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John Tileston Edsall: some selected biography and personal reminiscences

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Abstract

This paper has been written in honor of John T. Edsall. Its purpose is to review briefly the status of science during his active years and the combination of personal qualities and upbringing which resulted in his enormous impact on the field of biochemistry. There was an unusual combination of deep knowledge and interest in many intellectual areas by no means restricted to science; the large number of individuals he met by intent or by chance, many to become fast friends for life, who themselves became distinguished in science; and last but not least his influence on science policy through very clear statements and his moral positions on questions of the day.
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1. Introduction and early years

Rooted in his personality and century-long alertness of mind, John Edsall served and guided his science throughout an active career of much the same duration. His life can be chronicled into five stages which overlap to some extent in time: *first* his childhood and formal education through Harvard Medical School which included a very important 2 years leave of absence spent at Cambridge University and other locations in Europe trying his hand at research and meeting many of the people with whom he would interact through the rest of his career; *second* the period of full time laboratory research which ended when he closed his laboratory in 1971; *third* his formal teaching where the major component was the Tutorial Program in Biochemical Sciences for Harvard College undergraduates; *fourth* his major editorial work as Editor in Chief of the *Journal of Biological Chemistry* and the initiation and perpetuation of the review journal *Advances in Protein Chemistry* which, through his devotion and efforts, affected the

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[1] Introductory explanation: The authors of this paper, abbreviated FRNG and FMR, attended the same preparatory school 2 years apart, separated for college, and then found themselves, quite unexpectedly and unplanned, in the same unusual Department in the Harvard Medical School (Physical Chemistry!) as graduate students in the mid to late 1940s and early 1950s. The 2-year differential remained, of course, and our experiences and memories were not always the same, but the friendship was cemented.

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Fig. 1. John T. Edsall being unusually attentive to the camera.

careers of many protein chemists outside of his own research group; and *fifth* his interest and efforts in the social and policy aspects of science in general (Figs. 1 and 2).

As an undergraduate at Harvard College, Edsall was guided by Lawrence Henderson, a great correlator and author of 'The Fitness of the Environment', largely concerned with the internal milieu and its remarkable resemblance to ancient seawater. Significantly, Henderson presented a seminar series on the writings of Vilfredo Pareto, Italian economist and social scientist, a great correlator referred to in his day as the last of the great system builders. Henderson was responsible for the establishment of the Department of Physical Chemistry at the Medical School, the recruitment of E.J. Cohn and the later recommendation of Edsall to him. (This was the only such Department in any medical school then or since.)

Another very important shaping experience was his stay in Cambridge, England, a 2-year diversion from his medical studies in 1924. He was located in the Department of Biochemistry organized by Sir Frederick Gowland Hopkins, recognized internationally as the most active and forward-looking department in the field. Besides the exposure to the remarkable faculty, the young Edsall cemented his friendship with Jeffries Wyman, Jr. his closest lifetime colleague. Edsall reminisces with obvious pleasure about his vacation walking tour in Corsica in which they were joined by a junior friend from Harvard, J. Robert Oppenheimer.

Before the completion of his MD degree, Edsall had hands-on instruction on studies of muscle from Alfred Redfield, a distinguished physiologist and

Fig. 2. John T. Edsall in a frequently seen posture. See text.

his mentor for the year. This work led to a lifelong interest and key studies later in Cohn's laboratory especially with the elegant Swiss, Alexander von Muralt. Redfield suggested that Edsall talk with Edwin Cohn about joining his group. He did, and Cohn agreed to take him on. That decision established Edsall's major research collaboration over the next three decades.

2. The department of physical chemistry

Before 1940 this group was very actively engaged in testing the chemical properties of proteins, amino acids and peptides, particularly in terms of their ionization properties, salt interactions and solubility properties. The driving force for this pursuit was at first largely to test and thereby establish that biological molecules obeyed physical chemical rules of behavior. Strangely, many chemists early in the century believed that biological materials partook of some 'life-force' that would escape detection and quantitation by the usual criteria. The multiplicity of proteins in accessible body fluids such as blood meant that separation of components was a crude business, the results variable and enormously sensitive to the details of separation conditions. Taking the hard data from the pure amino acids and peptides and applying it properly to proteins, generally of uncertain composition and purity became the major effort of the whole Department.

