Pergamon

Stud. Hist. Phil. Biol. & Biomed. Sci., Vol. 30, No. 3, pp. 377–405, 1999

Printed in Great Britain
1369–8486/99 $-see front matter

www.elsevier.com/locate/shpsc

‘What Blood Told Dr Cohn’: World War II, Plasma Fractionation, and the Growth of Human Blood Research

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In October 1953, the death of Harvard Medical School professor Edwin J. Cohn inspired a number of journalistic accounts of his research contributions. One newspaper story, entitled ‘What Blood Told Dr Cohn’, described his method for fractionation of human blood as ‘one of the glories of American science . . . work that has proved to be as important and more difficult than that which gave us the antibiotics’.[1] Indeed, Cohn’s spectacular method for fractionating blood into its constituents had provided critical new therapies for military medicine and spawned a postwar industry of plasma fractions for civilian use. These medical advances grew out of a request by the Navy in 1940 for Cohn’s help in identifying a transfusible substance from bovine blood which could be stockpiled in preparation for war. Cohn’s group of researchers obtained a crystalline component from bovine plasma within a few months.[2] Unfortunately, the residual differences between cow and human blood proteins proved insurmountable: the antigenic irritants in bovine serum albumin could not be purified away biochemically, dooming the medical utility of the bovine protein for the casualties of war. But when the same methods were used to isolate the protein from human blood, the resulting serum albumin was not only pure, but exhibited remarkable effects when administered to injured persons as an antidote to shock (Starr, 1995). Furthermore, Cohn’s fractionation technique could be adapted to isolate other components of human blood of therapeutic utility, including fibrinogen and gamma globulins. The technologies proved

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[1]‘What Blood Told Dr Cohn’, clipping marked *Times*, Oct. 6, 1953, Cohn papers, HUG 4290.2, Pusey Archives, Harvard University.

[2]For an overview of the earlier uses of animal blood for transfusion to humans, see Diamond (1980).

PII: S1369-8486(99)00017-5

equally valuable to medical research on blood, providing a biochemical framework for the 'blossoming of hematology' after the war (Wintrobe, 1985).

The adoption of Cohn's fractionation methods, both in laboratory research and in pharmaceutical companies, relied on the constant flow of human blood as a research material and industrial feedstock. Ironically, this dependence upon civilian blood donation for the mass-production of such therapeutics was precisely what the military had hoped to avoid by developing a substitute from bovine blood. During the war, the Red Cross established its National Blood Donation service to coordinate blood donation, processing, and distribution; in the postwar period community-based volunteer donation of blood was supplemented by use of paid donors to process plasma components.[3] This paper relates the establishment of this infrastructure (for more detailed accounts, see Creager, 1998a, b) with an eye towards its consequences for biomedical research in the postwar period, focusing on the role of Cohn and his Harvard laboratory. In a pioneering essay on laboratory materials, Adele Clarke observed that the production of biomedical knowledge is intimately related to research materials and their infrastructures; interest in this relation has provided a new focus in history of biology during the past few years (Clarke, 1987).[4] Obtaining human materials for biomedical research poses particular logistical problems, as well as raising ethical issues of ownership and patient consent.[5] As Clarke notes, attention to infrastructures can complement the understanding of a historical 'ecology of knowledge' as framed by disciplines and institutions.[6]

One aspect of the ecology of research on human substances, such as blood, is that the demarcation between 'basic' and 'applied' research is mutable, technically and rhetorically. In the years after World War II, political debates in the US about government funding of research meant that the newly important category of 'basic' research was defined variously as pure or relevant, depending on the constituency involved.[7] I will argue that this new political situation favored the selection of *research materials*, such as human blood, that were directly pertinent to clinical

[3]See Titmuss (1971) on the debate about the incursion of the market onto the formerly altruistic practice of blood donation.

[4]Several historians have taken Clarke's lead: representative of the turn to materials in recent historical literature are essays by Lederman and Burian (1993), Lederman and Tolin (1993), Summers (1993), Zallen (1993), Kohler (1993), Holmes (1993), Clause (1993), and Burian (1993) (under the collective title 'The Right Organism for the Job'), Kohler (1994), and Rader (1995).

[5]These issues are well illustrated in the proliferation of HeLa tissue culture cells in biomedical research during the past four decades. This 'immortal' cell line was derived (without consent) from the cervical tumor of a black woman, Henrietta Lacks, who died at the age of 31 in 1951. Her husband's resentment of the supply industry which has sold his wife's cells is a well-known point of reference in discussions about the bioethics of use of human tissues. Hannah Landecker has recently written an excellent historical account of the HeLa cell line (Landecker, forthcoming); the scientific problems with HeLa cells as culture material are discussed in Gold (1986). On the ethical problems in the history of (intact) humans as scientific subjects, see the work of Susan Lederer (1984, 1985, 1995).

[6]On 'ecology of knowledge,' see the classic essay by Charles Rosenberg (1979).

[7]Although they are not directed at this precise point, for relevant discussions, see Kevles (1977) and Dennis (1994).

needs even as they were amenable to studies of a fundamental nature. In other words, the organization of research and publication around diseases and materials, such as blood, suited the postwar transition to enlarged public funding for 'basic' health-related research (Strickland, 1972).

At another level, the contingency that Cohn's medical breakthroughs relied on human plasma rather than the bloody by-products of Midwestern slaughterhouses linked the new therapies with the complex cultural meanings of human blood. One journalist declared, '"Blood will tell" is a well-worn phrase that carried a symbolic meaning because blood has always been a mysterious fluid. Dr Cohn stripped away the symbolism and made blood tell what it had never told before.'[8] The consistent fascination with the human derivation of the Cohn fractions in other media representations reveals that, contrary to this journalist's assertion, the biochemical partitioning of blood did not simply strip the fluid of its cultural meanings. Rather, the benefits of blood fractionation following upon World War II had particular redemptive associations which reinforced the public value of Cohn's research on blood proteins.

1. The Needs of War: Blood as a Source of Novel Therapeutics

The development of plasma fractionation technologies was inextricably linked to the early mobilization of science in the US for war. In 1940, the National Research Council (NRC), having provided advice on matters of science and medicine during World War I, was called on by the Surgeon General of the Army in the spring of 1940 to help anticipate military medical needs in transfusion and chemotherapy.[9] Walter Cannon, professor of physiology at Harvard Medical School, headed the NRC Committee on Transfusions, which included a Subcommittee on Blood Substitutes. In a report to the NRC scientists, Colonel Charles Hillman of the Army endorsed the use of blood banks if the war was close to home, but contended that battles in more distant places would require blood plasma.[10] The Navy, concerned about the quantity of plasma that could be stockpiled and transported, expressed interest in development of an alternative blood substitute. In addition to colloidal substances such as agar gum and gelatin, animal blood was a candidate.[11] Owen Wangensteen, a member of the Subcommittee on Blood Sub-

[8]Anonymous journalist, 'What Blood Told Dr Cohn', *op. cit.*, n. 1.

[9]On the beginnings of the NRC, see Kevles (1968), and on the NRC's activities in the interwar period, see Bugos (1989). The relationship between the NRC and the Office of Scientific Research and Development during World War II can be found in Stewart (1947). An insider's account of how Cohn came to be associated with the NRC committee can be found in Hastings (1989), p. 151.

[10]Minutes of Committee on Transfusions, May 31, 1940, NRC-DMS Bulletin on Blood Substitutes, Vol. 1, p. 2. Plasma is the liquid of blood separated from its cellular elements and to which an anticoagulant has been added; plasma can be stored in liquid or dried form for much longer than whole blood. Serum refers to the liquid separated from clotted blood. (Serum lacks fibrinogen, which is present in plasma.)

[11]On the development of blood substitutes during World War I (such as gum acacia), see Janeway and Oncley (1948).

stitutes from the Department of Surgery at University of Minnesota, had recently published promising studies on the use of bovine plasma in humans (Wangensteen *et al*., 1940).

