A SYMPOSIUM IN HONOUR OF THE CENTENARY OF VIRCHOW’S "CELLULAR PATHOLOGY" (1858-1958)

At the instigation of the Council of the Association of Clinical Pathologists the Editorial Board decided to devote this issue of the Journal to the publication of this Symposium on the pathology of the cell, which was held at the Royal College of Surgeons on October 2, 1958, to commemorate the centenary of the publication of Virchow’s classical volume. Participants of different interests in the cell were invited to contribute, and consequently it is hoped that in this issue readers will receive a wide and stimulating survey of the developments and the newer knowledge on the fundamental aspects of the physiology and pathology of the cell now being pursued.

1858

BY

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“For my part I am ready for anything, at a time when asphalt, India rubber, railroads, and steam are changing the ground we walk on, the style of overcoats and distances.” So remarks one of Balzac’s characters in his Deputy from Arcis as he curtly dismisses the 1830s. It was a time of transition from the splendours and miseries of the Napoleonic era to the calm of the later Victorian period, ruffled only by local revolution and minor wars. Technical invention had infiltrated art as well as ordinary existence. The invention of photography led to the dissemination of copies of great paintings and the revelation of styles. And when the American painter Rand found out how to make a collapsible tin tube whereby paints could be stored indefinitely and ready for immediate use, the mode of painting changed and Romanticism and Impressionism were born. This, too, was the age of the supreme romanticists in music, Robert Schumann, Johannes Brahms, and above all, Hector Berlioz and Richard Wagner. The Impressionists rejected the anecdotal and planned picture. “The great scandal of their painting was not that their pictures were bright,” writes Grosser, “but that they were unpremeditated.” Music broke from classical form and, with poetry, dared to give voice to the innermost emotions and flights of mind.

With the Congress of Vienna in 1815 was ushered in, for western Europe, 99 years of freedom from long and devastating wars. Populations expanded as wealth and comfort increased in some communities; in others, condemned to ignorance, poverty, and despair, they were fostered by better medical knowledge, and the breakdown of old customs and restrictions, early marriage, and the like. Nowhere was this change more apparent than in Germany. In the west, the traveller encountered a framework of rural life where compact villages were grouped around open fields or hamlets and scattered farmsteads stood in marshy valleys. As he journeyed eastwards, the more apparent it became that he was in a region conquered from Slavs. Most of the land was in the hands of the lord of the manor, vulgarly called the junker, who rigidly insisted upon a wide distinction between his family and the peasants. Many of the latter were no better than serfs, amenable to manorial jurisdiction and bound to the soil. In some of the quaint little grand duchies, electorates, and free towns of old Germany he was not too heavily taxed and life was tolerable though liable to sudden upsets according to the whim of the ruler. Many of the towns were, indeed, quiet backwaters of huddled roofs and spires, and even in 1850 the 12 largest towns of Germany accounted for a mere million and a third of people. Paris alone at this time had more than a million citizens.
With the effective exploitation of the Ruhr coalfields, the development of railroads and steamboats, the institution of a Customs Union in 1834, and the standardization of the coinage came a subtle change. The first German railroad was opened in Bavaria in 1835 despite the violent opposition of the Bavarian College of Physicians; in 1839 the newly completed line from Leipzig to Dresden carried more than 400,000 passengers in its first year, including ladies who kept needles between their lips to check familiarity in the single tunnel. By the 1850s, 3,000 miles of railroad had been built at an average cost of less than £11,000 per mile as compared with £40,000 in England. This meant more food, and with the introduction of chemical manures, as the result of Liebig's teaching in 1840, most of the sandy or heath-covered north German plain was at last accessible to cultivation.

Almost inevitably with these changes came labour troubles and the storms of revolution. The antiquated, absolutist bureaucracy encountered growing opposition from Liberals and Marxists. Unrest in the smaller states and the influx of political fugitives from France and Switzerland shook time-honoured dynastic loyalties, and the revolution that broke out in Poland in 1846, and swept through Paris in the February of 1848, flared up in Berlin in March of that year. Barricades appeared in the streets overnight and fighting broke out between the angry proletariat and the Prussian dragoons. King Frederick William IV was compelled to give way before the storm, a liberal, reforming ministry was appointed, and the King retired to Potsdam. In 1857 he went mad and his brother William took over the Regency. A rigid conservative, William was fully convinced of the divine rights of kings, but he detested police government. In 1858 he agreed to some reforms and seemed inclined towards a more liberal policy, but, reactionary elements prevailing, and ignoring the advice of his friend the Prince Consort of England, he reverted to the old policy of military alliances with German princes, absolute monarchial powers, and Army control. The same reactionary spirit prevailed in public health affairs, and Rudolf Virchow, in his capacity of Berlin politician and eminent scientist, played a foremost part in the fight for reform, just as he had rallied to the barricades with other ardent young Berliners in the turbulent weeks of 1848.

