Julius Cohnheim (1839–1884)
His Life and Contributions to Pathology

HAROLD M. MALKIN, M.D.

Oslerwelch Laboratories,
San Leandro, CA 94577

On August 15, 1884, the closing day of the International Medical Congress, Rudolf Virchow announced the death, at age 45, of his most distinguished pupil, Julius Cohnheim. It would seem timely, on the centenary of Cohnheim's death, to review and evaluate his work and contributions to the field of pathology.

Early Life and Studies at Berlin and Wurzburg Universities—(1839–1868)

Cohnheim was born July 20, 1839 in Prussia where he received his elementary education. In 1856, he went to Berlin to begin his studies in medicine. This was the same year that Rudolf Vir-
MALKIN

chow was called to Berlin, from his pro-

fessorship in Wurzburg, to establish his

famous Pathological Institute. Whether

Cohnheim, as a beginning medical stu-

dent, had any contact with Virchow
during the years 1856 to 57 is not men-
tioned by his biographer, Willy Kuhne.19

However, because Cohnheim in 1857 left
Berlin to go to Wurzburg to study his-
tology under Virchow's friend and col-
league, Albert Kolliker, it is not unre-
asonable to assume that Virchow had
some influence on this decision. In any
case, Cohnheim, after becoming an ac-


accomplished microscopist, returned to

Berlin in 1860, passed his examinations
for the M.D. degree, and started his
thesis under Virchow's guidance in 1861.

At this period the Berlin Pathological In-
stitute was a major center of intellectual
activity, and talented students came from
every part of the world to study with Vir-


chow. It was said at that time, because of Vir-

chow's leadership and inspiration for sci-

cientific inquiry, a new student would be
told by the older ones, "Poor fellow, you
too are going to be infected". It was no
different for Cohnheim, but as is often
the case with newcomers to a large re-

search institution, his day to day educa-
tion and stimulation came from Vir-

chow's assistants or colleagues, Willy
Kuhne in physiology, Ludwig Traube in


medicine, and Friedrich von Reckling-
hausen, and Edwin Klebs in pathology.

Although Cohnheim's thesis was first of
a series of publications on inflammation,3
which was to gain him an international
reputation, he also published with Willy
Kuhne, a student of both Carl Ludwig
and Claude Bernard, a paper on carbo-

hydrate enzymes (then called Fer-

ments).7 But it was Traube, called by
William Osler "one of the greatest

German clinicians" and a student of the

famous team of Karl Rokitansky, and
Josef Skoda, who emphasized to the
young Cohnheim the importance of

asking "why" certain disease processes
produce the structural changes at death,
rather than simply "what" are the struc-
tural changes themselves. Traube
stressed the importance of studying the
abnormalities in physiology produced by
disease, encouraged experiments in ani-
mals and inspired Cohnheim to establish
later the first school of experimental pa-


thology.

Cohnheim's career was interrupted in

1864 when he briefly served as a surgeon
in the German army during the war with

Denmark. On his return to Berlin, Vir-

chow appointed him chief assistant,
taking the place of von Recklinghausen
who was called to the professorship at
Konigsberg. The next four years were
difficult but productive, for in spite of the
considerable autopsy and teaching du-
ties, Cohnheim published several
papers, the most significant being his
classic, "Ueber Entzündung und Eiterung",
(On Inflammation and Sup-


puration).4,16,20 This research showed
conclusively that the leukocytes found in
inflammation are predominantly derived
from the blood by diapedesis through the
capillary walls. This was in opposition to
the position taken by his mentor, Vir-

chow, who believed that the leukocytes
in inflammation arose through local pro-

liferation of cells. Although diapedesis
had been seen much earlier by two other
investigators, William Addison,1,17 and
Augustus Waller,15 it was Cohnheim who
recognized and resolved the age old
question of the origin of pus cells in le-


Kiel Period (1868–1872)

In the fall of 1868, still only 29 years
old, Cohnheim accepted the chair of Pa-


thology at Kiel, where he studied the ef-

fects of venous obstruction and the
problem of arterial embolism, in which
he offered the important explanation that
varying pathological results depended
upon the presence or absence of collateral circulation beyond the point of obstruction. In the meantime, many objections were being made to his theory of inflammation. In order to substantiate his earlier work in which the vascular system was a vital component, Cohnheim, even though he was already a full professor, elected to go to Carl Ludwig’s laboratory for two months as a student, in order to learn the newest techniques in vascular research.