Cannon's colleague at Harvard, Edwin J. Cohn, was at this time well known for his studies of the physico-chemical properties of proteins. His Department of Physical Chemistry, admittedly an unusual unit for a major medical school, was sustained predominantly by the Rockefeller Foundation for its investigations of protein structure (Creager, 1998a). Around 1930, after a decade of work on protein solubility, Cohn and his coworkers turned their attention to the physical chemistry of the smaller and simpler units of proteins, amino acids and peptides (Edsall, 1950, 1979). In 1937, returning to studies of intact proteins, members of Cohn's laboratory began purifying serum albumin and serum globulin. Cohn's selection of these plasma proteins for investigation continued a longtime departmental interest in blood that began with L.J. Henderson's celebrated work on acid-base equilibrium. In effect, Cohn extended Henderson's interest in the regulation of small molecules in blood to the physiological role of macromolecules. Cohn's workers, however, were oriented entirely towards physical chemistry, not clinical utility: they assessed the purity and molecular behavior of the serum proteins by comparing the dielectric constant measurements to their electrophoretic and sedimentation patterns.[12] Cannon drew upon this local expertise in the spring of 1940 by asking his colleague Cohn to investigate the feasibility of the Navy's hopes for a blood substitute from bovine blood (Kendrick, 1964, p. 325 ff.).

Responding to this request, Cohn rapidly mobilized his laboratory to isolate a transfusible fraction from bovine blood. Serum albumin, which constitutes 50–60% of plasma proteins and exerts 85% of the osmotic pressure of plasma, was the best target for fractionation (Kendrick, 1964, p. 336; Blombäck and Hanson, 1979). Cohn's workers drew on their years of experience with the effects of solvents, pH, ionic strength, temperature, and protein concentration on solubility in devising a novel method for separating plasma into its constituents. Rather than relying upon salt precipitation as was conventional for protein separations in biochemistry laboratories (and which Cohn's workers had used to purify serum albumin and serum globulin in the late 1930s), their technique utilized ethanol at cold temperatures to separate the plasma proteins into five major fractions. After blood cells were removed by centrifugation, the fractions were recovered serially (also by centrifugation) from solutions of increasing ethanol concentration. Because newly developed lyophilizers could be used to remove ethanol from precipitates on a large scale, this method could be easily scaled up for industrial production (see

[12]Letter from J. W. Williams to Warren Weaver, Nov. 12, 1937, Rockefeller Archive Center (hereafter RAC) RF 1.1, 200, box 164, folder 2013. The Rockefeller Foundation had installed a Svedberg-type analytical ultracentifuge in Williams' laboratory, the only one in an American university, and so Williams frequently reported on his work to Weaver. In 1937 he had begun to collaborate with Cohn on serum albumin and serum globulin. A more detailed account of Cohn's research and its reliance on these new instruments can be found in Creager (1998a).

Figs 1 and 2).[13] Testing of the serum albumin (from Fraction V) proceeded along two lines. Cohn's group compared purified bovine serum albumin to purified human serum albumin, which they had also prepared by the end of 1940. Clinical trials also began with intravenous injections of purified bovine serum albumin into volunteers at a Massachusetts prison (Cohn, 1948; Harkness, 1996).[14]

Early results were sufficiently promising that the NRC approved funding in the spring of 1941 for construction of a pilot plant at Harvard to produce bovine serum albumin on a larger scale. A few months later the Committee on Medical Research

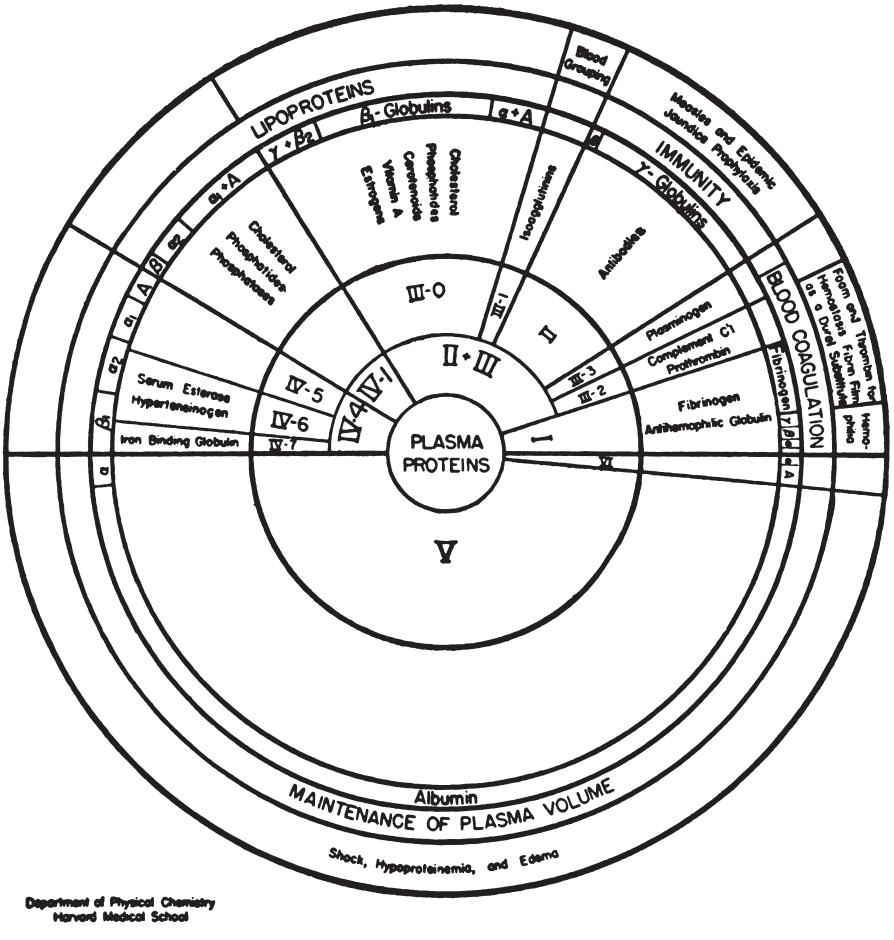

Fig. 1. Cohn's diagram depicting the separation of the various components of plasma into five major fractions. From Cohn (1948).

[13]Advances in equipment for lyophilization (vacuum-drying) in the 1930s, particularly by Sharpe and Dohme, were critical to the large-scale preparation of human plasma for the Armed Forces (Kendrick, 1964, pp. 280 ff.) as well as for mass-production of plasma fractions.

[14]On prisoner experimentation, including tests for the bovine serum albumin, see Harkness (1996).

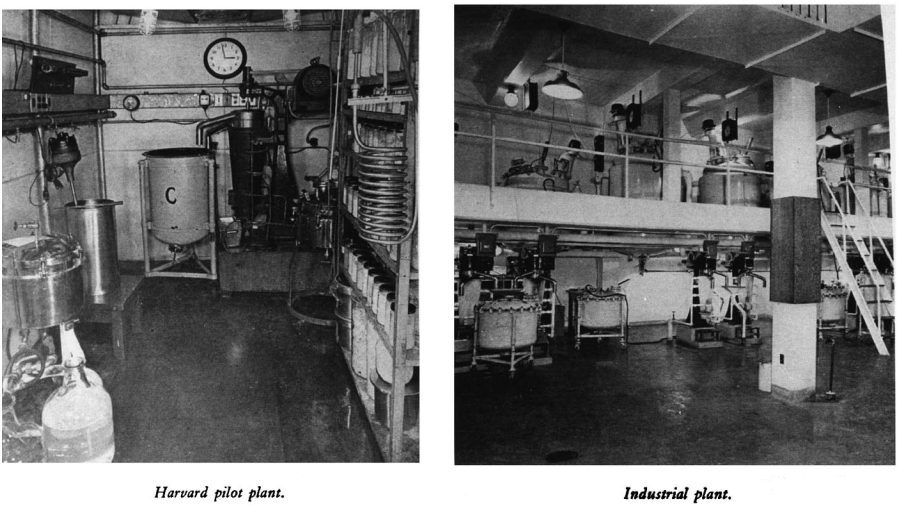

Fig. 2. Juxtaposed photographs showing the low-temperature fractionation room in the Harvard pilot plant (a) and an industrial plant (b). The centrifuge is the central apparatus, to the right of the clock in (a). From Cohn (1948).

(CMR) was constituted as a primary subdivision of the Office of Scientific Research and Development (OSRD). The OSRD-CMR provided Cohn's laboratory with substantial funding from late 1941 through 1946 (Cohn, 1950b). Armour Laboratories, located near the Chicago slaughterhouses, also began constructing a bovine plasma fractionation plant in 1941. Cohn's laboratory found that bovine serum albumin was nearly chemically identical to its human counterpart, in terms of solubility, isoelectric point, electrical charge, mobility, sedimentation in the ultracentrifuge, and migration in an electrophoresis apparatus. Only immunological techniques, such as a precipitin test, could distinguish them in the laboratory. Patients' bodies were equally discriminating, though: while most of the clinical testing was encouraging, the first serious instance of serum sickness from bovine albumin was reported in the summer of 1942. Cohn and his colleagues then sought to obtain a purer and more stable fraction, hoping that the reaction might be attributable to a contaminating substance. Armour Laboratories produced a bovine albumin with only 0.01 percent contaminating globulin; the Harvard pilot plant's bovine albumin contained 0.001 percent (Kendrick, 1964, pp. 326–330).