1858

No great perturbation shook the earth, no comet blazed its portents in the sky in that leisurely year of 1858. The British had captured Lucknow and rolled up the map in India for a few uncertain years when Lord Canning, the first Viceroy, declared an amnesty for the mutineers. Orsini tried to assassinate Napoleon III. The Princess Royal, Queen Elizabeth's eldest daughter, married Prince Frederick Albert of Prussia. China surrendered the left bank of the Amur River to Russia, and Jews were allowed to sit in the English Parliament. Yellow fever broke out in Lisbon in 1857 and so panicked the city that 50,000 inhabitants emigrated in a hurry. The Reverend Dr. Livingstone set out for Africa again, and a Jewish gentleman named Bravo brought an action against the Eastern Counties Railway Company for injuries sustained when the carriage into which he was stepping was suddenly propelled forwards. He was prevented for some weeks from performing the rite of circumcision, an operation which the Lancet characterized as one requiring "considerable nicety and skill." Professor Faraday declined the offer of the Chair of Chemistry at Edinburgh, which action the Lancet approved since "in these days the glories of the modern Athens have somewhat paled." A hippopotamus in the Paris menagerie gave birth to a calf which began immediately to swim about in the water in which it was born, "his voice being so strong an hour after his birth that people mistook it for that of the parents." Sir Benjamin Brodie, a surgeon of the highest eminence, was elected President of the Royal Society, and Mr. James Nolan of Carlow, Ireland, died at the age of 115 years and 9 months. Scotland achieved an unenviable preeminence in drunkenness, according to lunatic asylum and police returns.

"Even in Murray's Asylum, where there are so many patients of the higher classes that Dr. Lauder Lindsay says 'this circumstance gives a pleasing tone to our society,' the percentage of cases arising from intemperance is nearly double that of the Surrey County Asylum, which is wholly devoted to paupers. . . . For every person taken into custody in London for being drunk and disorderly, two are taken into custody at Edinburgh and three at Glasgow."

Captain Harrington of the good ship Castilian, hard by St. Helena, saw the sea serpent "lying like some large Doric column upon the waters, stretching away 200 feet or so in length, and 10 in diameter. He fastened home, and through the universal Times imported the intelligence to the wide world." A letter appeared in the selfsame Times, pleading for "a fig-leaf " to cover the regimental recruits when undergoing medical inspection preliminary to enrolment. The sanitation of many great cities was being heatedly debated. London was no exception, and Dr.
Barker of Bedford described experiments in which he exposed rats, mice, and dogs to the effluvia of sewage gas which "grew sick, restless, and diarrhoeal"; the Lancet sourly comments:

"It is no other than happens to the 2 millions of human beings who in London live in close chambers over sewers and cesspools... The hideous—the truly horrible, state of the river Thames" was at last "exerting a feeling of public indignation which will not be easily repressed." Someone called Kahn opened an exhibition in Coventry Street containing "additions of a most disgusting character... and days were set apart for the admission of 'ladies.'"

The abominations of the Strand slaughterhouses were arousing public indignation.

"The poisonous fumes from open cesspools pollute the air of the cellars in which the beasts are kept during two or three days, and in which, after being slaughtered, their flesh is suspended. The evil does not end here, for the putrefying offal is thrown into the sewers of this crowded neighbourhood, and become a fresh centre of infection."

Yet, according to the Lancet:

"the winter has been so unusually mild that the health of the people stands more than commonly high, while half the crowned heads of Europe have been on the sick list. The King of Prussia is suffering from a severe cerebral affection, from which no favourable issue can hardly be anticipated. The Grand Duke Ludwig of Baden, who has long been under strict medical surveillance,
FIG. 3.—London: old Covent Garden market in 1825 (painting by G. Scharf).

FIG. 4.—London: a dairy in 1825 (painting by G. Scharf).
died last week. The King of Sweden, slowly recovering from a severe illness, was thrown back by an attack of fever early last month, from which he is more convalescent. The King of Wurtemburg is reported to be fast breaking; he recently suffered from an attack of ‘grippe.’ Such a list affords ample food for the moralist.”

