. Farber, "Transfusion at the German Hospital", *Lancet*, 1874, ii, 541. Clearly, these fluids were used to overcome a variety of problems presented by blood.
21. "Transfusion with milk", *Lancet*, 1876, i, 937. W. S. Playfair pointed out that the operation was also supported by C. E. Brown-Séquard on the basis of animal experiments. W. S. Playfair, *A treatise on the science and practice of midwifery* (3rd edn, 2 vols, London, 1882), ii, 254.
22. "Blood drinking", *Lancet*, 1876, ii, 346.
23. An exception is found in Robert Barnes, who supported the addition of saline or milk to blood, as well as transfusion with animal blood: "To supply an answer to a vulgar dread that with the blood of animals some noxious vital principle may be imparted, it ought to be enough to remember that man lives upon the flesh and blood of animals." He went on to mention Galton's pangenesis experiments, in which blood of other species was injected into rabbits, as providing further evidence for the safety of foreign blood. Robert Barnes, *Lectures on obstetric operations* (3rd edn, London, 1876), 575–7, p. 577.
24. Summary of talk given to "Midwifery" section of the British Medical Association Annual Meeting. J. Braxton Hicks, "On transfusion, and new mode of management", *British medical journal*, 1868, ii, 151. I have drawn attention to the term 'saline' solution to underscore its meaning for those using it in the 1860s and 1870s. While we tend to assume a mixture of sodium chloride and water, they used it to describe the solution resulting from any salt dissolved in water.
25. It is unclear whether Hicks himself made the claim of safety (which would not be assumed today), or whether it was the journalist reporting on the annual meeting. Hicks, *op. cit.* (ref. 24), 151.
26. Braxton Hicks credited Pavy with this suggestion in the "Discussion" following E. A. Schaefer's presentation before the Obstetrical Society of London, "Report of experimental inquiry,

instituted to determine with what fluids and by what methods the operation of blood-transfusion may best be performed, and to ascertain the effects, immediate or remote, which result from the operation in animals", *Transactions of the Obstetrical Society of London*, xxi (1879), 316–47, p. 345.

27. Brief biographical sketches of several early British physiologists may be found in Edward Sharpey-Schaefer, *History of the Physiological Society during its first fifty years, 1876–1926* (London, 1927). Pavy's sketch is on p. 28. Pavy had received his medical education at Guy's and the University of London.
28. Hicks, *op. cit.* (ref. 24).
29. Andrew Elliot, "Transfusion: With special reference to intravenous infusion of saline solution" (M.D. Thesis, Edinburgh University, 1894), 16–22. Elliot appears to have studied medicine at the West London Hospital in 1892/93, then taken his M.D. thesis at Edinburgh. I am grateful to Michael Barfoot for kindly bringing this thesis to my attention.
30. For a review of the apparatus debate, see Pelis, *op. cit.* (ref. 9), 345–9.
31. "Committee to investigate the subject of transfusion", *Transactions of the Obstetrical Society of London*, xiv (1872); proposed by Charles Henry Felix Routh, p. 20. This committee was composed of the OSL's most esteemed members, including John Hall Davis, Alfred Meadows, and T. Spencer Wells. In 1873, Wells left the committee; in 1874, James Hobson Aveling joined it. It should also be noted that this inquiry was being conducted in the broader context of obstetricians' efforts to keep midwives out of the more profitable parts of their trade. One might hypothesise that a well-timed study of a potentially life-saving procedure that could be performed only by trained doctors would have aided their cause. For a participant's perspective on the midwife controversies, see James Hobson Aveling, *English midwives: Their history and prospects* (London, 1872; rev. edn, 1967). An excellent historical overview is given in Ornella Moscucci, *The science of woman: Gynaecology and gender in England, 1800–1929* (Cambridge, 1990).
32. "Transfusion", *Lancet*, 1873, i, 216.
33. William Priestley, "President's Address", *Transactions of the Obstetrical Society of London*, xvii (1875), 36–45, p. 44.
34. Henry Madge, "On transfusion of blood", *British medical journal*, 1874, i, 42–44, p. 44.
35. The Council's approval for this physiological study appears in William Priestley, "Annual address", *Transactions of the Obstetrical Society of London*, xix (1877), 17–36, p. 29. It is discussed in W. S. Playfair, "Annual address", *Transactions of the Obstetrical Society of London*, xxii (1880), 55–72, p. 61.
36. The state of English physiology at mid-century is discussed in several sources. See Gerald L. Geison, "Social and institutional factors in the stagnancy of English physiology, 1840–1870", *Bulletin of the history of medicine*, xlvi (1972), 30–58; and Richard D. French, *Antivivisection and medical science in Victorian society* (Princeton, 1975). For a review of the complex lineage and basic ideas of nineteenth-century Continental physiology, Karl E. Rothschuh, *History of physiology* (Huntington, NY, 1973).
37. After taking his M.D. at Edinburgh in 1823, Sharpey studied anatomy in London, surgery and natural history in Paris, and physiology (under Johannes Mueller's teacher, Karl Rudolphi) in Berlin. In 1836, he was offered the chair of General Anatomy and Physiology at University College, London, which he held until 1874. Sharpey-Schaefer, *op. cit.* (ref. 27), 17–19.
38. Stella Butler provides a detailed account of Sharpey's efforts to establish physiology in Britain — from his place on the General Medical Council to his nurturing efforts to grow his own department at University College. Stella V. F. Butler, "Science and the education of doctors in the nineteenth century: A study of British medical schools with particular reference to the development and uses of physiology" (Ph.D. thesis, University of Manchester, 1981),