During this same period, the American Red Cross began laying the groundwork for a national blood donation system, making human blood more readily available to Cohn's group. In February 1941 nineteen weekly donors began giving blood for the Harvard research group to fractionate (Cohn, 1948, pp. 367–68). Clinical trials of human serum albumin were launched, and the human preparation, unlike bovine serum albumin, caused no adverse reactions (Kendrick, 1964, pp. 337–38). When war came on December 7, 1941, the laboratory shipped human serum albumin to treat casualties of the Pearl Harbor attack. It yielded striking results on the

few wounded and burned soldiers treated. A transfusion unit of normal human serum albumin was only one-fifth as bulky and one-sixth as heavy as an equivalent unit of dried plasma—important considerations for the Navy—and albumin could be heat-treated to inactivate any contaminating hepatitis virus, unlike plasma (Edsall, 1984). In January 1942 the Surgeon General of the Navy authorized contracts for the commercial preparation of human serum albumin, while hoping a bovine material could still be developed. Ultimately, however, the bovine project was canceled following a second serious reaction in February 1943.[15] At that time Armour Laboratories converted their plant to process human plasma, adding to recent production of normal human serum albumin by Eli Lilly, Squibb, Cutter, Lederle, Sharp and Dohme, and Upjohn (Cohn, 1948).

The demand for human serum albumin as well as plasma challenged the existing infrastructure for blood collection, the limitations of which had motivated the Navy to ask Cohn to develop a bovine blood substitute in the first place. The American Red Cross established their blood donation service in the fall of 1941, responding to what seemed an overwhelming request from the military for material (mostly plasma) for 300,000 transfusions. The following year, military demand for civilian blood increased six-fold.[16] The mass production system for dried plasma and serum albumin required the voluntary participation of millions of donors in order to provide raw material for the processing, and novel mechanisms were set in place to induce donation. The Red Cross organized donations at factory work-sites and solicited them through conventional advertising campaigns in newspapers and magazines (see Fig. 3). Donors were also recruited in motion picture showings through the cooperation of theaters with the War Activities Committee of the Motion Picture Industry. The various publicity campaigns were even more successful than the Red Cross expected. Blood donation became an important avenue of public participation in a war away from home. During the week in 1944 following the Allied invasion of Normandy, the American public contributed over 123,000 pints, well above the required weekly bleedings for scheduled production of transfusion supplies (Dulles, 1950, pp. 417–18).

The enormous reserve of collected blood allowed for exploration of other medical applications of blood derivatives. Cohn recognized that the human plasma proteins being discarded as by-products of serum albumin preparation could also be clinically useful. His separation method was further refined to yield five biomedical

[15]This reaction confirmed doubts raised by an earlier fatality in conjunction with the testing on Massachusetts prisoners in the Norfolk State Prison Colony in 1942. As Harkness has recounted (Harkness, 1996, pp. 73 ff.), the prisoner who died, Arthur St Germaine, was given a exceptional posthumous pardon in honor of his courageous contribution to the war effort as a volunteer experimental subject. See also Kendrick, 1964, chapter XII, 'The Bovine and Human Albumin Programs'.

[16]Minutes of National Research Council, Division of Medical Sciences acting for the Committee on Medical Research of the Office of Scientific Research and Development, Conference on the Preparation of Normal Human Serum Albumin, at the Department of Physical Chemistry, Harvard Medical School, Faculty Room, Boston, Massachusetts, June 6, 1942; Rare Books Room, Francis Countway Library of Harvard Medical School.

THE NEW YORK TIMES, THURSDAY, AUGUST 26, 1943.

JAPANESE TRANSPORT JOINS THE FLEET OF SUNKEN VESSELS

Crew members huddle against the rail to the right of the tentlike covering forward as a stick of bombs from a Liberator blasts the ship in an attack off Mussau Island, in the Southwest Pacific. This picture was made by a B-24 as it came in low to release the bomb that sent the craft to the bottom.

The New York Times (U. S. Army Air Forces)

370 WOUNDED MEN ON NEW ARMY LIST

Only 36 Were Injured Outside North Africa, Sicily and Southwest Pacific

TWENTY TWO NEW YORKERS

New Jersey and Connecticut Have 11 Representatives Each on Roll of Honor

Special to THE NEW YORK TIMES.

WASHINGTON, Aug. 25—The War Department made public today the names, with next of kin, of 370 United States soldiers wounded in action on half a dozen fighting fronts. All but thirty-six of these casualties occurred in the North African, which includes Sicily, and Southwest Pacific areas.

There are twenty-two New Yorkers and eleven men each from New Jersey and Connecticut on today's list. All enlisted personnel unless otherwise specified, they are:

New York

European Area

WIEGAND, ARTHUR H., second lieutenant; mother, Mrs. Isabelle E. Wiegand, Mount Vernon.

North African Area (Including Sicily)

CUFFNEY, ROBERT V.; mother, Mrs. Mildred Cuffney, Sonyea.

DWYER, ROBERT J., second lieutenant; father, William A., Dwyer, 78-12 35th Ave., Jackson Heights.

FORSYTHE, GILBERT D.; sister, Mrs. Ruth E. Eldred, Binghamton.

GALVIN, EDMUND C.; father, Robert J. Galvin, Buffalo.

GILHOOLY, JOSEPH F.; father, John J. Gilhooly, 895 E. 137th St., New York.

GOLDBERG, NORMAN R.; father, Samuel Goldberg, 1372 Riverside Dr., New York.

GORCE, WILLIAM J.; wife, Mrs. Dorothy Gorce, 410 E. 178th St., Bronx.

KUZ, HARRY M.; mother, Mrs. Michael Kuz, Scottsville.

LOHNES, ROBERT E.; mother, Mrs. Clara Lohnes, Roslyn Heights.

MULLIGAN, WALTER V.; brother, Frank L. Mulligan, 4401 Avenue D, Brooklyn.

OLSON, ARTHUR T.; mother, Mrs. Sarah Johnson, 160 East 84th St., New York.

OSTERMAN, WILLIAM M.; friend, Margaret H. Neugebauer, 19 Ingram St., Brooklyn.

O'DONNELL, MAURICE C.; aunt, Mrs. Elizabeth Dolan, 243 West 21st St., New York.

PARISI, JOSEPH A.; mother, Mrs. Carmila Parisi, Buffalo.

REYNOLDS, RUSSELL R.; mother, Mrs. Delia Reynolds, Seneca Falls.

SANTARSIERO, Frank J., mother, Mrs. Mamie Santarsiero, Port Chester.

Southwest Pacific Area

BEARDSLEY, WILLIAM C.; father, Ray Beardsley, Harrisonville.

DODD, CHESTER O.; mother, Mrs. Oscar Dodd, Windsor.

DRAKE, CHARLES H.; father, Joe H. Drake, West Clarksville.

HUNTLEY, HARVEY J., second lieutenant; wife, Mrs. Mary F. Huntley, Buffalo.

KIJANKA, WALTER; brother, John Kijanka, Buffalo.

New Jersey

Middle East Area

POWERS, JOHN J.; wife, Mrs. Dorothy C. Powers, Union City.

North African Area (Including Sicily)

AIKEN, RICHARD S., second lieutenant; wife, Mrs. Ruth P. Aiken, Ventnor.

LUCCHI, EDWARD R.; mother, Mrs. Nathalie Lucchi, Ridgefield Park.

MERICO, HAROLD, First Lieutenant, father, Michael C. Merico, Somerville.

RICE, JACOB G.; father, Effridge G. Rice, Madison.

STUTZER, JOHN; father, Charles Stutzer, Woodbine.

WINNICKI, ANTHONY; mother, Mrs. Anna Winnicki, Hillside.

YANKO, GEORGE, First Lieutenant; father, Jacob Yanko, Red Bank.

Southwest Pacific Area

BETZ, GEORGE W., mother, Mrs. Sarah B. Wiggins, Mount Holly.

PIQUETTE, THOMAS A., Jr., Second Lieutenant; mother, Mrs. Patience E. Piquette, Plainfield.

WHITSON, ANGUS M.; mother, Mrs. Margaret Whitson, Tenafly.