Even the size range of protein molecules, if indeed they should be so-called, was the subject of much debate. The discovery by Sumner that enzymes were proteins would at first sight seem to clinch the notion that numerous specific proteins make up any initially isolated material mixture, and that the magic was in the multiplicity. However, on the one hand, coenzymes and other factors were being discovered before 1930 and the notion could be sustained that the protein moiety of an enzyme had the role of a carrier, not a participant in catalysis. On the other hand, methods for the direct determination of the size range of proteins were very limited. Many attributed protein behavior to materials of modest size. A turning point came with the joint papers of Cohn and Conant in 1926 in which it was shown that the rigorous removal of salt and other solutes from the solutions of proteins in phenol reduced the freezing point lowering to very low values consonant with a large molecular weight of the protein solute, which the data indicated to be greater than 10 000. Likewise, Svedberg's ultracentrifuge studies established the macromolecular nature of proteins, a result much to his surprise since he started out thinking that they were colloidal aggregates.

Svedberg concerned himself with some dissociable protein systems, exhibiting different molecular sizes according to changes in pH or other variables. The Swedish investigators had experience with colloidal systems dispersed in the laboratory into ranges of sizes depending on precise conditions for their generation. The multiplicity of characteristics reflected in size and electrophoretic distinctions of proteins could be viewed as analogous to those of artificial preparations of colloidal dispersions. The exquisite sensitivity to environmental conditions of isolation of pure proteins seemed to have little parallel in chemistry outside of recipes for preparing simple minerals or artistic triumphs such as gold sols in the colloidal state. Svedberg's suggestion that proteins had an underlying mass of approximately 17 000 daltons or multiples thereof, proved a useful working hypothesis in certain systems accessible to study at the time. Cohn argued vigorously for the individual and specific sizes and characteristics of proteins. However, he was to dabble in numerology in the last months of his life by attempting to predict protein structure from knowledge (meager at the time) of amino acid composition. In this area he could be said to have anticipated the valuable empirical correlations of amino acid sequences with structural elements set out by G.D. Fasman two decades later.

The remarkable collaboration between Cohn and Edsall beginning in 1926 at the Department of Physical Chemistry reached a culmination in the masterful book '*Proteins, Amino Acids and Peptides*' with its subtitle 'As Ions and Dipolar Ions'. It was completed in 1941 and published in 1943. It was the good fortune of FRNG to be assigned it as a text in a class at McGill University in 1944. The preface names 23 collaborators in the research portrayed in the book and carefully correlated with work in other laboratories. The leadership of Cohn and Edsall was augmented in the laboratory by J. Lawrence Oncley who provided physical chemical acumen in the laboratory second only to the role of George Scatchard at M.I.T., Edsall and Cohn provided strong leadership over the 15 pre-World War II years of this stage of their collaboration. Anyone working with E.J. Cohn filled perforce a supporting role. Edsall brought understanding and humor to the collaboration, his greatest skill perhaps lay in the gracing of an argument with the utmost logical reliability and awareness of the needs of his audience. In this he has always drawn on a formidable memory.

As an example, FMR remembers, with some embarrassment, his own lecture in Edsall's seminar course, the assignment being a section on multiple equilibria in Wyman's recent review on heme proteins. He was caught trying to sidle around one of the particularly relevant equations. John, very politely, said 'Fred maybe it would be well to show the group the derivation of this equation'. FMR admitted that he had spent 2 full days trying to derive the equation without success and handed the piece of chalk to Edsall. The latter went to the board and without a moments hesitation wrote down the derivation in approximately 2 min, while carefully explaining the interchange of the subscripts of the four relevant variables which, of course, made everything appear very easy. The end of a promising graduate career seemed clearly in sight at that moment.

The contrasting styles of thought of Drs Cohn and Edsall came out one weekend afternoon at Cohasset, Massachusetts as guests of Professor and Mrs Cohn. A tennis party of Cohn and Edsall and Oncley was assembled and FRNG found himself as Oncley's partner at doubles. Seen but not heard. At the point of 30–40 or 40–30, Oncley asked the pertinent question as a good scientist: ''What's the score?'' Cohn broke into a smile and kept silent while Edsall gestured back and forth, ''Now let me see....'' At this point Cohn spoke up: ''That's the difference between John and me. I know the score and he can remember everything that happened and will work it out, eventually''.