**Breslau Period (1872–1878)**

In 1872, Cohnheim moved to Breslau where he built a Pathology Institute, and continued to draw on the knowledge of outstanding pioneers in other fields such as Rudolf Heidenhain in physiology, and Ferdinand Cohn in bacteriology. By this time he was so well known in academic circles, that, like Virchow in Berlin, he was able to attract excellent colleagues and students, many of whom were to become outstanding leaders in their respective fields; Paul Ehrlich, Carl Weigert, William Henry Welch, Albert Neisser, Ludwig Lichtenheim, Ottomar Rosenbach, Carl Julius Salomonsen, Charles Roy and William Councilman. Weigert, Cohnheim’s chief assistant, was one of the most famous pathological anatomists of the 19th century, and a quotation from Carl Salomonsen’s “Reminiscences of the Summer Semester, 1877, at Breslau”, reflects Cohnheim’s increasing emphasis on experimental pathology, and his reliance on Weigert for the pathological anatomy:

“**Weigert was the real pathological anatomist of the institute, prosector as well as microscopist. Cohnheim himself was tired of the prosectorship; he had become the complete experimenter. He only entered the dissection room when all postmortems were finished; then he selected something for his courses; only once, on the first day after vacation, did we have the opportunity of admiring the elegance and skill with which he dissected and taught at the same time; otherwise he willingly left postmortem dissections and microscopic investigations to Weigert as his equal as a prosector, and as a microscopist, perhaps his superior . . .”**

Cohnheim would also in a joking way chide the morphologists, particularly Paul Ehrlich with reference to his being a “master dyer” and “painter”, although the staining techniques of both Ehrlich and Weigert greatly advanced our understanding of cells and other tissue components. But as Virchow encouraged research and men in his institute whose talents and interests were somewhat different from his own, so too did Cohnheim in the Breslau institute. Another example of Cohnheim’s ability to recognize ability and talent is the famous story of his reaction when Robert Koch came to Breslau in November 1875. This famous bacteriologist, who was a country practitioner at the time, had been invited to demonstrate his cultures and experiments on anthrax to Ferdinand Cohn, the most learned man on bacteria at the time. Cohnheim heard of the experiments, went over to Cohn’s laboratory, witnessed the elegant experiments of Koch, went back to his institute and said to his assistant, Weigert:

“**Now leave everything as it is, and go to Koch. This man has made a magnificent discovery, which, for simplicity and the precision of the methods employed, is all the more deserving of admiration, as Koch was shut off from all scientific associations. He has done everything of himself and with absolute completeness. There is nothing more to be done. I regard this as the greatest discovery in this domain and believe that Koch will again surprise and put us all to shame by further discoveries.”**

Then to enable Koch to leave his medical practice and continue his work in
bacteriology, Cohnheim used his influence to persuade the German government to appoint Koch to a position as a member of the Imperial Sanitary Commission in Berlin. In 1877, Cohnheim, with Salomonsen, did crucial experiments that showed unequivocally that tuberculosis was a transmissible disease. As these experiments were described in Koch's most famous paper on the identification, isolation and proof that the mycobacterium was the etiological agent in tuberculosis;