Connecticut

BURMA DRIVE SEEN UNDER NEW LEADER

Continued From Page One

tion in the Pacific when they stressed the emphasis that had been placed on Pacific strategy, but also early action.

2. The long-discussed campaign to retake Burma, entering wedge to southern China, to which communications must be established if the Japanese are to be ex-

tive duty in this war. He also saw sea service in the last war. He served in everything from U-boats to battleships and labored on the intricate problem of naval communications in the days when it was strictly in the experimental stage.

At the start of the war he commanded the fifth destroyer flotilla in the Kelly. Twice the Kelly was badly damaged, once by a mine and once by a torpedo. Lord Louis got her back both times. The Kelly finally went down off Crete in April, 1941.

Lord Louis got the D. S. O. and

Fig. 3. An advertisement in The New York Times *for blood donors adjacent to the US Army's published casualty list. August 26, 1943, page A4. Copyright © 1943 by the New York Times Co. Reprinted with permission.*

products from human plasma: serum albumin, serum gamma globulin, fibrin foam with thrombin, blood grouping globulins, and fibrin film. The highest priority product continued to be normal human serum albumin, but the other biologicals also began to be prepared by contract for the Navy from late 1943 through 1945 (Cohn, 1948, p. 376) (see Fig. 4).

These therapeutic products began to have an impact on civilian as well as military medicine. In 1944, the Red Cross set aside $1.5 million dollars 'for the nationwide distribution of immune serum globulin to state health departments, and it was reported that a sufficient quantity was available to give immunity from measles to more than 400,000 children' (Dulles, 1950, p. 418). By 1945, donated blood was transformed industrially into plasma derivatives used on battlefields and in civilian

Fig. 4. Medical products from fractionation of human blood plasma. From Cohn (1948).

clinics to achieve transfusion to shock victims, immunization of soldiers and children, reconstruction of the brain covering after neurosurgery, clotting in hemophiliacs, and typing of blood.

2. After the War: The Allure of Blood

By the end of the war, Edwin Cohn was something of a celebrity, as reports of the Plasma Fractionation Project appeared in newspapers, *Collier's*, *Atlantic Monthly*, *Life*, *McCall's*, as well as on television and radio programs. OSRD funding for the fractionation project ceased in 1946, and, like many researchers involved in the war effort, Cohn was expected to return to his prewar investigations. However, Cohn had filed for several patents on his fractionation process, and did not want to give up his work on blood-based therapeutics.[17] In fact, Cohn vacillated immediately after the war in choosing a course for research. Before reviewing the various ways in which human blood might have served as 'the right material for the job' (Clarke and Fujimura, 1992) for Cohn's postwar research laboratory, I will focus on the difficulties Cohn faced in articulating his research enterprise in terms of the 'applied' versus 'fundamental' categories to which he felt accountable. His dilemma reflected tensions in the larger political economy of science, as various science policies were considered and debated in the US after World War II. I suggest that the organization of biomedical research around key materials and diseases served as a way for scientists to achieve autonomy in laboratory research while ensuring medical relevance—and funding.

For Cohn, the motivations to continue working on blood grew out circumstances at hand, not simply the medical or commercial applicability of the research. The Dean of Harvard Medical School pointed to the many research opportunities generated by the war work in writing the Rockefeller Foundation for postwar funding:

> [Cohn's] group and the resources of their division should now, in my opinion, be prepared for a new attack on the fundamental problem. These young men and their colleagues have accumulated a vast amount of knowledge during the extraordinary opportunity of the five years. They have seen during this period more *material* than they might expect to see in an ordinary lifetime. Important scientific assets are here and should be preserved by a proper transfer of the efforts of this group from the applied to the theoretical area. During the past five years it has been necessary to postpone fundamental work which was simply crying to be done, in order to meet a series of deadlines in essential production—deadlines created by military emergency. [Emphasis added][18]

[17]Copies of various patent applications can be found in folder 'Patent Matters 1952', Edwin J. Cohn papers, Rare Books Room, Countway Library. It is worth noting that Cohn never earned any money from his patents. He did exercise substantial power in the pharmaceutical industry in terms of product quality control, but he was never motivated by financial gain *per se*. For more on the non-profit bodies Cohn established to administer the patents and license products, see Creager (1998b).

[18]Letter from Dean C. Sidney Burwell to Frank Hanson Blair of the Rockefeller Foundation, February 1945, as quoted in Cohn (1952).

Just a few years before Sidney Burwell made this funding plea, Cohn's work on plasma fractions had been presented to the Rockefeller Foundation Trustees as a payoff for their investment in abstruse research. The success of Cohn's plasma fractionation method was promoted as a 'neat job in applied science [which] provides a beautiful demonstration of the bread-and-butter value of theoretical research'.[19] Burwell presented the opposite argument, contending that applied work yields basic problems, in the form of research material, which deserves to be pursued. He emphasized how the needs of the war forced Cohn's coworkers to set aside work 'simply crying to be done', which in his view should no longer be neglected after their contributions to the victorious war effort.

Whether basic research is presented as the source of applications, or applied work is seen as generating fundamental problems, the value placed on undirected research in these excerpts echoed the arguments of those lobbying for a federal agency to support scientific research (the classic text being Bush [1945], 1960). The scientist's articulation of basic research prioritized the autonomy of the investigator above the mandate of societal needs. Cohn expressed his own views on science funding in a 1952 pamphlet entitled 'History of the Development of the Scientific Policies of the University Laboratory of Physical Chemistry Related to Medicine and Public Health, Harvard University'. In reviewing his laboratory's activities during the war, Cohn readily admitted that mistakes may have been made in managing the balance between the 'basic' and 'applied' work:

> It is probable that a fundamental error was made during World War II when most of the work in the Department of Physical Chemistry was committed to the development and control of methods of plasma fractionation. It was for this reason, in a reaction to the program of the war years, that retraction of the activities of the Laboratory, to exclude all but fundamental studies, was determined upon in 1946 . . . This project was equally in error; for the retraction which appeared necessary, in the interest of reestablishing the Laboratories' dedication to fundamental research, was greater than proved possible to establish, or desirable to continue. Thus, it has never appeared wise to discontinue, to the extent then contemplated, research or training in pilot plant methods in biochemistry, biophysics and biomechanics. This error in judgment has been a continuing embarrassment to the Administrators of the University and to myself, since the laboratory space which I assured President Conant would be adequate, has proven completely inadequate, and since the funds which I assured the Rockefeller Foundation would be adequate have also proven completely inadequate. (Cohn, 1952, pp. 4–5)

Cohn's equivocation in the above passage reflected the two competing aims of the longer text: that of convincing the readers of the importance of generous funding for 'fundamental' research, which should not be limited by programmatic or public mandates, and that of justifying the continued involvement of his 'fundamental' protein research laboratory in (expensive) activities related to pharmaceutical

[19] 'Wanted: Blood for 300,000 Transfusions,' Rockefeller Foundation Trustees Bulletin, RAC, RG 1.1, 200D, box 141, folder 1743.

production. In accounting for his war work, Cohn resorted to the conventional argument that basic scientific research generates technological innovations, in his case the development of an industrially useful plasma fractionation method. At the same time, he contended that the pilot plant work which he continued after the war should be regarded as 'fundamental' research in biomechanics. In one of his more florid passages, Cohn declared himself a '"conscientious objector" to announcing "projects" in advance, or reporting them in any but the tried methods of universities, scientific academies, or learned societies' (Cohn, 1952, p. 11).

Cohn's objections to project-oriented research were characteristic of the terms of debate about the federal funding of science in the US. One of the issues at stake in the postwar debates over the establishment of a National Science Foundation was the degree to which government-funded research would be responsive to perceived needs in society, and whether such responsiveness would (as Cohn feared) destroy creativity in research (see Penick *et al*., 1965; Kevles, 1977). The meaning of 'basic research' remained contested in the 1950s, as did the degree of constraint placed on a researcher by contract funding. One NSF official defended the freedom of investigation in government-sponsored research: 'The concept "basic research" may comprise the systematic endeavor, without preconception, to increase our knowledge and understanding of nature. It is the kind of research that some of our colleagues characterize as "pure science". If it is indeed pure, it derives that quality from uncompromising objectivity, unconcern over specific aims, and absence of intent to exploit results' (Klopsteg, 1955, p. 781). Speaking from an industrial perspective, the research director at Shell Oil Company differentiated pure from basic research: 'For my requirements', he wrote, 'I suggest three categories. We have pure research, which I define as the inquiry after knowledge for its own sake, without consideration or hope of practical gain. We also have applied research, the investigation carried out in response to immediate, direct, and obvious needs. Basic research is in between. By basic research, then, I mean the scientific inquiry carried on, not under pressure of immediate needs or in hope of quick profit, but with reasonable hope of some eventual payout' (Spaght, 1955, p. 785). He recognized that these categories were context dependent: in the case of Shell-sponsored research grants to university chemists and chemical engineers: 'These men are working on problems of their own selection; to us it is basic, to them it is pure.'