3. Bench research

Two of Edsall's early research projects in the 1930s were of particular importance. The *first* was the use of the recently discovered Raman spectroscopy to show that at neutral pH both the carboxyl and amino groups were charged and that the molecules were dipoles and not neutral species, resolving a considerable debate in the organic chemical community at that time. The *second* was the development with Alex von Muralt of the flow birefringence procedure which permitted the measurement of the asymmetry of macromolecules. This was initially used on actomyosin preparations and provided an explanation at the molecular level of the observed optical birefringence of intact muscle preparations. The procedure was further developed by using a pair of concentric cylinders to provide, in the space between, accurately known and adjustable shear gradients. This allowed determination of the axial ratio of much less asymmetric proteins than actomyosin, thus providing shape factors for many proteins. A famous figure, prepared by Larry Oncley, published in the late 1940s showed two-dimensional ellipsoid models, drawn to scale, for the few proteins for which there was both molecular weight and shape information at that time. Some were remarkably close to today's low resolution pictures while others have turned out to have much more complex shapes than could possibly be derived from the experimental procedures available at that time. Electron microscopy, X-ray crystallography, and high resolution NMR were still in the developmental phases.

Edsall's highly systematic thinking process and elegant development of an argument are evident in everything that he wrote and in his teaching and editing. As Cohn would occasionally remark, his own style was somewhat different: a retentive memory for details of experiments, especially for observations that did not fit in with expectations, and ability to retain apparently conflicting facts or hypotheses for decades. To the extent that these distinctions were justified they made for a strong collaboration, and attracted a large group of additional coworkers with a great diversity of interests engaged in Cohn's laboratory or in other departments and institutions. The closely associated collaborators cited in the preface to Cohn and Edsall's book were: George Scatchard, John G. Kirkwood, Hans Mueller, J. Lawrence Oncley, Ronald M. Ferry, William T. Salter, Jeffries Wyman, Jr., Alexander von Muralt, Marcel Florkin, Thomas L. McMeekin, Arda Alden Green, Jesse P. Greenstein, Norman F. Burk, Norman R. Joseph, Danella Straup-Cope, V.E. Morgan, Jacinto Steinhardt, John A. Luetscher, Jr., Harry L. Fevold, Gertrude E. Perlman, Isidore Fankuchen, Walter L. (Pete) Hughes, Jr. and Lawrence E. Strong.

4. The department in World War II

The entry of the USA into World War II changed the efforts of the Department of Physical Chemistry dramatically as it did for so many academic institutions. The focus became the development of pilot plant procedures for the separation of the proteins of blood plasma, procedures that could be scaled up to an industrial level. These materials could be stored for a considerable time and greatly assisted medical procedures in the military services. Many in the Department continued their contact with Cohn's laboratory during the war years supporting the work on plasma fractionation by the use of ethanol–water mixtures of controlled pH, ionic strength, protein concentration and temperature. The technical aspects of this work were based on the experience of the laboratory since its inception over 15 years before. Cohn arranged for leaders of the laboratory such as Oncley, Edsall, Hughes and Strong to specialize in the different plasma fractions. Plasma albumin, gamma globulin, and other products could be distributed to other laboratories in previously unavailable quantities. The isolation of albumin and gamma globulin by essentially these methods continues to the present day. Edsall's area of responsibility lay with the asymmetric proteins, fibrinogen and the polymerized products derived from it. Hughes and Strong worked brilliantly on the isolation and scaling up of the albumin preparations and Oncley directed the gamma globulin isolation.

Medical application in the war zones was on a massive scale; likewise, physiological studies had a wide scope. A bulky July 1944 issue of the *Journal of Clinical Investigation* was devoted to the latter studies. FRNG remembers a subsequent comment by a leading clinical investigator at the adjacent Children' Hospital, Charles A. Janeway, to the effect that quite apart from the direct medical applications, the work repaid the effort in terms of basic physiologic knowledge. An example in point: at a time when internal protein degradation was poorly understood, it was found that a human subject could be maintained in nitrogen balance with no other nitrogen source than intravenous albumin. Many other studies dealt with the medically essential osmotic characteristics of the albumin preparations.

The plasma fractionation studies required intellectual demands as stringent as the earlier systematic studies in which Edsall had taken a prominent part. The exploitation of the five-variable isolation technique mentioned above was potentially too complicated to maximize by systematic adjustment of one variable at a time. For example, the effects of ionic strength regulated through pH buffers could be explored at the same time as variations in ethanol mole fraction, the first suitable for enhancing selective solubility of certain proteins, the latter to adjust solubility of various classes of proteins. Maximization of conditions was accomplished by following up clues from initial modest improvements.

