"History is simply the biography of the mind of man; and our interest in history, and its educational value to us, is directly proportionate to the completeness of our study of the individuals through whom this mind has been manifested."

—OSLER

Contributions by Medical Undergraduates to the Science of Preventive Medicine

By WILLIAM C. GIBSON, M.D., D.Phil.

THE AVERAGE student today is likely to greet with a mixture of amusement and pity any suggestion by his teachers that he might make a lasting contribution to medical science. Students have wallowed through mountainous academic seas for so long in convoy fashion—the speed of the fleet being set by the speed of the slowest ship—that their imagination has been blunted, if not embalmed. It is in the hope of resurrecting some of the keenness of students' first bright days in medical school that the following essay on student contributors of the past is presented. The inquiring, restless mind of the uninhibited undergraduate is still our greatest asset in medicine and the greatest deterrent to smugness in research.

Educators and administrators also would do well to review in retrospect the lives of past contributors in the field of preventive medicine, for in such a study there may be found the key to further recruiting and development of exceptional personnel. I mention educators because the critical ingredient—gray matter—passes through their hands. Their attitude, as we shall see throughout this paper, can be absolutely determinative. They can foster discovery, or they can impede it. I mention administrators, for they face a dilemma—they have to make existing methods work while insuring that they are not brushing aside as a "nonconformist" some potential discoverer.

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Smallpox

Appropriately, this review is opened with a reference to Edward Jenner, who combined early vision, fortitude in the face of powerful critics, and a life-long delight in clinical investigation. Jenner found himself, in 1768 at the age of 19, a quaking medical apprentice noting down a patient's history, possibly one of his first. The patient was a milkmaid who, on being questioned about any possible smallpox in her history, replied, "I cannot take that disease for I have had the cowpox." Thus, the fledgling Jenner encountered early in his career the common belief among the country people of Gloucestershire that there was a harmless preventive of smallpox. Perhaps his newness to the study of medicine caused him to listen

long enough to this patient's replies to gain something of value. His countryman William Withering was to stumble on the virtues of digitalis in a similar rural setting in Shropshire.

Jenner became, as have many since, a student unpopular with his teachers, for he kept bringing up his fantastic theory, as from the back pasture. However, he lived in John Hunter's house while studying in London, and his patron greatly encouraged the thoughtful undergraduate. Hunter's philosophy was couched in his immortal advice to Jenner, "But why think, why not try the experiment."

Jenner graduated at the age of 22, and, despite an offer to accompany Captain Cook on a world-circling expedition, he returned to his native Gloucester to practice and to build up a set of records on simple, clear observations. So cautious was Jenner that he vaccinated no one for 30 years after his undergraduate conception of vaccination. Then came Sarah Nelmes—the source—and James Phipps—the subject. And Jenner's campaign, for he was a campaigner, was launched.

John Hunter had been dead 5 years by the time Jenner was ready to publish the results of his inquiry. Jenner turned to the Royal Society in 1798 for an audience and was rebuffed with the advice that he "should be cautious and prudent . . . and ought not to risk his reputation by presenting to the learned body anything which appeared so much at variance with established knowledge, and withal so incredible."

The same advice had been given Franklin by the same body in 1752 when he reported on his derivation of electricity from the clouds. The type of advice offered Jenner, who happens to have been a keen balloonist, was 140 years later to be tendered another aeronaut Frank Whittle, the jet propulsion pioneer, on the grounds that he was still a Cambridge undergraduate and his theory was "incredible."

Tuberculosis

In another area—that of tuberculosis—one is struck by the student contributions of the impecunious, observant, and industrious René Theophile Hyacinthe Laennec. Before graduation in Paris in June 1804, he had written papers on mitral valvular disease and on "inflammation of the peritoneum" under the stern and powerful Dupuytren. He had discovered the subdeltoid bursa and had also shown that hydatid cysts were due to parasites. In March of 1804, he gave an address on what he called "pulmonary tuberculosis," in which he showed "phthisis" to be tuberculosis of the lungs.

Laennec learned of percussion from Jean-Nicolas Corvisart, who brought this clinical application of an innkeeper's barrel-tapping technique into use 47 years after Leopold Auenbrugger had first described it. Laennec's great book on auscultation appeared in 1819, and by 1825 we find William Stokes, as an Edinburgh medical undergraduate, singing the praises of the method in his book, the first work in English on auscultation, entitled "An Introduction to the Use of the Stethoscope with its Application to the Diagnosis in Disease of the Thoracic Viscera; Including the Pathology of Various Affections."