For medical research, considerations of federal funding of science were also connected to political debates about government involvement in health care and medical education (Strickland, 1972). The Public Health Service Act of 1944 enlarged the authority of the agency to 'pay for research to be performed by universities, hospitals, laboratories, and other public or private institutions' beyond the area of cancer investigations; the Division of Grants Research was soon expanded to assimilate unfinished OSRD contracts.[20] However, critics of the Public Health

[20]US Congress, P.L. 410, 78th Congress, 2nd session, 1944, as quoted in Strickland (1972), p. 19.

Service (many in private medical schools) vigorously opposed the interference by the federal government in medical research and education (Marks, 1992). National Institute of Health (NIH) officials had to defend the legitimacy of government research funding to prominent medical scientists at the same time as they had to protect 'their new authority to conduct a broad extramural program' from being assimilated into the proposed new national research agency (Fox, 1987, p. 460). With voluntary health agencies launching a research-based 'war with disease' in the wake of World War II, the NIH also expanded its funding of 'categorical' research.[21] Within this emerging political economy (discussed further below), human blood research could be viewed as basic or applied, clinically relevant or fundamental, depending on the context and particular situation.[22]

As long as his laboratory investigated blood, Cohn continued to receive research material from the Red Cross. The benefit of this alliance for Cohn's laboratory was obvious: the vast majority of the papers published from Cohn's laboratory for several years after the war were based on materials obtained from the Red Cross (see Fig. 5). Most of the studies used physical chemical methods and instruments (ultracentrifugation, electrophoresis) to characterize the purified plasma proteins. In the 1950s, Cohn's group was particularly interested in the interaction of blood proteins with each other and with other molecules, such as heavy metals (Cohn *et al*., 1953). Given that the starting material for the fractionation was pooled plasma from many donors (whose proteins would be slightly different due to genetic variation), the success of Cohn's laboratory in treating the plasma proteins as homogeneous species is striking. The limits of this approach were most pronounced

Year	Blood research papers	Total number papers
1940	0	13
1941	0	17
1942	1	12
1943	1	10
1944	23	28
1945	21	30
1946	12	16
1947	29	32
1948	15	20
1949	14	20
1950	15	22

Fig. 5. Number of papers published by the Department of Physical Chemistry at Harvard Medical School, 1940–1950, and proportion dealing with material prepared from blood donated by the American National Red Cross. Numbers taken from Cohn (1950a).

[21]On the role of voluntary health agencies in postwar science funding and policy, see Creager (1999) and Gaudillière (1998). On the rapid expansion of funding for categorical research, see Strickland (1972).

[22]I am not trying to suggest that perceived problems with the aptness of the fundamental *versus* applied categories for medical research were new in the postwar period; the novelty, rather, lies with the political context, with the US federal government beginning to sponsor 'basic' research contracts on a large scale.

in the study of antibodies, for the antibodies retrievable as gamma globulin (even from a single individual) are a whole population of proteins which bind many different antigens (Oncley, 1953).[23] In fact, physical chemical studies of gamma globulin contributed to the growing recognition of the diversity of antibodies in circulation. Cohn's group also continued to investigate the clinical efficacy of plasma fractions in collaboration with physicians (e.g., Thorn *et al.*, 1946). At the same time, the fractionation methods were being further refined using the pilot plant; as industries were using Cohn methods 5 and 6, the laboratory had developed Cohn method 10 (Björling, 1979, p. 30).

The Red Cross also benefited from their cooperation in supplying Cohn's laboratory with material, in that the usefulness of their donated blood in furthering biomedical research at Harvard helped further justify attempts to re-establish a national blood donation service for civilian health, which were slow and met much opposition. The new program was officially launched in January, 1948, at which time the ongoing blood donor projects in Massachusetts were brought under national control. On October 1, 1949 General George Marshall took up the presidency of the American Red Cross (Dulles, 1950, chapter 30, 'Toward the Future', pp. 525–39). Marshall was a prominent champion of Cohn's blood research and lobbied for greater public support of his laboratory (Lear, 1951). This alliance had its detractors: army surgeon Edward Churchill, a critic of the 'oversimplified physicochemical' approach to transfusion materials from the outset of the war, claimed that the Red Cross's commitment to plasma and plasma fractionation reflected 'a huge vested interest [which] had been built up starting from assumptions and erroneous thinking' (Churchill, 1972, pp. 45 and 48).

In his preference for working with a large team of researchers and collaborators, his patents, and his publicity, Cohn struck an image far from that conventionally associated with a university professor. One writer for *Collier's* weekly noted:

> In any scientific gathering, Dr Cohn is always the man who looks least like a scientist. The perpetually new-scrubbed pink of his upholstered cheeks, the immaculate white of the fringe around his pate, the perfect fit of fashionable cloth across his shoulders, and the well-brushed sound of British phrasing in his speech all hint the presence of a brisk and debonair investment-banker–clubman. The impression is disconcerting to those who look for a vague and dreamy personality to fit Cohn's world-wide reputation as a pure—i.e. theoretical—protein chemist. Nevertheless, it is amazingly accurate. For within the research realm this Harvard professor operates on a scale that would be fully appreciated only in the world of industrial finance. (Lear, 1951, p. 12)

Cohn's coworkers recognized the ways in which he resembled an industrial manager. One was quoted as saying, 'Most scientists are quiet, meek little guys who like to sit in a corner and think. Cohn is a tycoon. He runs his lab like General

[23]By contrast, in hyperimmune plasma or serum, antibodies to a single antigen are abundantly produced, making the gamma globulin fraction less heterogeneous, at least in terms of antigen binding.

Motors. The kind of team work he demands often makes it impossible to tell with whom any scientific idea originates' (Lear, 1951, p. 13). In a similar vein, a Rockefeller Foundation officer wrote in 1950, 'E.J. Cohn is not a first-class scientist, but is an excellent entrepreneur and promoter. His main weakness however is that he directs his laboratory so completely that the chance of their observing and finding anything "sideways" is negligible and in this he seems therefore to resemble the worst of industrial research'.[24] In the wake of debates in Congress over the merits and flaws of directed research programs, this comment upon Cohn's penchant for control was very pointed. At the same time, the pursuit of scientific knowledge by the management of large teams was rapidly gaining legitimacy and funding in physics (Galison and Hevly, 1992).

One research venture which engaged Cohn's laboratory in the early 1950s particularly caught the public imagination. Cohn had become dissatisfied with the way in which his plasma fractionation scheme denatured some therapeutically valuable blood components (Tullis, 1990; Tullis *et al*., 1956). Aiming to preserve the short-lived proteins and blood cells which could not survive plasma fractionation, he constructed a blood fractionator which could be attached directly to a blood donor's arm (Fig. 6). A *New York Times* reporter wrote of its sensational introduction:

> The world's tiniest chemical processing plant, about the size of a card table, was wheeled into a Yale University lecture room here this morning and demonstrated at the annual meeting of the National Academy of Sciences. The tiny plant, of plastic and stainless steel, performs chemical engineering steps that are virtually as complex as those of a vast petroleum refinery.[25]

Cohn patented the machine, and the Arthur D. Little company was producing the first customized models when Cohn died in 1953.[26] Cohn's longtime collaborator at Children's Hospital in Philadelphia, Joseph Stokes, Jr, first adapted the ADL Cohn Fractionator for plasmapheresis in the mid-1950s, an important precedent for further developments in blood-derived therapies, such as the isolation of clotting factors (Stokes and Smolens, 1957). Interest in Cohn's machine survived him; *Life* magazine featured the new blood automated plasma collection and fractionation method on April 23, 1956.

Can the evident public fascination with research on human blood be fully accounted for by interest in high-tech plasma-processing machines and improved therapeutics? The cultural meanings of blood are so varied, vast, and entrenched in society that the available symbolic associations with Cohn's blood fractions were myriad. The popularization of Cohn's research may have mobilized deeply held notions of blood as life-giving on the one hand, or as linked to racial identity on

[24]WFL diary, September 15, 1950, RAC, RF 1.1, 200D, box 141, folder 1746.