Cohn reveled in the variety of requirements of the fractionation work which called on all manner of laboratory and clinical expertise. He made a habit of calling on leading experts of all sorts. In this his shrewd style reminds one of the vision of Vladimir the Second of Kiev who chose to steer his Viking band towards a monotheistic faith by summoning spokesmen for the four options, ultimately to choose on logical grounds, Byzantium.

It might be well at this point to note the status of the methods available in the 1930s and 1940s for the separation and characterization of the components of any solution as complex as blood serum. Most of the procedures that could be scaled to the industrial production level involved differential precipitation or crystallization, when possible, of the components, or the reverse, selective extraction from bulk precipitates. Although the Russian chemist Tswett had developed chromatography decades earlier, Western Europe and America somehow failed to recognize its significance until after WWII. Amino acid analysis was carried out by gravimetric or microbiological growth procedures applied to dried samples of the amino acids from an acid hydrolysate of the whole protein or peptide separated by fractional crystallization. The available data on the composition of proteins was crude at best. Methods using column chromatography for accurate analysis were not worked out until the late 1940s by Stein and Moore, with chromatographic separation of the proteins themselves coming along a few years later. Many of the biophysical instruments for characterization of the proteins, common today, had not even been invented at the time: lasers and all of their applications, the atomic force microscope, and so forth.

5. Teaching

John Edsall's broad education and career experience prepared him for the role of teacher and editor. The study of proteins during the past century has required the integration of very many approaches, physical, chemical and biological, and seen the application of this work to many fields. Edsall's breadth of knowledge served the science by looking carefully at each new experimental option and encouraging the diversity of approach and correlation of evidence that the field requires.

John Edsall's teaching reflected his breadth of interest and his attention to individual students. The best example of these qualities probably was his role on the Board of Tutors in the Biochemical Sciences. The College did not have a Biochemistry Department for many years. In its place was a board made up perhaps of a dozen active, often younger biochemists in various departments and hospital laboratories in Cambridge and Boston. The Board members were chaired for many years by John Edsall. Students who, as sophomores, elected the field of concentration in Biochemical Sciences were guided by members of the Board in the selection of their courses in Biology, notably one taught by Edsall and Wyman, and other appropriate choices. Students would make appointments with Board members at the Board's offices and conference rooms, availing themselves of a well-stocked library. For the less-advanced students, guidance sessions might last for 20 or 30 min monthly. For the most advanced students the sessions often lasted 1 h per week by the stage of the senior year. FRNG joined the Board at John Edsall's invitation when a graduate student. In keeping with the cliché, every Board member felt a student himself. Equally universal was the sense of humility in the face of the talent and commitment of the undergraduate students in our care. A number of the Tutors filled in the gap by serving as well as freshmen advisors. John Edsall lead the way in maintaining later contact with those he had taught in this setting.

Of course for graduate students and postdocs the most important teaching was informal; one on one discussions and the apprenticeship relationships as is usually the case. As usual also, such interactions are very hard to summarize because they are different for each individual.

6. Life in the department

What was it like to be a student in Cohn's Department? Intense! Few students were on hand before the war years. Some, like Joseph S. Foster were postdoctoral students during the years of the furious work on plasma protein fractionation. Foster later worked at the Carlsberg Laboratories and at Purdue University where he produced a remarkably astute series of studies on plasma albumin. Protein chemistry lost a true leader at his death in 1975.

Those of us who arrived after 1945 found the pace unremitting and the faculty uninclined to stop to explain anything for a second time. We caught the drift from exchanges of outside advisors with the faculty. Our colleagues, pre-doctoral and postdoctoral, came from very disparate backgrounds. The mood of the University was set by returning veterans committed to disciplined study. Postdoctoral students included medical students at various stages of their studies such as David M. Gibson, Ray K. Brown, Robert S. Gordon, Edward Leonard, Alexander Rich, David Gitlin and Herbert Scheinberg. The distinguished dermatologist Walter Lever found time from his practice at the Massachusetts General Hospital. One member of the junior staff was Douglas N. Surgenor who contributed liaison with the hemotologists such as James Tullis and others studying materials concentrated in various plasma fractions while ably coordinating the work of a number of students and visitors. Many of these came from abroad to catch up after the wartime disruption, often bearing scars of their experiences which we tried to assuage in ways that one must feel in retrospect to have been haphazard at best. One person who reassured the drifting Europeans was John Edsall. His benign manner, beautiful enunciation, familiarity with their world and, yes, idiosyncrasies, were reassuring qualities for a classic Herr Professor of the best sort.