Robert Brown, the eminent botanist and explorer, whose name has achieved immortality in “Brownian movement,” Johannes Müller, renowned for his researches in zoology and embryology, Robert Hare, the inventor of an oxyhydrogen blowpipe with which he was able to fuse platinum, and Baron von Welsbach, who invented the incandescent gas mantel, died in this year. Births included those of Max Planck, whose law of radiation brought about a major revolution in scientific thought, Christiaan Eijkman, the co-discoverer with Gowland Hopkins of vitamins, E. M. Crookshank, who founded in King’s College, London, the first bacteriological laboratory to be established in Britain, Rudolf Diesel, who built the first successful diesel engine in 1897, Robert Hadfield, the discoverer of manganese steel, and Leoncavallo and Puccini, the Italian composers. In this self-same year, too, Charles Dickens was writing *A Tale of Two Cities*, Anthony Trollope completed *Doctor Thorne*, and George Eliot was at work on her *Mill on the Floss*. Richard Wagner had just written *Tristan and Isolde*, Samuel Clemens was piloting a Mississippi river steamer and steadily moving forward to his literary rebirth as Mark Twain. On July 10 Charles Darwin and Alfred Russel Wallace communicated their papers on evolution and natural selection to the Linnean Society of London, and Rudolf Virchow’s “Cellular Pathology” was published in Berlin on August 20.

Of London itself, much has been written. An observant, fastidious young American, Henry Adams, who visited the city in 1858, found in “the long, muddy, dirty, sordid, gas-lit dreariness of Oxford Street . . . a certain style (that) dignified its grime. . . . The eighteenth century held its own. . . . Vanity Fair was alive on Piccadilly in yellow chariots with coachmen in wigs, on hammer-cloths, footmen with canes, on the footboard, and a shrivelled old woman inside; half the great houses, black with London smoke, bore large funereal hatchments, every one seemed insolent, and the most insolent structures in the world were the Royal Exchange and the Bank of England.” (Figs. 1–4.)

An amalgam of well-nigh unlimited wealth and grinding poverty, of luxury and Victorian stability...
side by side with filthy stews, misery, and starvation, it was no better nor no worse than a dozen cities of its rank in Europe and America.

**Berlin in 1858**

Built on a barren, sandy plain without a vestige of a hill and traversed by the muddy, sluggish Spree, Berlin is oppressively hot even in May and bitterly cold during the long-drawn-out winter. To young Henry Adams of Boston it appeared as “a poor, keen-witted, provincial town, simple, dirty, uncivilized, and in most respects disgusting. Life was primitive beyond what an American boy could have imagined. Overridden by military methods and bureaucratic pettiness, Prussia was only beginning to free her hands from internal bonds. . . . German manners, even at Court, were sometimes brutal, and German thoroughness at school was apt to be routine. . . . The condition of Germany was a scandal and nuisance to every earnest German, all of whose energies were turned to reforming it from top to bottom.” Adams came to appreciate the “simple character, the good-natured sentiment; the musical and metaphysical abstraction; the blundering incapacity of the German for practical affairs. . . . Germany had no confidence in herself, and no reason to feel it. She had no unity, and no reason to want it. She never had unity. . . . Until coal-power and railways were created, she was mediaeval by nature and geography.”

But a certain simple charm emanated from the well-planned streets of Berlin, lined as they often were with lime trees beneath which the people sat
at night listening to the band. Entrance from the west by the Brandenburg Gate, an imitation of the Propylaeum of Athens, with its large figure of Victory in her chariot drawn by four horses and bearing the Prussian eagle, led to the broad Unter den Linden and the royal palace (Figs. 5 and 6). Many of the buildings were imposing and built of brick and stucco. The old or eastern part of the city was given up to business, and was traversed by long, stone alleys, with footpaths on either side raised above the centre or separated by a kennel lined by small rough stones (Fig. 7). There were many squares (Figs. 8 and 9), some spacious and surrounded by tall, handsome buildings with little or no ornaments, seldom paved or turfed and often treacherous from stagnant water. The left bank of the Spree was dead flat so that its water often overflowed the pavements.

Between the Brandenburg Gate and the palace were crowded together the guard house, the university, arsenal, opera house, and the new theatres. The palace was a roomy plain building, fronted with large parade grounds. Outside of the Brandenburg Gate stretched an extensive plantation bounded to the south by small handsome villas and on the north by the Spree, whose bank was dotted with coffee houses, rustic benches and tables beneath limes and elms, and numerous beer houses. This was the famous Thiergarten much frequented by squads of schoolboys and beloved by the Berliner and his family, rivalling in his favour the Palace of Charlottenburg, two miles from the city, where Frederick the Great had kept his sculpture. A small Doric temple, among cypresses and weeping willows, marked the tomb of Queen Louise of Prussia, who had rallied the people against Napoleon.