chs 2 and 3.

39. Both Schaefer (who later changed his name to Sharpey-Schaefer) and Pavy were founding members of the Physiological Society. Sharpey and Charles Darwin were named Honorary Members. Sharpey-Schaefer, *op. cit.* (ref. 27), 13.
40. Sturdy and Cooter, *op. cit.* (ref. 11); Lawrence, *op. cit.* (ref. 11). See also S. E. D. Shortt, "Physicians, science, and status: Issues in the professionalization of Anglo-American medicine in the nineteenth century", *Medical history*, xxvii (1983), 51–68. For the American parallel to this story, with an emphasis on the embrace of science as a professional strategy, see Gerald L. Geison, "Divided we stand: Physiologists and clinicians in the American context", in Morris J. Vogel and Charles E. Rosenberg (eds), *The therapeutic revolution: Essays in the social history of American medicine* (Philadelphia, 1979), 67–90. A more recent study of experimental medicine in America, which attempts to combine explanations from science and culture, is John Harley Warner, "The fall and rise of professional mystery: Epistemology, authority and the emergence of laboratory medicine in nineteenth-century America", in Andrew Cunningham and Perry Williams (eds), *The laboratory revolution in medicine* (Cambridge, 1992), 110–41.
41. Playfair, *op. cit.* (ref. 35), 41. Of course, the actual influence this report had on the way ordinary, individual general practitioner-obstetricians did or did not perform transfusion is another matter. To answer such questions of day-to-day practice, if at all possible with extant records, would take an overwhelming amount of detective work: a problem which, in itself, sheds light on the complex issues surrounding any detailed appreciation of the relations between clinic and laboratory in the last third of the nineteenth century.
42. Moscucci, *op. cit.* (ref. 31), provides a good example of how, in the 1880s, hospital surgeons effectively prevented many obstetricians with gynaecological aspirations from performing ovariotomies.
43. According to Butler, Guy's gave the most active support to physiology research of the London teaching hospitals during the nineteenth century. Butler, *op. cit.* (ref. 38), 82. It may be no coincidence that Guy's also was a leading location for the study of transfusion.
44. Schaefer, *op. cit.* (ref. 26), 319. During the 1870s, blood transfusion was being used to treat an increasing array of conditions, from chronic anaemia to bacterial infection. While such efforts were being carried out in England, too, English transfusion remained firmly in obstetrical hands until the final decade of the century.
45. Schaefer repeated many of these experiments, both *in vitro* and *in vivo*; confirming Landois, he described what would now be called a haemolytic reaction: destruction of red cells, bloody urine, potential for emboli, and possible death. Schaefer, *op. cit.* (ref. 26), 316–19. It would be another twenty-five years before Karl Landsteiner recognized that human blood itself came in different types, which could be mutually incompatible.
46. Schaefer, *op. cit.* (ref. 26), 320, 321. Schaefer's blood pressure measurements were on animals. At this time, blood pressure apparatus, though popular in laboratory experiments, were not yet adapted for use at the bedside. Yet, after 1896, when clinical apparatus became available, English clinicians in general tended to prefer the measurement of their trained finger to that of the instrument. Lawrence, "Moderns" (ref. 11), 9–10.
47. Schaefer, *op. cit.* (ref. 26), 319. The physiologist Ernest Starling confirmed that this post-haemorrhagic blood dilution had been "known to physiologists for the last fifty years". E. H. Starling, "On the absorption of fluids from the connective tissue spaces", *Journal of physiology*, xix (1896), 312–26, p. 314. Schaefer's confident interpretation of this observation was, however, far from conventional clinical wisdom in 1879.
48. Schaefer, *op. cit.* (ref. 26), 319–20.
49. Schaefer, *op. cit.* (ref. 26), 321. The emphasis is Schaefer's.