The Department was divided between two locations, opposite ends of the C and E wings in the Medical School. FMR occupied a tiny lab in the 4th floor of the C wing with an 8-foot bench and a single chair. For a graduate student this was luxurious. This lab was immediately adjacent to John Edsall's office which was if anything smaller. Along with a writing desk there was just room for three chairs. In the absence of a specific appointment John would frequently come out of his office inevitably reading a book or a journal and humming to himself. ''Hmmm, hmmm, yes, Uhmm, hmmm'', (eyes glued to the reading material) ''good morning Fred'' (still reading) Uhmm, 'yes', hmmm, (no motion of head) ''Have you seen this latest volume of J.A.C.S. hmmm, hmmm''. (The answer was almost always ''no'' regardless of the specific book or paper.) The origin of Edsall's phenomenally broad and comprehensive knowledge was obvious; he could walk, read, and talk all simultaneously without missing a beat. By this time he would be out in the corridor.

The corridor was a famous place. The labs on every side were regular labs, but the corridor was elegantly paneled in wood, and encircled just below the ceiling with a frieze engraved with gold letters. The letters spelled out the names of practically all of the famous physical chemists of the previous two centuries. There was one empty space which was of a size that would neatly accommodate 10 letters and 4 spaces. There was never any doubt among the graduate students as to whose name would appear in that space in due time. When especially famous guests were visiting the department, a table for lunch would be set in the corridor that was long enough to seat just the number of individuals that seemed appropriate to Cohn.

Despite the stresses of the laboratory environment, the individual student found the demands offset by substantial support within the group and in the wider Harvard community. An example would be the experience of FRNG in characterizing the Beta-lipoprotein (renamed low density lipoprotein or LDL) in his thesis according to its protein characteristics of solubility, carriage of lipid substance in blood, electrophoretic and ultracentrifugal characteristics, and susceptibility to oxidation of its lipids according to a peroxide pathway. In certain quarters this was heresy. The support of Robert Woodward, the distinguished organic chemist whose work on the lipoperoxides was the basis of that part of the study was especially appreciated at the thesis defense. This work was supervised by J. Lawrence Oncley who continued to pursue the field skillfully and thoughtfully. The very significant ultracentrifugal studies on individual plasmas, revealing the wide range of LDL levels and behavior to be encountered in a population, brought Gofman and Lindgren at Berkeley a very mixed reception and years of underappreciation.

A brief story will illustrate the careful support provided by E.J. Cohn to FRNG after he later developed an ulcer. Considering the notions of etiology of the day it was only natural that Cohn should suggest that he might have asked too much, putting the point in unforgettable words, ''You know, Frank, you're no longer expendable''.

7. The start of structural biology at HMS: (before the phrase was invented)

Cohn had great foresight as to the direction in which the field would go. Even though Perutz had spent years in applying X-ray crystallography to protein crystals there was no evidence that a detailed structure would ever be produced. The absence of computers was an enormous stumbling block among a whole lot of other difficulties. Cohn recounted how he made up his mind to tackle the problem on the basis of a private lunch with the leading mathematician, John von Neumann. The latter covered a napkin with calculations and pronounced that the computation would be feasible. This Vladimir-style episode was apt, considering the almost religious degree of commitment that has come to mark those who have been drawn to the field. Once Cohn was convinced that it was going to work, he got Barbara Low to join his department as an assistant professor.

Barbara was well known already for her work with Dorothy Crowfoot (later Hodgkin) in solving the structure of penicillin which was a tremendous contribution to the war effort through the development of the beta lactam antibiotics. She arrived in 1948 intending to work on insulin, work she had started with Dorothy in England. She got her first graduate student immediately.