In spite of the general air of cleanliness and order, Berlin had its black spots. Even in 1873, as young William Osler wrote:

"The drainage is everywhere deficient, and in the greater part of the city the sewers are not even covered but skirt the pavement on each side, sending up a constant odour, which until one gets acclimatized is peculiarly disgusting."
The incidence of typhoid fever and kindred diseases was high and epidemics were frequent. Poverty and crime were common enough, and concentrated in those areas where the railways crept inwards from the four points of the compass. The journey from London to Berlin, via Ostend, a distance of 765 miles, took 40½ hours. Hospitals and charitable institutions were numerous, but medical teaching was centralized around the Royal Charité. A sequence of illustrious teachers had, however, made Berlin the focus of the medical scientific world. The newly erected Pathological Institute at the Charité, presided over by Virchow, was a Mecca for pathologists. A heavy drinking, smoking, duelling set of students thronged the lecture rooms and wards. To young Osler they seemed

"a hard-working set, much given to long hair and slouched hats, and a remarkable number of them wear glasses. They possess the virtue, quite unknown as far as my experience agrees, among their English or Canadian brethren, of remaining quiet while waiting for a lecture, or in the operating theatre. . . . Field sports, such as cricket and football, are entirely unknown among the students, but they have a curious habit of forming small societies of 10 or 12, who have a room at some restaurant where they meet to drink beer, smoke, or discuss various topics. . . . Drunkenness is not common, at least not obtrusively so, but they appear to get a fair number of cases of delirium tremens in the Charité."

For those who lived in a residential institution such as the training school for army surgeons, where Virchow received his education, life was severely disciplined. The lecture time-table is positively frightening. The youthful Virchow and his fellow student Helmholtz slogged away at 48 lectures each week with 12 hours of revision classes. Helmholtz wrote to his parents in 1838, "The food in the Institute is not so bad as most people make out,* though less good than in a private home. We can have two helpings of soup and vegetables, but only one of meat. Or instead of vegetables we may have sauce over the meat, with potatoes." Helmholtz shared a large room with one or two others, had his own piano on which he played the sonatas of Mozart and Beethoven, and ran a kind of glee club. In the evenings he read Goethe and Byron and sometimes integral calculus! Apparently he was not regarded as a prig or freak by the tough army set. The numerous letters of young Rudolf Virchow to his parents, though harassed by the educational treadmill, give no hint of unhappiness or persecution.

*Largely sauerkraut, sausage, and beer, so Henry Adams assures us. A far more serious feature was the dislike of fresh air.

Virchow in 1858

This selfsame Rudolf Virchow was born in 1821 in the tiny Pomeranian county town of Schavelbein. His father was a small farmer who dabbled unsuccessfully in petty commerce. Of Virchow's mother we know scarcely anything. She seems to have been a fretful, worrying woman who played little part in the development of her son. Their life was narrow and colourless and copied that of the junkers of eastern Germany, from whom was emerging that man of iron will, Bismarck. Contemporaries of Virchow included Helmholtz, the physicist, Schliemann, the excavator of Troy, Flaubert and Baudelaire, the French writers of genius, and Mary Baker Eddy, the founder of Christian Science. Virchow was slightly junior to Claude Bernard, Karl Marx, Queen Victoria, and John Ruskin, and slightly older than Louis Pasteur, Francis Galton, and Lord Kelvin.

A school career at Cöslin marked Virchow as a brilliant scholar and a rebel against authority. Despite strong competition, he gained a place at the Friedrich-Wilhelm Institute in Berlin in 1839, where he underwent training as an army doctor. From the Institute came Helmholtz, Loeffler, Gaertner, Behring, and many distinguished doctors, yet instruction was largely empirical and speculative. But though training was stern and harshly Prussian, with long hours of study and little leisure, there was some let-up from time to time, as Helmholtz's account of his life shows, and the didactic classes and revisions were lightened by the university lectures of three of Germany's greatest medical teachers, Johannes Müller, the physiologist, J. L. Schoenlein, the clinician, and Casper, the toxicologist. To the former, young Virchow owed his initiation into scientific method; a letter to his father exists in which he asks that some rabbits be secured for some experiments he wished to conduct when he came home.