50. Schaefer comments about the transfused dog that "the patient was strong enough to run about, and take its usual food the next day". This and the above quotations from Schaefer, *op. cit.* (ref. 26), 328.
51. Schaefer, *op. cit.* (ref. 26), 328.
52. I use the terms "shock", "collapse", and "exhaustion" with qualification. Throughout the nineteenth century (and, indeed, into the twentieth), they were used with a kind of fluidity that prevents any simple description of their respective meanings.
53. Little himself described the lineage of saline infusions for cholera treatment . W. J. Little, "Notes of unsuccessful and successful cases of saline alcoholic injections into the veins for relief of collapse of malignant cholera, treated during the epidemic of 1848–9", *Clinical lectures and reports, by the medical and surgical staff of the London Hospital*, iii (1866), 132–68.
54. I should stress that transfusion was thought of as an operative procedure, relying as it did upon 'cutting down' on veins. This operative status would persist into the twentieth century, arguably even until blood banking replaced hospital-based donation.
55. Charles Egerton Jennings, *Transfusion: Its history, indications, and modes of application* (London, 1883), 3.
56. Jennings, *op. cit.* (ref. 55), 1–2. Jennings was one of the few doctors of his day to bring attention to the dangers of infection, both to donor and patient. He continued his story by pointing out that the poor donor might develop "an ugly-looking pulsatile tumour" where the blood had been taken, giving him the role of hospital patient. Slightly later (p. 3), he mentioned — in passing, but still significantly — the dangers inherent in emergency transfusion, when there was no time to determine whether the donor had syphilis or "other specific communicable diseases".
57. Jennings, *op. cit.* (ref. 55), 2.
58. Jennings, *op. cit.* (ref. 55), "Author's preface". The emphasis is Jennings's.
59. Jennings, *op. cit.* (ref. 55), 5.
60. Charles Egerton Jennings, *On transfusion of blood and saline fluids* (2nd edn, rev., London, 1883), "Author's preface to the second edition".
61. T. Spencer Wells, "Special preface", in Jennings, *op. cit.* (ref. 60). Wells qualifies, with Jennings, that this substitution would be "within certain limits".
62. The most significant textual change comes in the second edition's inclusion of several cases in which blood or saline had been used to treat a variety of conditions other than acute haemorrhage. Included in this list is Mackenzie's work on using intravenous saline for treatment of diabetic coma. Jennings, *op. cit.* (ref. 60), 35–37.
63. Jennings, *op. cit.* (ref. 60) described both his donor difficulties (p. 5) and the case itself (p. 25), which appears to have occurred in August 1882.
64. Jennings, *op. cit.* (ref. 60), 48. (He cites Schaefer's work on p. 51.) Jennings was elected as a Fellow of the OSL in 1882.
65. He continues: "which, whilst sternly denying to us the right of experimenting on lower animals, in no way prohibits, and probably never contemplated the performance of experiments on men!" Jennings, *op. cit.* (ref. 60), 49.
66. Charles Egerton Jennings, "Report of two experimental transfusions on dogs, performed in Guy's Hospital Laboratory", *Lancet*, 1883, ii, 364–6, p. 364.
67. Jennings, *op. cit.* (ref. 60), 57.
68. Jennings, *op. cit.* (ref. 60), 57. The emphasis is again Jennings's. In preserving a place for blood's nutritive property, Jennings did believe that a blood/saline combination would be better than saline alone "in some *rare* cases, such as carbolic acid poisoning and some of the varieties of chronic anaemia".