“...opponents of the infective theory strove to prove that tuberculosis could be induced by the inoculation with non-tubercular material. To the decision of this question Cohnheim and Salomonsen contributed largely by selecting for inoculation, in a moment of inspiration, the anterior chamber of a rabbit’s eye. By this means it is possible to separate the cases in which successful inoculation with tubercular material has been accomplished from those in which some other infective material has been introduced with the tubercular virus. Subcutaneous inoculation with such material often causes a more or less widely diffused cheesy infiltration, not unlike that of tubercle. But in the eye these substances give rise only to a general inflammation of short duration, which cannot in any case be mistaken for the slow and characteristic development of tuberculosis resulting from inoculation. The course of a successful tubercular inoculation can be watched throughout by the experimenter. After a fairly long inoculation period, single grey nodules, barely visible to the naked eye appear in the iris, starting from the piece of material introduced. The number of nodules gradually increases, they enlarge, become yellowish in the center, caseate, and show macroscopically as well as microscopically all the typical characters of the true tubercular nodule. The tubercular infection, however, does not remain limited to the eye, but invades later the whole organism, spreading to the neighboring lymphatic glands, the lungs, spleen, liver and kidneys. Cohnheim and Salomonsen, as also the observers who repeated these experiments, unanimously state that in no case did tuberculosis of the iris follow an inoculation with non-tubercular material.”

At Breslau, another event occurred in April 1877 which was to have a great impact on medicine and pathology in America. This was the time that William Henry Welch came to Breslau to learn experimental pathology before his return to America and his long and illustrious career as the father of American pathology. Originally Welch went to Germany to study with Virchow, but Carl Ludwig, with whom Welch worked during the last half of 1876 and the early part of 1877, persuaded him to go to Breslau to study with Cohnheim. When Welch arrived at Cohnheim’s institute, he wrote to his father, comparing Virchowian pathology as represented by the Leipzig professor, Ernst Wagner, to that of the Cohnheim school:

“Prof. Cohnheim and Prof. Wagner are in some respects the antipodes of each other. Wagner has perhaps a greater array of facts at his disposal... has gone deeper into the microscopic details of a pathological change, but while Wagner is often satisfied with the possession of a bare fact, Cohnheim’s interest centres on the explanation of the fact. It is not enough for him to know that congestion of the kidney follows heart disease or that hypertrophy of the heart follows contraction of the kidney, or that atheroma occurs in old age, he is constantly inquiring why does it occur under these circumstances. The result is that Cohnheim has taken for especial studies such common subjects as inflammation, dropsy, embolism and through
his investigations these have become perhaps the only subjects in pathology in which our knowledge approaches in exactness what is known concerning a physical or chemical process.

"Pathology and even practical medicine have entered upon a new era since Cohnheim's discoveries in the process of inflammation for there is hardly a disease of which our conception is not thereby modified. He is almost the founder and certainly the chief representative of the so-called experimental or physiological school of pathology. That is, he occupies himself . . . with the study of the diseased processes induced artificially on animals."

Welch was assigned the problem of attempting to determine the mechanism of the production of pulmonary edema during cardiac failure. This work was coauthored by both pathologists in 1877.

**Leipzig Period (1878–1884)**

In 1878 Cohnheim moved for the last time to Leipzig, where he wrote the last volume and the second edition of his famous Lectures, and continued his research on the effects of the occlusion of the coronary arteries. He also investigated the circulation of the kidney with Charles Roy of Great Britain. These were his last projects because of his chronic illness with gout from which he ultimately died in August 1884. In June of that year, William Osler who went to Leipzig to observe Cohnheim's work, wrote back to his colleagues in America:

"The Pathological Institute is conducted very much on the model of Virchow's, and is in charge of Professor Cohnheim, with whom are associated Professor Weigert and Privat-Dozent Huber. As, I dare say, most of your readers have heard, Prof. Cohnheim is seriously ill, and there is, unfortunately, no prospect of his recovery, as he has chronic Bright's disease (gouty). The loss will be most serious. As an experimental pathologist, he has no rival in Europe, and his lectures on General Pathology, a second edition of which was issued last year, show a grasp of the principles of disease not inferior to his great master, Virchow, and a clearness of exposition quite as great. It is a pity the work has not been translated. The charge of the laboratory is virtually with Professor Weigert, to whom medicine is under a deep debt of obligation for the introduction of the use of aniline dyes in histological work, as well as for the unravelling of many knots in pathological histology."