[25]Robert K. Plumb, 'A Tiny New Plant Processes Blood', *The New York Times*, 7 Nov. [1952], clipping in Cohn papers, HUG 4290.2, Pusey Archives, Harvard University.

[26]See correspondence under 'Plasmapheresis Grants', Joseph Stokes, Jr, papers, American Philosophical Society, B: St65p.

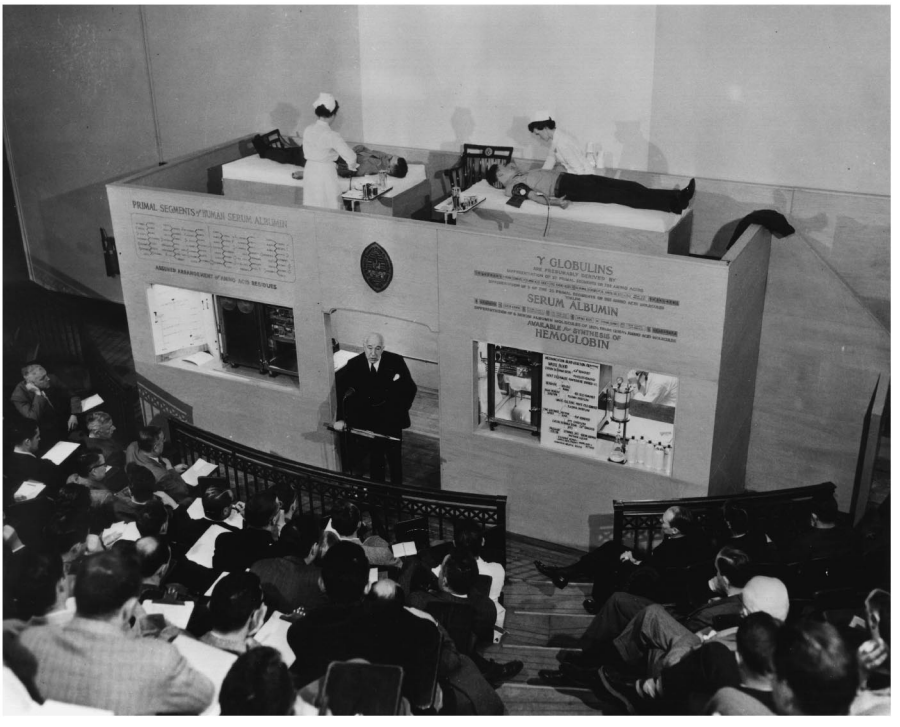

Fig. 6. Demonstration of Cohn's portable fractionator with the two blood donors, assisted by nurses, situated above the centrifuge and separation apparatus. The seal of the University Laboratory of Physical Chemistry related to Medicine and Public Health, which Cohn designed for the laboratory's opening in 1950, is depicted on the supporting enclosure, along with printed information about therapeutically useful plasma proteins. Reproduced by permission from Harvard University Archives, Pusey Library.

the other (Wailoo, 1997). However, the most striking explicit connection offered by his contemporaries was that of his blood research as a means for transforming death into life. Cohn's contributions to plasma fractionation were repeatedly used to justify the costly war to the public, and to rationalize the scientific mobilization for the war on the basis of the benefits it yielded to civilian life. A newspaper article reporting on Cohn's work, in *The New York Times* on September 13, 1944, opened with these lines:

> This war, which has caused the flowing of more rivers of blood than ever before in human history, has also led to the greatest progress in our knowledge of this vast ocean of life, its multiplicity of constituents and the mechanism of its many systems, according to Prof. Edwin J. Cohn of Harvard. The new knowledge, which is already saving countless lives of our fighting men on the battle fields, promises in the generations to come to give back to mankind more lives than the war has taken.[27]

[27]William L. Laurence, 'War Speeds Study of Blood System', *The New York Times*, September 13, 1944, RAC, RG 1.1, 200D, box 141, folder 1744.

Similarly, Yale physiologist John F. Fulton, writing for the *Atlantic Monthly* in 1945 on medical advances from the war, introduces Cohn's contributions in this way:

> When one turns to blood and the advances that have been made in the study of this circulating tissue, one becomes acutely aware that wars, whatever their horrors, may contribute to creative human endeavor in that they stimulate work of such quality as has come out of the blood-fractionation program. (Fulton, 1945, p. 111)

The impact of plasma fractionation on civilian medicine was presented as a means for redemption after a devastating war. The powerful appeal of Cohn's contributions to saving the lives of bleeding soldiers and extending the lives of civilians was that it provided a counterweight to the strong association of blood with killing and the losses of war. As the achievements of researchers such as Cohn were extolled as one way of finding meaning in the war, they were also useful for justifying new levels of public funding for scientific research.

While the advances in transfusion technologies became an important example of how advances in medicine during war benefited public health, the military interest in blood substitutes never entirely receded. The brewing Korean war secured the re-establishment of the Red Cross's national blood donation service, and motivated the military to once again stockpile plasma and serum albumin (Dulles, 1950). Cohn's attention to the formed elements of blood (the blood cells which were discarded in plasma fractionation) in the early 1950s grew out of hopes for developing methods for preserving whole blood and its cellular constituents in order to have better reserve therapeutics in case of military emergency. Research on white cell preservation by James Tullis, who was directing Cohn's Blood Characterization and Preservation Laboratory, was supported by the Atomic Energy Commission with the aim of developing medicine for the age of the atomic bomb. As described to the public by John Lear, writing for *Collier's* magazine, Tullis's preserved blood corpuscles 'hold man's first glimmering hope of replacing, by transfusion, the disease-fighting white cells destroyed by gamma rays in atomic-bomb explosion victims' (Lear, 1951, p. 59). Cohn's blood laboratory was well-suited to both medical needs and public anxieties in the atomic age.[28]

3. Blood Groups: Organizing Postwar Research by Material

Due in part to his substantial contributions to the development of a new industry of blood-derived therapeutics, Cohn is remembered more often for his contributions to blood research than to protein chemistry (see e.g. Dameshek, 1950a, p. 390). In part, the special recognition of Cohn's role in blood research derives from the coalescing of hematology as an important medical specialty in the mid-twentieth

[28]For a different understanding of the intersection between the atomic age and postwar biology, see Rasmussen (1997).

century (Wintrobe, 1985). Blood research was not new to biochemistry: scientists had been using blood (animal or human) as a material for chemical investigation since at least the nineteenth century. A review of some of the more prominent chemists who worked on blood shows that Cohn's assimilation into the history of (bio)medicine might be understood as part of a new postwar ecology of knowledge.

When Arne Tiselius developed his electrophoresis apparatus in the 1930s, his model demonstration was the separation of α, β, and γ globulins from horse blood serum (Tiselius, 1937; Kay, 1988, 1993a). Tiselius and his colleague Kai Pedersen were among many prominent protein chemists who analyzed the binding of small molecules to serum albumin. The binding of bilirubin to albumin proved a fruitful model for protein binding, and Pedersen's coworkers recalled that they 'studied this problem in different clinical conditions with the aid of electrophoresis and ultracentrifugation' (Blombäck and Hanson, 1979, p. xv). Tiselius and Pedersen's mentor The Svedberg also used serum proteins (albumin, globulin) in the early 1930s to study protein structure in the analytical ultracentrifuge (Pedersen, 1983, p. 49). Hemoglobin, the most thoroughly studied blood protein (but not a plasma protein), has served as a key model protein in numerous research programs aimed at understanding vital processes using the tools of chemistry and physics (Kamminga, 1993; de Chadarevian, 1996). To cite one instance among dozens, Svedberg's experiment sedimenting hemoglobin in 1924 in his analytical ultracentrifuge has attained something of a mythic status for demonstrating the discrete molecular nature of proteins (Pedersen, 1983, pp. 240–41). For protein chemists since the eighteenth century, clinical materials and problems have been essential resources to be exploited for furthering the science of proteins, but their research efforts remained, by and large, 'fundamental' and based on protein models which were not clinically derived (Holmes, 1995).