69. Spallanzani's ideas, which he set forth in 1803, challenged Lavoisier's belief that respiration, as well as the production of animal heat, took place when the blood passed through the lungs. An elegant presentation, and interpretation, of the eventual acceptance of tissue respiration is Charles A. Culotta, "Tissue oxidation and theoretical physiology: Bernard, Ludwig, and Pflueger", *Bulletin of the history of medicine*, xliv (1970), 109–40.
70. Culotta, *op. cit.* (ref. 69), 116–20 (on Bernard); 120–8 (on Ludwig and his school). Culotta emphasises that neither Bernard nor Ludwig *denied* that respiration occurred in the tissues; rather, they objected to the view that the tissues, and not the blood, controlled the process (p. 128).
71. Culotta, *op. cit.* (ref. 69), 139–40, 130. Rothschuh, *op. cit.* (ref. 36), 226, further underscores the teleological framework in which Pflueger viewed his physiological studies.
72. I have found the following description of Ringer's typical workday such a striking portrait of a London clinician's determination to conduct both clinical and laboratory work — at a time when institutional structures hardly facilitated such efforts — that I quote it at length: "he would rise early, dispatch a hasty breakfast at eight, and the next few minutes would see him on his way to hospital, always on foot, carrying, perhaps, with him some casual co-breakfaster, astonished at the celerity of things. The hospital visit would generally, in pharmacological days, conclude with a quick-change appearance in the physiological laboratory — Ringer the physician transformed into Ringer the pharmacologist.... 'Fielder!' would have been hailed, a tracing taken, various suggestions made, and off he was again on his way back to Cavendish Place and the morning's consulting work.... The afternoon would be filled with visits, consultations, the hospital round, a *post-mortem* examination, and again, when possible, and for as long as possible, a visit to the laboratory. His attraction to this workshop was quite wonderful. Nothing could withstand it, not even the college palings, over which he clambered in the dark, upon one occasion at least, when the gates would not yield." "Obituary, Sidney Ringer", *British medical journal*, 1910, ii, 1384–6.
73. William F. Bynum, "Sydney Ringer", *Dictionary of scientific biography*, xi, 462–3. Butler, *op. cit.* (ref. 38), 214–20, describes the contrast between the Univerity College lab's openness to a wide variety of projects, and the focused investigations that took place in Michael Foster's Cambridge lab. On Foster and his laboratory, see Gerald L. Geison, *Michael Foster and the Cambridge school of physiology: The scientific enterprise in late Victorian society* (Princeton, 1978).
74. Ringer described his work in a series of papers published in the *Journal of physiology* between 1882 and 1885. His findings came independently of S. A. Arrhenius's work on electrolytic dissociation. Bynum, *op. cit.* (ref. 73), 462–3.
75. To twenty ounces of distilled water, Jennings added sodium chloride and, in lesser amounts, potassium phosphate, "sulphate of soda", "carbonate of soda", and "phosphate of soda". He carried pre-prepared packets of this salt mixture (as had Little before him) in his apparatus case. In some cases — again, following Little — he added "absolute alcohol" to his saline mixture. Jennings, *op. cit.* (ref. 60), 56.
76. Elliot, *op. cit.* (ref. 60), 22–23, cites several Continental reports of successful saline infusion from 1881–82.
77. Jennings mentions this research trip in the 1888 edition of his transfusion treatise. Charles Egerton Jennings, "Author's preface to the third edition", *On transfusion of blood and saline fluids* (3rd edn, London 1888).
78. Jennings, *op. cit.* (ref. 77). It is here that Jennings thanks Schaefer, Ringer *et al*. for "discussing various scientific points at length with me".
79. Jennings, *op. cit.* (ref. 77), 57. That Jennings continued to hold to blood's nutritive value, and did not simply omit revisions of this passage from the earlier editions, is strongly suggested

by a discussion held on a transfusion apparatus presented to the Harveian Society in 1885. Jennings, having championed the case of saline, qualified his assertion, which was noted in the *Lancet*'s summary of the evening: "the nutritive value of blood was not to be underrated; and where transfusion was indicated for the sake of nutrition, the employment of whole blood would be better than that of defibrinated blood." "Meeting, Harveian Society of London", *Lancet*, 1885, i, 664.