Just as he had helped Robert Koch obtain a position in Berlin, Cohnheim was very influential in obtaining the first professorship of pathology for Welch. In early 1884 shortly before he died, he wrote to President Gilman who was organizing the Johns Hopkins Hospital and Medical School that:

"the person best fitted for the chair of general pathology is Mr. Welch of New York. Welch, indeed, worked with me for a long time and I regard him as an astute as well as thoughtful investigator."

As regards to Welch's thoughts when he returned in the winter of 1884 to work again in Carl Ludwig's laboratory, he wrote back to Gilman:

"... since Cohnheim's death there is no prominent teacher of general (experimental) pathology in Europe, so that I think that I can profit more by work in physiological laboratories where much experimentation is done than in strictly pathological laboratories. . . . Experimental physiology is the basis of experimental pathology. Cohnheim's superiority as an experimental pathologist was
largely due to his training under Ludwig.”

Contributions to Pathology

Because of his early death, Cohnheim’s scientific discoveries were not numerous, and he published only 41 research papers. Certainly his research on inflammation and his dictum “without blood vessels there can be no inflammation” is still valid today, but many of his papers were of only minor significance. Perhaps most significantly he was a catalyst for the development of experimental pathology which was strongly based on contemporary physiology. It was his departure from the purely morphological, and his refreshingly new perspective on pathology gained by his associations with Kuhne, Ludwig, and Traube that made his institutes in or during the late 19th century meccas for the young pathologists such as Welch, Ehrlich, Salomonsen, Neisser, and Roy. In the rapid development of scientific knowledge, it is difficult for an individual to maintain leadership over a long period of time, and the best students quickly overshadow the masters. As Osler stated in his famous “fixed period” speech:10

“. . . The effective, moving vitalizing work of the world is done between the ages of twenty-five and forty—these fifteen golden years of plenty. . . . In the science and art of medicine, young or comparatively young men have made every advance of the first rank. Vesalius, Harvey, Hunter, Bichat, Laennec, Virchow, Lister, Koch—the green years were yet upon their heads when their epoch-making studies were made.”

Cohnheim was the leader in the 1870’s, as Virchow’s creativity and leadership, monumental in the 1850–1870 period, waned. He created at Kiel, Breslau, and Leipzig an atmosphere that was stimulating and tolerant, and his background was sufficiently broad to direct the creative minds of the younger men without necessarily insisting on specific older experimental approaches. And as with Virchow earlier, and Welch later in the United States, Cohnheim was the pathologist consulted by medical school deans when looking for outstanding young pathologists for new departments and institutes. Specifically it was largely Cohnheim’s “Lectures in General Pathology” that helped establish his leadership. These lectures, published in three volumes during the years 1877–1880 are remarkable in their degree of modernity when compared with Henle’s “Rational Pathology” (1846), Rokitansky’s “A Manual of Pathological Anatomy” (1846), or even Virchow’s “Cellular Pathology” (1858) even considering the time elapsed between the publications. Exerpts from the Introduction to his Lectures as translated in 1889 by Alexander McKee for the New Sydenham Society are given here to emphasize the vision and perspective of Cohnheim regarding pathology.

“We speak of a disease where the regulative mechanisms, acting in opposition to one or more vital conditions, are no longer adequate to secure that the various vital processes shall proceed undisturbed . . . one individual may be better able than another to adapt himself to one and the same external condition; or, in other words, that disease may be produced in one person by causes which have no effect on another. Disease is nothing more or less than a deviation from the normal vital process, brought about by the action of external conditions and the reaction of what may be called in general terms the internal regulative capabilities or the organism.