FMR also arrived in 1948 fresh from his Bachelors degree at MIT. He had taken a full year course in X-ray diffraction as an elective with Bert Warren in the Physics Department, was intrigued with the possibilities and could extend an interest in geometry developed in a prep school math course. Warren used metal alloys as examples of complex structures where the lattice sites could be either perfectly crystalline or randomly disordered. There were lots of electrons to scatter and discuss. In private discussions with FMR about the application of X-ray crystallography to proteins Warren was less than enthusiastic. He thought the diffracted beams would be much to weak to measure accurately since the low atomic number atoms C, N, O had so few electrons. He can be excused because, as a physicist, he had not followed the work on small molecule organic structures which were beginning to flow out of the chemical X-ray labs.

The first protein structure was still a decade away, but there was quite a bit that could be done, and the program fitted in nicely with the department's interest in the interaction of metal ions with proteins in which, by this time FRNG was heavily involved. Barbara's office was just across the corridor from John Edsall's, an accident of fate for FMR who thus had easy daily access to all sorts of advice on both the chemical and X-ray sides.

There were also somewhat strange incidents in 1953 the last year of Cohn's life. For example, having just received his PhD degree FMR was made a post-doctoral assistant to Dr Cohn for 1 year. He was set to work on trying to apply the recently developed zinc–ethanol plasma fractionation procedure to the separation of the protein components of milk, another protein-rich, readily available, biological fluid. During this study Cohn decided that the Boston area needed some instruction on what was going on in his Department, and milk seemed to be simpler to explain to the public than blood. Arrangements were made to have a farmer + a cow + a milking machine + FMR + a line of sterile centrifuges connected in series on the stage of the Boston Museum of Science. FMR appeared in a clean white lab coat, which he never normally wore, but the audience could immediately classify him as a scientist and would, thus, distinguish him from the farmer. The farmer was there, thank god, to hook up the milking machine and collect the milk and separate off the cream. From there on the milk was FMR's responsibility, and he also had to explain what was happening in the centrifuges and WHY. We believe that the only thing the audience got out of it was the conversion of the cream into butter which was done on the side in a Waring Blender. Like so many Broadway shows this one had the benefit of a short run. FMR does not know to this day whether or not Cohn ever knew anything about the actual show that he set in motion, but FMR certainly hoped that Edsall and Low did not know anything about the whole affair since he was counting on them for letters of recommendation for a fellowship.

8. Communication and editing

There is a thread that runs through all of Edsall's life that we really cannot do justice to in this short paper. It came to the fore particularly later in life. There have always been two aspects to research: one is the actual experimentation and data collection, and the second, equally important, the conversion of the notebook material, for most of us an inscrutable jungle, into a crisply written form which makes the data and conclusions available to others. The quality and effectiveness of scientific papers varies enormously. John had a natural talent in this direction. This was recognized by others, of course, and resulted in his appointment as Editor in Chief of the *Journal of Biological Chemistry* from 1958 to 1968. He demanded high quality in the writing and got it both through suggestion and through much rewriting by himself. All this was done with a benevolence which made the authors anxious to please. His efforts raised the Journal to the peak in its area, and the changes in administration which he initiated attracted excellent authors and have led the Journal to its current enormous size.

Seldom is a single laboratory responsible for generating a 'big picture'. Usually the results of many are required and these have to be digested, organized and reinterpreted for maximum use to the scientific public. Thus, the importance of review articles and the so-called secondary literature which we believe to be a misnomer. Through the urging of the then president of Academic Press, Kurt Jacoby, and a feeling that protein chemistry as a field was not properly represented, John Edsall and Tim Anson started the series *Advances in Protein Chemistry* whose first volume appeared in 1944. This required the same editorial attention that was given to the JBC but there was no limit on the length of the article. The series is now up to Volume 58. For the most part the authors were, and are, selected by the editors, and John was remarkably successful in convincing them to accept the offer and then to actually supply the manuscript. Over the years there have been some real gems in this series, articles which have changed peoples' thinking and started new directions. The importance of a well-constructed review cannot be overstated.

9. Ethics in science

During the past three or four decades the world has seen a crescendo in scientific fraud. This behavior has paralleled the increase in the association of industry and academia. Whether these are related in any causal way is the subject of considerable debate at this time. John always had a very clear picture in his own mind as to what was right and what was wrong in the conduct of science. He shared these feelings and concerns with a large part of the scientific community, but he had taken more direct action than most.