80. Peter Horrocks, "Saline transfusion", *British medical journal*, 1892, ii, 491.
81. On the young Wooldridge (he was 32 when he died), see W. J. O'Connor, *British physiologists, 1885–1914: A biographical dictionary* (Manchester, 1991).
82. L. C. Wooldridge, "The coagulation question", *Journal of physiology*, x (1889), 329–40. This paper was published posthumously, with a note by Michael Foster. The article is in fact a spirited defence of his own work against the critiques of W. D. Halliburton.
83. William Hunter, "Summary of three lectures on transfusion: Its physiology, pathology, and practice", *British medical journal*, 1889, ii, 116–19, 237–40, 305–9. Hunter's work came at a time when several European investigators, whose studies he cited, were reaching the same conclusions.
84. Elliot, *op. cit.* (ref. 29), 20.
85. Whereas Elliot, following Jennings, tended to use around two pints of saline, Bernard Pitts, at St Thomas's hospital, infused between four and thirteen pints into his patients. Bernard Pitts, "The history of transfusion, with short notes of cases in which the method of infusion of saline fluid into the veins has been adopted", *Saint Thomas's Hospital reports*, xxi (1893), 253–70, 262–4. Both authors describe these patients as "collapsed" or "exhausted"; Pitts adds "moribund" and, in one instance, refers to the condition as "shock".
86. Moscucci, *op. cit.* (ref. 31) tells this story in ch. 6.
87. My initial review of later literature suggests that obstetrical interest in blood transfusion was only rekindled in the 1930s, when concerns about maternal mortality became acute.
88. Elliot, *op. cit.* (ref. 29), 53. The case of 13 transfused pints is in Pitts, *op. cit.* (ref. 85), 263. It is possible that Wooldridge and Horrocks were conducting the work at Guy's in the 1880s that encouraged the use of mass infusions; further research must be done before this hypothesis can be stated with more certainty.
89. Peter C. English, *Shock, physiological surgery, and George Washington Crile: Medical innovation in the progressive era* (Westport, CT and London, 1980), ch. 6.
90. English argues that Crile's use of blood pressure measurement was key to his understanding of the nature and treatment of shock. English, *op. cit.* (ref. 89), chs. 5 and 6. In hospital, where most doctors were estimating the effects of saline, blood pressure measurements were not yet taken. At the same time, it is also possible that Crile's ideas about blood itself had some considerable bearing on his interpretation of the relative efficacy of the two fluids.
91. Butler, *op. cit.* (ref. 38), ch. 3, describes this process. Geison, *op. cit.* (ref. 73), 151, suggests that the addition of physiology in 1870 to the subjects examined for the MRCS "may have been the single most important factor in the transformation of late Victorian physiology".
92. Wooldridge was one of three men who shared the position of teaching practical physiology at Guy's. It was not until several years later that the position was consolidated and filled by a single individual. C. C. Michel, "Starling: The formulation of his hypothesis of microvascular fluid exchange and its significance after 100 years", *Experimental physiology*, lxxxii (1997), 1–30, pp. 2–3.
93. Not only did Starling take Wooldridge's position at Guy's, he also eventually married Wooldridge's widow. Michel, *op. cit.* (ref. 92), 2–6. Jens Henriksen's biography of Starling appeared last year; however, I have not yet been successful in my efforts to find a copy. Jens H. Henriksen, *Ernest Henry Starling (1866–1927), physician and physiologist: A short biography*

(Copenhagen, 2000).