. . . We regard the clinical symptoms and the anatomical changes as equally valuable factors in the estimation and de-
The knowledge of the symptoms gained by observation at the sick bed, and the knowledge of the anatomical changes, as revealed with but few exceptions by post-mortem examination, are alike indispensable to the understanding of a disease. Neither of them alone is sufficient, just as little as in normal physiology the most minute and accurate knowledge of the conformation and structure of a muscular fibre permits a surmise as to the contractile power of the muscle, or the most strict observation of its action, even when conjoined with a determination of its collective physical properties, allows of an approximate guess as to its structure. To pathology this applies, if possible, in a still higher degree. It is impossible, from the post-mortem appearances in case of typhoid, to sketch a picture of the course and symptoms of this disease, having even a remote resemblance to the reality, nor to take a chance example from the microscope—can anyone in the least deduce the characters of the urine 'intra vitam' from fatty degeneration of the renal epithelium or from amyloid degeneration of the renal vessels.

Etiology can be nothing more, I believe, than an enumeration and discussion of very different factors, having only one feature in common, namely, a capacity to act as exciters of disease.

I am persuaded that it is far more to your advantage to concentrate our united energies on the other branch of general pathology, namely, 'morbid physiology'. This science, as its name indicates, bears the same relation to normal physiology as does morbid to normal anatomy. While in morbid anatomy we learn the modifications undergone by the morphological (or chemical) constitution of the individual organs in disease, morbid physiology teaches 'how the functions of the affected organs are performed under abnormal circumstances'.

... the subject matter of normal physiology is not sufficient for our purposes in general pathology. It is of course perfectly true that the laws of physiology fully apply to the diseased organism as well as to the healthy one; but since physiology explains the process of healthy life alone, i.e. of the life under ordinary conditions, it does not without more ado help us to an insight into the processes going on within the organism when the conditions are essentially changed. No-where does physiology afford information as to what occurs when, in addition to the ordinary food, a perfectly foreign substance, such as phosphorus, for example, is absorbed by the body. From physiology we receive the most detailed intelligence as to the normal circulation, i.e. where heart, vessels, and blood are healthy; but of the state of the circulation when the valves do not close in consequence of previous disease, or when the vessel walls are altered, or when the blood is coagulated in some part, we learn nothing from physiology.

... Just as modern physiology has long broken with all speculative systems, and become an explanatory science after the manner of physics and chemistry, so do we banish from us in pathology all the systems which have succeeded one another in large numbers in the course of centuries. Far be it from me to deny our indebtedness to these manifold systems for many a great and important advance in pathology; but they have as such, whatever be the names they bear, a purely historical interest.

The method of investigation is the same in morbid as in normal physiology. You know what the most essential aid of physiology is, that one by which she has become an inductive natural science in the sense that chemistry and physics are such; it is experiment—and where purely physical and chemical experiments are inadequate,—express physiological experiment. By experiment, as is well known, the single possible factors
are tested as to their performances, and the conditions in which an organ works are varied in order to obtain information as to the significance of the individual factors. The results of physiological experiment are in the first place of service to pathology; then, however, we make use of pathological experiment, which was first practiced in England by John Hunter, and in France by Magendie, yet was only raised to the rank it at present occupies as our most important fundamental aid by the researchers of Traube and Virchow in the fifth decade of this century.

... Every dead body is equally valuable so far as the anatomy of the normal lung is concerned, provided this organ has been healthy; it is otherwise with the inflamed lung. Here it is very different whether the individual has died on the second or third or as late as the eighth day; for inflammation of the lung is progressive, while anatomical examination can evidently only supply information as to the condition of the lung which prevailed at the moment of death. This gap is filled by pathological experiment. By its aid we are in a position to work out the anatomical history of many highly important processes, either following them by continuous observation, or at least subjecting them to examination at whatever intervals we please; thus our most valuable knowledge of the processes of morbid development and growth, of intoxications, of the processes of inflammation, thrombosis, and embolism, of dropsies, and of many other subjects is owing to experiment.

Of particular interest is the definition of disease given in the first paragraph of the quotation. It is clear that Cohnheim was thinking of disease as a failure of what Walter Cannon was to develop and call "homeostasis" a quarter to a half century later. It is all the more remarkable considering that the fields of bacteriology, immunology, endocrinology, and autonomic nervous system physiology were either non-existent or in their infancy. The field of pathology advanced greatly because of the leadership of Julius Cohnheim.

References

12. Ibid, p. 94.