A predecessor in the chemistry of blood much closer to Cohn was his mentor L.J. Henderson, for whom the Department of Physical Chemistry was founded (to keep Henderson at Harvard when he was offered a professorship at Johns Hopkins).[29] Henderson worked on the physiology of blood from a more holistic perspective than his protégé. Rather than fractionating blood into its components for characterization, Henderson studied blood as a system of molecular equilibria. Deriving a general expression for acid–base equilibrium (the so-called Henderson–Hasselbach equation), he applied this quantitative principle to blood as a chemical system based on observations of the interrelated amounts of various molecules. In his classic papers, 'Blood as a Physicochemical System', I and II, he presented nomograms 'of all the physicochemical factors which are known to be involved

[29]Letter from David Edsall, Dean of Harvard Medical School to A. Lawrence Lowell, President of Harvard College, regarding the establishment of a Department of Physical Chemistry, 29 Jan. 1920, Deans' Files, 'Departments, HMS and HSDM: Physical Chemistry, 1920–49', 1:580, Harvard Medical School Archives at the Rare Books Room, the Francis Countway Library of Medicine. See Edsall (1950, 1979); Creager (1998a), for more on the early years of the department.

in the complex equilibrium of the blood' (Henderson, 1921, Henderson *et al*., 1924, Hankins, 1999).

Cohn saw himself as following in Henderson's path. In 1946 he delivered the Silliman Lectures at Yale University, and he intended to transcribe them into a book entitled *Blood: A Study in Protein Chemistry*, after Henderson's monograph, *Blood: A Study in General Physiology* (Henderson, 1928), drawn from the Silliman lectures of 1928 (Edsall, 1961). Yet one cannot help but be struck by the differences between the approaches of Henderson and Cohn, one classically holistic and one a chemical reductionist, even as both worked as physical chemists on blood in the very same laboratory.[30] Moreover, Henderson's interests in physiological regulation were much broader than his interest in blood. Leaving the Department of Physical Chemistry in Cohn's able hands, Henderson focused his energies in the 1930s on the Fatigue Laboratory he helped establish at Harvard Business School (Dill, 1967).

While blood and blood proteins had been important in the development of protein chemistry from the nineteenth century, World War II proved to be a turning point for the development of blood as the organizing material for a field of research. This transition was marked by the establishment of a new journal in 1946, *Blood: The Journal of Hematology*.[31] The first volume opens with a foreword penned by editor George Minot, the noted Harvard professor of medicine, and the very first article is 'Blood: A Brief Survey of Its Chemical Components and of Their Natural Functions and Clinical Uses' by Edwin J. Cohn. An endnote to the first volume calls attention to the fact that 'the emergence of a new journal with universal appeal should coincide with the first year of peace after so many years of bloodshed', drawing on the same cultural significances invoked in presentations of Cohn's work. In addition, this endnote offers a rationale for the journal's bold title: 'At first glance, it seemed too striking, but the more one thought about it, the more right it seemed to be. Hematology seemed to denote more the strictly morphological approach, whereas present day studies of the blood were often functional and had to do with *the blood itself*' (Anonymous, 1946; emphasis added). Publications included both laboratory studies and clinical reports, with particular attention to new therapies as well as scientific meetings.[32] The perceived need for an international journal devoted to this key biomedical material was confirmed; within a year the journal achieved a world-wide circulation of 2500 subscribers. In fact, the editor noted that there was much 'talk about the country regarding the prospects of founding a national society for the study of the blood' (Dameshek, 1947).[33]

The ascendance of blood as a material for organizing research communication

[30]For more on Henderson, see Parascandola (1971), Cross and Albury (1987), and Amsterdamska (1998), pp. 62–64.

[31]Published, beginning in January 1946, by Grune and Stratton.

[32]For examples of special attention given new therapies, see Dameshek (1949, 1950b).

[33]The interest in new societies for blood research and therapy was not restricted to the US. 1948 saw the founding of both a European Society of Hematology and an International Society of Hematology, which were then merged in 1965 (Bernard, 1992, pp. 200–3).

marked the formation of a new postwar political economy of biomedical research, in which diseases and clinically relevant materials were used to mobilize research support and organize research units. This approach drew strength from the innovative fund-raising and research support around the disease of poliomyelitis by the National Foundation for Infantile Paralysis (best known by their annual fundraising campaign, the March of Dimes) (Benison, 1972, Creager, 1999). It flourished as a means of organizing federal support for biomedical research after World War II, especially for the National Institutes of Health, which became a major postwar supporter of life science research.[34] Of the twenty organizational components of the National Institutes of Health in 1976, nine were named after organs and diseases, and six of those were established between 1948 and 1950.[35] Cohn was a founding member of the Study Section on Hematology in the newly established National Institutes of Health Research Grants Program in 1949, funding which enabled the expansion and maturation of this field (Wintrobe, 1985). Support from NIH enabled Cohn to build a new Blood Preservation and Characterization Laboratory at Harvard, dedicated on January 8, 1951. Cohn's re-orientation of his laboratory around human blood and its components was mirrored by a trend in publication, as gauged in *Index medicus*. The length of research listings per volume of both 'blood' and the more specific 'blood proteins' increased rapidly from 1945 to 1955, and even more striking is the dramatically increased percentage of listings under 'blood' which were sublisted as 'blood proteins' (Fig. 7). The Cohn fractionation method provided a technical framework for this productive research field and the new blood donation infrastructure supplied material.

One challenging issue which accompanied the expansion of research on blood and blood proteins was that of standardization. Investigators in a variety of settings, as well as in several national contexts, had previously isolated various human blood proteins. Establishing which of these prior isolates were the 'same' as the products of plasma fractionation became an important and demanding task. For instance,

[34]G. Burrough Mider, in his extensive study, 'The Federal Impact on Biomedical Research', asserts the following: 'Support [for medical research in the US] first came from private sources, followed by public philanthropic organizations, typically American, from industry, and finally from governments, principally the federal purse. The varied interests complemented and supplemented each other's efforts. Yet medical research failed to flourish until the categorical approach, spearheaded by the March of Dimes, made a strong emotional appeal to a public acutely conscious of the diseases that afflicted them. Consequently, legislators voted larger and larger sums in response to the demands of their constituents who were being systematically barraged by propaganda from the same agencies that solicited funds to support research in the diseases of their special interest' (Mider, 1976, p. 806).

[35]My numbers are taken from Mider (1976); the nine to which I refer are the National Cancer Institute (1937), National Heart and Lung Institute (1948), National Institute of Dental Research (1948), National Institute of Allergy and Infectious Diseases (1948), National Institute of Arthritis, Metabolism, and Digestive Diseases (1948), National Institute of Mental Health (1949), National Institute of Neurological and Communicable Disorders and Stroke (1950), National Eye Institute (1968), and the National Institute on Aging (1974). The National Cancer Institute is the sole exception to the *postwar* timing of the inauguration of institutes around organs and diseases; established in 1937, it provided another American precedent (similar to the March of Dimes funding of polio virus research) for the expansion of disease-based research support after World War II.

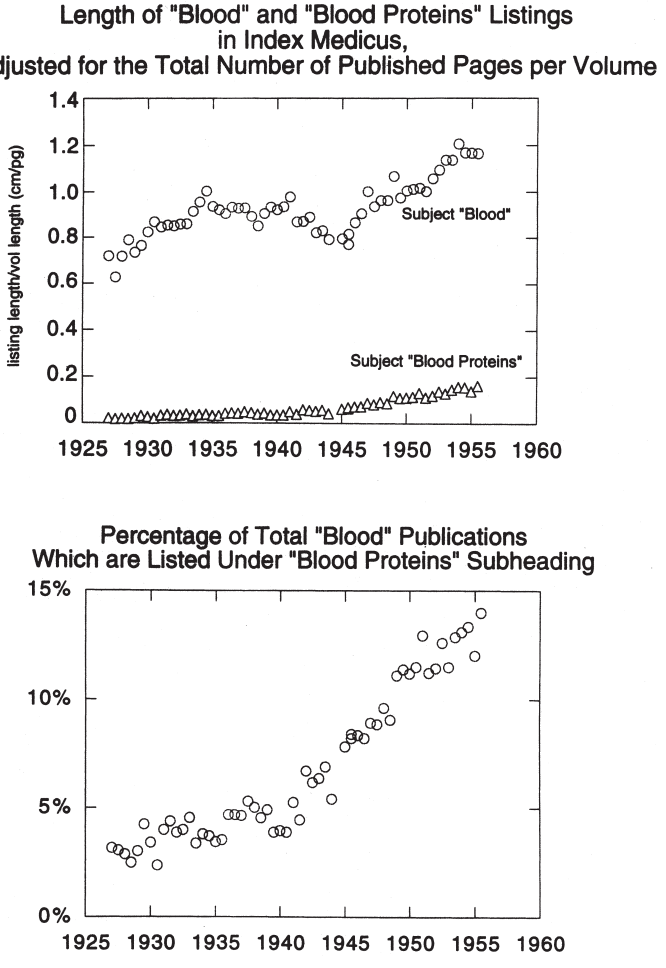

Fig. 7. (a) Length of 'Blood' and 'Blood Proteins' listings in Index medicus, *adjusted for the total number of published papers per volume. (b) Percentage of total 'Blood' publications which are listed under 'Blood Proteins' subheading in* Index medicus.