94. Michel, *op. cit.* (ref. 92), 3. Starling was awarded scholarships by the British Medical Association and the Grocer's Company.
95. Butler, *op. cit.* (ref. 38), 80–82.
96. Starling lays out pieces of Heidenhain's theories and evidence in his own publications; Michel brings them together nicely. Michel, *op. cit.* (ref. 92), 6–7. In his presentation of Heidenhain's work, Rothschuh is relatively cautious about vitalistic labels, arguing that, principally, Heidenhain abhorred over-hasty reductionism, preferring biological explanations while avoiding vitalism proper. Rothschuh, *op. cit.* (ref. 36), 231–2. This may well be so: I have not studied Heidenhain's work directly. It is clear, however, that Starling and his collaborator saw a vitalistic component in Heidenhain's interpretations: "the force which causes absorption ... is clearly something more than osmosis, and that it originates in the vital properties of the intestinal epithelium, Prof. Heidenhain argues, is rendered probable...." J. B. Leathes and Ernest H. Starling, "On the absorption of salt solutions from the pleural cavities", *Journal of physiology*, xviii (1895), 106–16, p. 107. Quite possibly, the answer simply comes down to one's definition of the ever-slippery concept, 'vitalism'.
97. Michel plausibly suggests that Wooldridge encouraged Starling to take up the question of lymph formation. Michel, *op. cit.* (ref. 92), 6.
98. Michel clearly and systematically lays out how Starling overturned each of Heidenhain's hypotheses. Michel, *op. cit.* (ref. 92), 7–9. See Leonard G. Wilson, "Starling's discovery of osmotic equilibrium in the capillaries", *Episteme*, ii (1968), 3–25.
99. In the final chapter of her dissertation, Butler argues persuasively that Starling, in the early part of the twentieth century, articulated a holistic concept of the body (based on his hormone work) that, in Bernardian fashion, relied on physico-chemical explanations but saved a special place for life in organization itself. Butler, *op. cit.* (ref. 38), ch. 7.
100. Starling's ongoing fascination with Claude Bernard's *milieu interieur* was most fully realized in 1923, in his Harveian Lecture. Ernest Starling, "The wisdom of the body", *Lancet*, 1923, ii, 865–70.
101. Aaron J. Ihde, *The development of modern chemistry* (New York, 1964, 1984), 410–13, provides a good summary of nineteenth-century work on osmotic pressure.
102. I have found that the botanical experiments of Hugo de Vries provide a good illustrative example of osmosis. When he placed a plant in plain water, the plant became turgid. When he placed it in a moderately concentrated salt solution, it withered. Finally, when he used a solution that had the same salt balance as was found in the plant itself, the plant remained unchanged. Ihde, *op. cit.* (ref. 101), 411.
103. Ernest Starling, "Contributions to the physiology of lymph secretion", *Journal of physiology*, xiv (1893), 131–53.
104. Starling and Alfred H. Tubby, "On absorption from and secretion into the serous cavities", *Journal of physiology*, xvi (1894), 140–55; Leathes and Starling, *op. cit.* (ref. 96).
105. Starling, *op. cit.* (ref. 47), 312–13, 313. Orlow had originally demonstrated this in 1894.
106. Starling, *op. cit.* (ref. 47), 317.
107. Starling, *op. cit.* (ref. 47).
108. Ernest Starling, "The glomular functions of the kidney", *Journal of physiology*, xxiv (1899), 317–30. For an overview of the history of renal physiology, with particular reference to Starling, Leon G. Fine, "British contributions to renal physiology: Of dynasties and diuresis", *American journal of nephrology*, xix (1999), 257–65.
109. Starling, *op. cit.* (ref. 108), 322.
110. Starling, *op. cit.* (ref. 108), 328.

111. Michel, *op. cit.* (ref. 92), 3. Starling was a firm believer in the value of collaboration.
112. Bayliss married Starling's sister in 1903. For a first-hand review of the Starling/Bayliss collaboration, see A. V. Hill, "Bayliss and Starling and the happy fellowship of physiologists", *Journal of physiology*, cciv (1969), 1–13. (This was, in fact, the "Third Bayliss-Starling Memorial Lecture".) Also, P. R. Fleming, "The other Bloomsbury set: Bayliss, Starling, and Thomas Lewis", *International journal of microcirculation*, xiv (1994), 91–94. The pair are perhaps most famous for their discovery of secretin in 1902.
113. Butler, *op. cit.* (ref. 38), ch. 5.
114. Ernest Starling, "The chemical correlation of the functions of the body", *Lancet*, 1905, ii, 339–41, 423–5, 501–3, 579–83, p. 340. Butler argues that Starling's hormone concept mirrored his ideas for the reform of medical education, thereby providing scientific justification for his social ideas. Butler, *op. cit.* (ref. 38), ch. 7. There is certainly an overlap in Starling's thinking about the functions of hormones and the ideal system of medical education. And, there is that coincidence of timing between Starling's hormone work and his move to University College. Yet, it seems that one must take account of Starling's earlier interest in Heidenhain's theories to decide whether he developed the science to substantiate the social, or instead tended to see the world generally in these organizational terms.
115. Ernest Cowell, "Wound shock in front line areas", in W. G. Macpherson, A. A. Bowlby, Cuthbert Wallace, and Crisp English (eds), *Official History of the War — Medical Services — Surgery of the War* (2 vols, London, 1922), i, 58–78, p. 59.
116. Several historians of medicine have underscored what appears to be a sudden interest on the part of physiologists in clinically-relevant questions during the war. In the war-time debate on fluid replacement, we see a complex set of interactions between physiologists, surgeons, and several who fall between the two categories in a fashion seemingly related to the institutions that gave them their medical training. I will develop these relationships more fully in my forthcoming monograph.
117. L. Bruce Robertson, with a note by C. Gordon Watson, "Further observations on the results of blood transfusion in war surgery", *British medical journal*, 1917, ii, 679–83, p. 683.
118. On the Canadian support of blood, see Pelis, *op. cit.* (ref. 3).
119. Starling was, in fact, named chairman of the Medical Research Committee's special committee on shock. By this time, however, his physiological interests lay elsewhere. (He was also working on gas poisoning and nutrition.) When he resigned from his position on the shock committee in March 1918, it was Bayliss who became chairman. "Special committee on shock and allied conditions. Minute Book", 13 March 1918, Public Records Office, London, PRO FD1/5262.
120. Frank P. Knowlton, "The influence of colloids on diuresis", *Journal of physiology*, xliii (1911), 219–31, p. 220.
121. Knowlton, *op. cit.* (ref. 120), 231. From Cincinnati the following year, James J. Hogan and Martin H. Fischer published their independent findings on the effects of gelatine on fluid retention. James J. Hogan and Martin H. Fischer, "Zur theorie und praxis der transfusion", *Kolloidchemische Beihefte*, iii (1912), 385–416. I have done no further research on Hogan and am therefore uncertain as to why he decided to publish his work in German.
122. Starling, on the other hand, did join the Royal Army Medical Corps, but found that his personal philosophy of integrated collaboration and the army's preference for hierarchy and discipline didn't mix. Starling soon decided he would serve his country's interests better back in London and resigned his commission. Michel, *op. cit.* (ref. 92), 5. It should also be noted that British physiologists did not confine their efforts to improving the defensive part of the war effort. On the war work of the Medical Research Committee and the Royal Society, see Steve Sturdy, "From the trenches to the hospitals at home: Physiologists, clinicians and oxygen