This action took the form of many letters both personal and open and extensive articles on specific topics. As examples: References to him or OpEd letters from him may be found in the NY Times archives: (1981) A Split Soviet Image on Nuclear War; (1982) Updating Man's Ancestry; (1984) The MX (missile) is Counterproductive to Our Security; (1985) Science, Sakharov and the Soviet. The following are two examples of specific fraud accusations: (1) What is known as the 'Gallo affair' (the origin and use of the HIV virus in the Gallo laboratory) was initiated by a very long and influential article by John Crewdson in the Chicago Tribune. John Edsall became concerned about the approach by government agencies to the accusations and the apparent whitewashing. He presented a carefully written critique in a letter to Representative John Dingell who was Chairman of the Subcommittee on Oversight and Investigations. (2) He was even more involved in the 'Baltimore affair' (Imanishi-Kari with Margot O'Toole as the whistleblower). In this case he gave testimony in support of O'Toole in Congress before the Dingell committee in addition to his writings on the subject some of which appeared in the journal *Ethics and Behavior* (1994).

10. Move to the main campus

As Cohn's final illness[2] progressed he seemed to jump ahead of facts on some occasions, not so much in responding inappropriately to the evidence brought before him but rather in the stage of hypothesis formation for medium- to long-term planning. It is not uncommon for creative people to over-commit to certain objectives in their last year or so. Whatever the process, John Edsall

[2] At his death in 1953 Cohn was found to have died of a complication of an undiagnosed pheochromocytoma. This tumor of the adrenal medulla characteristically releases adrenaline (epinephrine) that raises the blood pressure and mediates the fight or flight response. In this case the diagnosis was doubtless obscured by a long-standing condition of angioedema which was treated by injection of the same chemical, adrenaline, to combat the characteristic swelling.

recognized that he had little further role at Cohn's side and left the Medical School for the College where he was naturally most welcome and integrated with the evolving biochemistry faculty there. Earlier Ronald Ferry, as Master, had invited John Edsall and Jeffries Wyman to become Tutors in John Winthrop House. The whole process brought more focus to his responsibilities and paved the way for the editorial and leadership roles in which he shone.

John Edsall's balance, generosity and consideration for others was reflected in his home. Margaret Dunham Edsall came from New York. She would reminisce about her adolescent trips with her mother to visit Mister Tiffany to discuss suitable gifts. She came prepared for the Boston scene with a great knowledge of art, architecture and music gained in North America and Europe. Particularly enjoyable to a frequent guest were occasional glimpses of the Scot's irreverence in her sparkling eyes. If they happened to be one of John's tutees grape juice and cookies were added to the warm words of greeting.

Anyone who has dealt with John Edsall knew him as morally and intellectually incorruptible. As an overnight guest of John and Margaret in Cambridge or Greensboro, Vermont, FRNG had many occasions to see him in unguarded moments. Their oldest son Lawrence, now deceased, enjoyed talking of music, a subject he knew very well. It was the second son, David, who offered the comment approximately 45 years ago that he had long wondered about his father's imperviousness to any form of unfairness or strong-arm tactics. What he said was approximately ''I used to think that Father didn't notice unfairness or deceit but now I see it as part of his technique to avoid legitimizing the contemplated action''. Seen in that light, John Edsall has been the touchstone of the virtuous man.

This paper is filled with personal anecdotes and a very rough history of an extraordinary man. It is not intended to be a serious, fully documented, biography. Thus, specific references are not given in the text, but most of the non-personal facts have been taken from one or more of the following sources.

11. Some suggested reading by and/or about John T. Edsall

Biographical or review articles

Further reading

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[17] (Investigation of the Gallo and Baltimore cases each lasted for a number of years, and there is a huge amount of information available to the public on both. They will not be discussed further in this paper.)

[18] Letter from John Edsall dated 4 Feb 94 to Representative Dingell http://home.t-online.de/home/Bernhard.Hiller/wstewart/CelebratedCases/GalloCase/LettersFolder/Edsall4Feb94.html.

[19] Additional information on some items referred to in the Edsall letter can be found through the site: http://home.t-online.de/home/Bernhard.Hiller/wstewart/CelebratedCases/GalloCase/RichardsReport/ReportOfTheRichardsCom.html.

[20] John T. Edsall, On Margot O'Toole and the Baltimore Case: A Personal Note on the Evolution of My Involvement, Ethics & Behavior, 4 (3) (1994) 239–247 or consult the Web site http://home.t-online.de/home/Bernhard.Hiller/wstewart/CelebratedCases/BaltimoreCase/Edsall94.html.