C.-B. Laurell reviewed the various terms for blood clotting factors in 1952 for readers of *Blood*, attempting to specify the multiple synonyms in the literature for the various implicated factors (Laurell, 1952). The universalization (i.e. literal internationalization) of human blood components was aided by increasingly prevalent reference to the Cohn method of fractionation, which brought welcome standards for reproducibility to the field.[36] As one review author asserted, 'Plasma

[36]In the historical introduction to a 1976 book on plasma proteins, Kai O. Pedersen stated, 'The introduction of the cold ethanol method for the fractionation of plasma proteins and its importance can hardly be overrated. It opened possibilities for preparing plasma proteins efficiently and in a reproducible way. . . . The Cohn method is now used in a number of countries all over the world, and it has been further developed.' (Blombäck and Hanson, 1979, pp. 11–12)

fractionation with ethanol has become a technically routine procedure, ever since the extensive work of E.J. Cohn and his group at Harvard Medical School' (Heide *et al*., 1977, p. 548). Notably, in the years following the war, Cohn's Harvard laboratory was flooded by investigators who came from abroad to master Cohn's methods.[37] To this day blood protein researchers make reference to the various 'Cohn fractions' in their publications.[38]

4. Conclusions

The selection of human blood as a material for biochemical fractionation irrevocably altered the career of Edwin Cohn, drawing him into the world of high-profile medical breakthroughs. This was no mean feat. In an evaluation of his work for the Rockefeller Foundation in 1944, one officer reminded colleagues of Cohn's former realm of protein research.

> The scientific level of the work in this laboratory has always been distinguished. But it is certainly true that the work over the first ten or fifteen years was pretty abstract and theoretical. Professor Cohn and his colleagues carried out a large number of difficult and precise experiments to determine the physical-chemical properties of large protein molecules. As late as 1938 the Rockefeller Foundation, making an appraisal for itself of this project, included in its statement the sentence, 'The work has been painstaking, abstruse, and likely only slowly to come to widespread recognition for its essential importance.'[39]

By contrast, in 1952 Cohn was listed among 'The 100 Most Important People in the World Today' (Robinson, 1952).

I have contended that Cohn's material, human blood, played an important role in the transformation of his career. But perhaps my argument about the significance of his material can be confronted most directly asking this question: What difference did it make that Cohn's laboratory shifted their scientific focus from cow's blood to human blood during the war?[40] At the level of infrastructure, the reliance on human donors was very consequential, and depended on the cooperation of the Red Cross. Blood is the easiest to procure of all human tissues, at least in limited amounts. One historian and former hematologist has speculated that the ease of obtaining human blood was a major factor in the rise of hematology as a research specialty (Tauber, personal communication). Cohn's biochemical approach, devised

[37]From 1946–1948 alone, twenty visiting investigators worked in the laboratory, and only four were from the US. Most of the international researchers came to Cohn's laboratory to learn his plasma fractionation method; they came from Belgium, Switzerland, Argentina, England, Canada, Finland, China, France, Scotland, and Sweden (Scatchard, 1948).

[38]A Medline search on June 17, 1998 for the term 'Cohn fraction' in the title of publications turned up 50 recent references.

[39]Summary of history of Department of Physical Chemistry, January 26, 1944, RAC, RG 1.1, 200D, box 141, folder 1744.

[40]I am indebted to Susan Lindee for this formulation.

for the mass-production of therapeutics, required blood on a new scale; his fractionation technology and the Red Cross National Blood Donation service grew up together under the conditions of World War II. The push for pharmaceutical products during the early years of fractionation meant that a host of less urgent scientific questions awaited medical researchers after the war. Cohn's laboratory continued consuming blood for research after the war in large part because the pilot plant and the association with the Red Cross were already in place.

What did the transition from bovine blood to human blood mean in terms of public perception? Pragmatically speaking, the reliance on human material was attributable to the failure of bovine blood substitutes rather than to any symbolic preference for human blood. If cow's plasma could have been made to work as a source for a transfusion material, there is no reason to think that it would have been rejected or devalued in the imagination of patients or the public. Horse blood had provided the material for serum therapy for decades, and in her study of xenotransplantation, Susan Lederer has found that ordinary people in the first third of the twentieth century were surprisingly unsqueamish about the prospect of receiving animal skin or parts (Lederer, 1998). Lederer's findings suggest that the animal/human boundary, while significant, may not have been as symbolically fraught in the first half of the twentieth century as we tend to imagine. But once the therapeutic advantage of human blood as a source for serum albumin had been demonstrated, the provenance of the new medical products enabled the public perception of Cohn's fractions as civilian sacrifice incarnate, the literal end-products of what Americans gave to save their fighting men. At the same time, plasma fractions were never conceptualized as carrying human identity to the same degree as donated whole blood: at a time when transfusible blood was classified by not only the blood group of the donor but also the race (Wailoo, 1997), plasma fractions, produced from pooled donated blood, were apparently universal.

Developments in blood protein research after Cohn died have served to reinforce the molecular approach to hematology which his techniques helped set in motion. Cohn's chemical methodology drew on the similarity between the same blood proteins from different individuals in order to purify macromolecules from pooled plasma. The pooling of blood to purify statistically 'normal' constituents has been fruitful not only for research but for therapeutics, particularly the mass-production of gamma globulin and clotting factors (Janeway *et al*., 1966, Kasper and Lusher, 1993). But another of the striking postwar success stories in blood protein research has concerned molecular diversity: the study of hemoglobin from patients with sickle cell anemia, which provided by the early 1960s the largest ensemble of human molecular variants in biomedical research (de Chadarevian, 1998). Ingram's breakthrough observation in 1958 that the sickle cell phenotype was due to a single amino acid change in the hemoglobin polypeptide chains confirmed Linus Pauling's formulation of genetic disease as seen in sickle cell anemia (Pauling *et al*., 1949;

Ingram, 1956, 1957), and in this sense exemplified the salience of genetics for molecular medicine.[41]

The turn to genetic engineering in the production of new drugs in the last two decades may supplant the chemical approach to blood medicine developed during World War II. However, the legacy of Cohn's fractionation for health technologies may be viewed more broadly. First, the addition of plasma fractionation to the pre-existing practices of whole blood transfusion expanded the scope of exchanges of blood and its constituents. The large-scale, anonymous sharing of blood as a source of therapeutics, established under conditions of war, has proliferated in postwar civilian medicine (bringing its own health hazards). The distribution of blood derivatives relies on both willing donors and mediating laboratories to universalize (often literally de-antigenize, and so de-individualize) materials from the human body. Second, the circulation of blood and its parts among donors, industries, hospitals, laboratories, and patients set a precedent for the medical exchange of many other body constituents, requiring other new infrastructures for human materials. From organ transplants to the donation and sale of gametes for *in vitro* fertilization, biomedical technologies have permitted the increasing bodily fragmentation and reassembly of individuals.[42] If the philosophical deconstruction of the self exists as 'postmodern' issue, it is in the laboratories of biochemists, immunologists, and molecular biologists that the material boundaries of the body have been challenged (Tauber, 1995). In the history of the fragmentary and redistributed human body, Edwin Cohn's Plasma Fractionation Project would stand as an important chapter.

Acknowledgements—I thank Susan Lindee, Gerry Geison, Charles Gillespie, Charles Rosenberg, and participants at the workshop on Human Materials at Princeton University, March 15, 1995, for their comments and criticisms in response to the original version of this paper. Since that time, Harmke Kamminga, Bill Creager, and an anonymous referee offered valuable suggestions for its revision, for which I am grateful. I am also indebted to John Edsall, Douglas Surgenor, and Alfred Tauber for profitable discussions related to the scientific aspects of this paper, although I alone am responsible for the perspective taken (and any errors) in this account. Finally, I thank Richard Wolfe at the Countway Library and Thomas Rosenbaum at the Rockefeller Archive Center for their generous help with archival materials, and Douglas Starr for sharing sources.

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[41]See Kay (1993b), pp. 274–75.

[42]On transplantation, see Brent (1997).

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