therapy, 1914–30", in John V. Pickstone (ed.), *Medical innovations in historical perspective* (Basingstoke, 1992), 104–23.

123. It is quite possible that T. R. Elliott, the Medical Research Committee's official liaison in France, alerted Bayliss to the problem. Elliott had been conducting physiological research at Cambridge for several years before coming to University College in 1906 to study medicine. In 1910, he was appointed Assistant Physician at UC Hospital. In France during the war, Elliott was concerned quite early on with the treatment of acute blood loss and may well have asked Bayliss to work on the problem. The official announcement of the impending formation of the "shock committee" came in March 1917. "Memorandum upon surgical shock and some allied conditions", *Lancet*, 1917, i, 502–5.

124. W. M. Bayliss, "Methods of raising a low arterial pressure", *Proceedings of the Royal Society of London*, B, lxxxix (1917), 380–93. Bayliss submitted the paper on 29 August 1916. As was commonly done through the First World War, Bayliss divided the condition once called "collapse" into two clinically similar, but etiologically distinct, categories. On the one hand, there was haemorrhage, with its evident fluid loss; on the other, was "pure shock", which was not, he argued, the result of fluid loss, but of "peripheral vaso-dilation". The relations between these two categories is too complex for consideration at this time; therefore, I will treat only his work on haemorrhage.

125. Bayliss, *op. cit.* (ref. 124), 380. During the war, advocates of both blood and blood substitutes claimed that their choice was the most "efficient" fluid.

126. This was Poiseuille's Law, applied to blood vessels by the likes of Mueller and du Bois-Reymond. Bayliss, *op. cit.* (ref. 124), 382.

127. Bayliss, *op. cit.* (ref. 124), 386–7.

128. Bayliss, *op. cit.* (ref. 124), 388; 393. A year earlier in the United States, James Hogan — whom we saw working on colloids earlier — advocated instead the addition of gelatine for the treatment of shock. James J. Hogan, "The intravenous use of colloidal (gelatin) solutions in shock", *Journal of the American Medical Association*, lxiv (1915), 721–6. In this article, Hogan greatly simplifies his colloidal studies for his medical audience.

129. Bayliss, *op. cit.* (ref. 1), 80. Bayliss appears to have chosen gum acacia over gelatine shortly after submitting this paper. The best proportion of acacia was debated by those who used it.

130. Bayliss, *op. cit.* (ref. 1), 85. Gum acacia was comprised of "a mixture of polymerised anhydrides of galactose ... and of a pentose sugar, arabinose ... in varying proportions".

131. Although surgeons and physiologists technically worked together to solve the problem of shock in wartime, their collaboration was far more complex than has generally been appreciated.