Qualifying in 1843 at the age of 22, Virchow served as "company surgeon" in the Charité Hospital, where he picked up some chemistry and histology from Robert Froriep, the prosector, whom he succeeded three years later. Meanwhile, his reputation as a teacher mounted, and in 1845 appeared his first publication on fibrin and "white blood," forerunner of his justly celebrated work on embolism and leukaemia. On May 3, 1845, in an oration commemorating the birthday of the Friedrich-Wilhelm Institute he urged that all sorts of methods be employed in extending clinical research, stressing the impor-
Dr. Samuel D. Gross, the eminent American surgeon, visited the Institute in 1868 and tells us that the laboratory

"is a model in its way, admirably adapted to the wants of the student for improvement in the use of the microscope and the examination of morbid specimens, which are passed round in jars or on plates on a near little railway carriage, so that every one may have a full opportunity of inspecting them. Microscopes are provided in great numbers. . . . Virchow is a most patient and laborious investigator, and yet he never seems to be in a hurry. His dissections seldom occupy fewer than two and a half to three hours each. Every organ of the body is thoroughly explored. For years past his habit has been to open, every Monday morning, a cadaver in the presence of his private pupils with a view of instructing them in the art of conducting autopsies—holding the knife, using the saw, and taking notes, the whole being supplemented by microscopic inspection of the more important diseased structures. . . . A work from his pen on the subject of autopsies was lately issued at Berlin. On Wednesdays and Saturdays he devotes two hours before his class to the illustration of pathological anatomy."

The first assistants were Hoppe-Seyler, the great biochemist, and von Recklinghausen. Pupils flocked to him from far and wide, and the next few years saw the publication of some of his greatest works. Supreme among them is the "Cellular Pathology, based on physiological and pathological histology" which appeared on August 20, 1858. Based on a series of lectures given early that year to Berlin medical practitioners, it sums up what he had been thinking and writing over the previous 12 years. Of this work Lister said that it had

"established the true and fertile doctrine that every morbid structure consists of cells which have been derived from pre-existing cells as a progeny. . . . Even those morbid structures which deviate most from the normal structures are known to be derived as a progeny from normal tissue—from normal cells, driven to abnormal development by injurious agencies."

These principles are developed brilliantly in Virchow's other great work, *Die krankhaften Geschwüste*, published between 1863 and 1867.

For us in England it is pleasing to record Virchow's staunch friendship for our own country. He had been brought up at a time when Europe felt strongly the reaction that followed the Napoleonic Wars and England alone stood for political freedom. He had seen, at close quarters, a bureaucratic and feudal régime in action in Prussia, and had suffered for the part he had taken in the revolution of 1848. Virchow made many close friends in England, amongst them Huxley, James Paget, Lister, Pye-Smith, Kanthack,

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*tHis illustration of the theory of disease, "I know a family—a very exalted one—in which the grandfather had softening of the brain, the son hardening of the brain, and the grandson no brain at all" was well understood in Germany to refer to the three kings of Prussia. Frederick William the Second, Third, and Fourth. Virchow made little secret of his contempt for the national religion. He was an agnostic and denied the existence of a hell and the devil, of whom he said "only a bumptious Mecklenburg parson could be so foolish as to believe in him." (Semon, 1902.)

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1858
and Shattock. He was well informed about British medical writings and he frequently acknowledged the great services of John Goodsir of Edinburgh in the creation of cellular pathology as a discipline. Felix Semon, who knew him well and has written down, with devastating frankness, his weaknesses and oddities, says that the warmth of his receptions in England filled him with deep gratitude. When he gave the Croonian and Huxley Lectures in London he experienced a triumphal progress which almost overwhelmed him.

It is surely right and proper that we pause for a few moments to recall with gratitude and respect Virchow's great achievement given to the world just one hundred years ago. What this has meant to medical science you will learn from the distinguished contributions that follow. May I conclude by quoting a moving remark of Socrates.

"Although my mind is far from wise, some of those who come to me make astonishing progress. They discover for themselves, not from me—and yet I am an instrument in the hands of God."

Fortunate, indeed, is he about whom this may be said.

In the preparation of this paper I have received much help from many friends, especially from Dr. Helmut Drubba of Essen, Dr. Walter Pagel of London, and the Cultural Attaché of the German Embassy, London.

Figs. 1–4 are reproduced by permission of the British Museum, and Figs. 5–9 by permission of the Landesbildstelle, Berlin.

I have drawn fully upon the authoritative works of the following and upon innumerable shorter papers in British, American, and German journals.