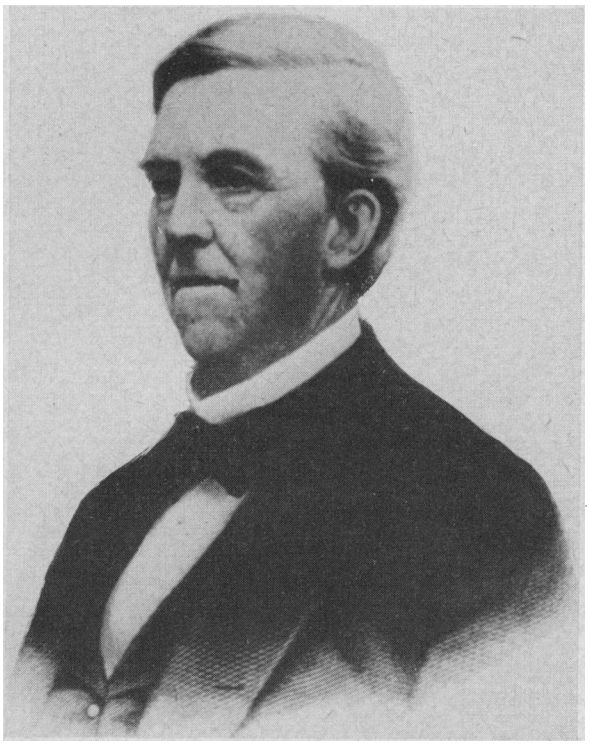
An unsung American contributor in the history of tuberculosis is James Jackson, Jr., of whom Osler wrote: "Jackson's name . . . will always be associated with the studies on emphysema, and he is the discoverer of the prolonged expiration in pulmonary tuberculosis." As an undergraduate Jackson studied with the great French clinician and pathologist Louis. In 1832 he sent home to New England an article on cholera based upon his experience with Louis in an epidemic in France. While preparing to write his M.D. examinations at Harvard, he was stricken with dysentery and died at the age of 24. Louis' letters to Jackson's father asking if the son could not spend another year in his clinic in Paris are very touching.

Another American pioneer in tuberculosis was James Blake (1815–93). In 1860 he was recommending and practicing the open-air rest treatment in a sanatorium on the summit of Monte Sol in California to the east of Mount St. Helena where Robert Louis Stevenson later lived. Blake's student contribution had been the arranging of the elements into a periodic table on the basis of their physiological effects. This was done when Blake was an undergraduate in London, aged 23. Mendelejeff, usually credited with the periodic table, was 4 years old at the time of Blake's publication. Blake's student discovery was made under the benev-

olent eye of William Sharpey, as were those by Lister and Huxley.

Puerperal Fever

Ignaz Philipp Semmelweis and Oliver Wendell Holmes had interesting student preparations for their eventual encounter with puerperal fever. As an undergraduate Semmelweis was experimenting on rabbits with tartar emetic, at that time a preferred "remedy" for



". . . not to take authority when I can have facts, not to guess when I can know . . ."—Holmes.

pneumonia. Holmes, like Semmelweis, had spent a brief apprenticeship in law—a discipline which was to serve them, and humanity, well in the struggle to which their methodical investigation brought them. Holmes began the study of medicine under James Jackson, Sr., in Boston and continued it in Paris, along with Jackson's son already mentioned. In a letter sent to his home in Boston, he alluded to his student "discoveries": "I have more fully learned at least three principles since I have been in Paris: not to take authority when I can have facts; not to guess when I can know; not to think a man must take physic because he is sick. . . . My aim has been to qualify myself . . . not for a mere scholar, for a follower after other men's opinions, for a dependent on their authority—but for the character of a man who has seen and therefore knows, who has thought and therefore has arrived at his own conclusions." Holmes, the Bostonian, a nationally known poet at 21, little suspected that a fiercely independent Hungarian practicing in Vienna unknowingly would be his ally. Holmes' pen was mightier than the swords of his obstetrical compatriots. Semmelweis maintained his doctrine against frightful persecution because he knew he was right and he had the support of his teachers Rokitansky, Skoda, and Hebra.

Cellular Pathology

One of the great concepts introduced in the last century was that of "cellular pathology." Rudolf Virchow as an undergraduate in Berlin decided to test the prevailing theory that inflammation was vascular in origin by studying it in the cornea, a nonvascular tissue. His graduation thesis, written in 1843, was entitled, "De rheumate praesertim corneae." We believe from a letter of 1841 written to his father in the country, asking for more rabbits, that he had been engaged on it at least 2 years prior to graduation. Virchow's student work on the cornea determined his later opinions on the cellular basis of inflammation and doubtlessly influenced his outlook on the fundamentals of pathology.

The distinguished physician-educators Sir James Paget and Sir William Osler were student investigators, strangely enough, in the same field. As an undergraduate at St. Bartholomew's Hospital Medical School, London, Paget in 1835 discovered the cysts of *Trichinella spiralis* in the muscles of the cadaver he was dissecting. In 1870, William Osler, a first-year medical student at the University of Toronto, was removing these trichinae from a cadaver and trying to infect cats, dogs, and rabbits with them. Osler entered medicine with training in the preparation of biological specimens, received at the skilled hands of James Bovell and Father Johnson at their school in Weston, Ontario. On graduation at McGill Medical

Faculty in 1872 his thesis was accompanied by such excellent histological preparations that he was awarded a special prize. Osler's early bent toward pathology was evident throughout his long clinical career. It remained for an undergraduate at Johns Hopkins Medical School, Thomas R. Brown, to discover in 1898 the eosinophilia seen in trichinosis.

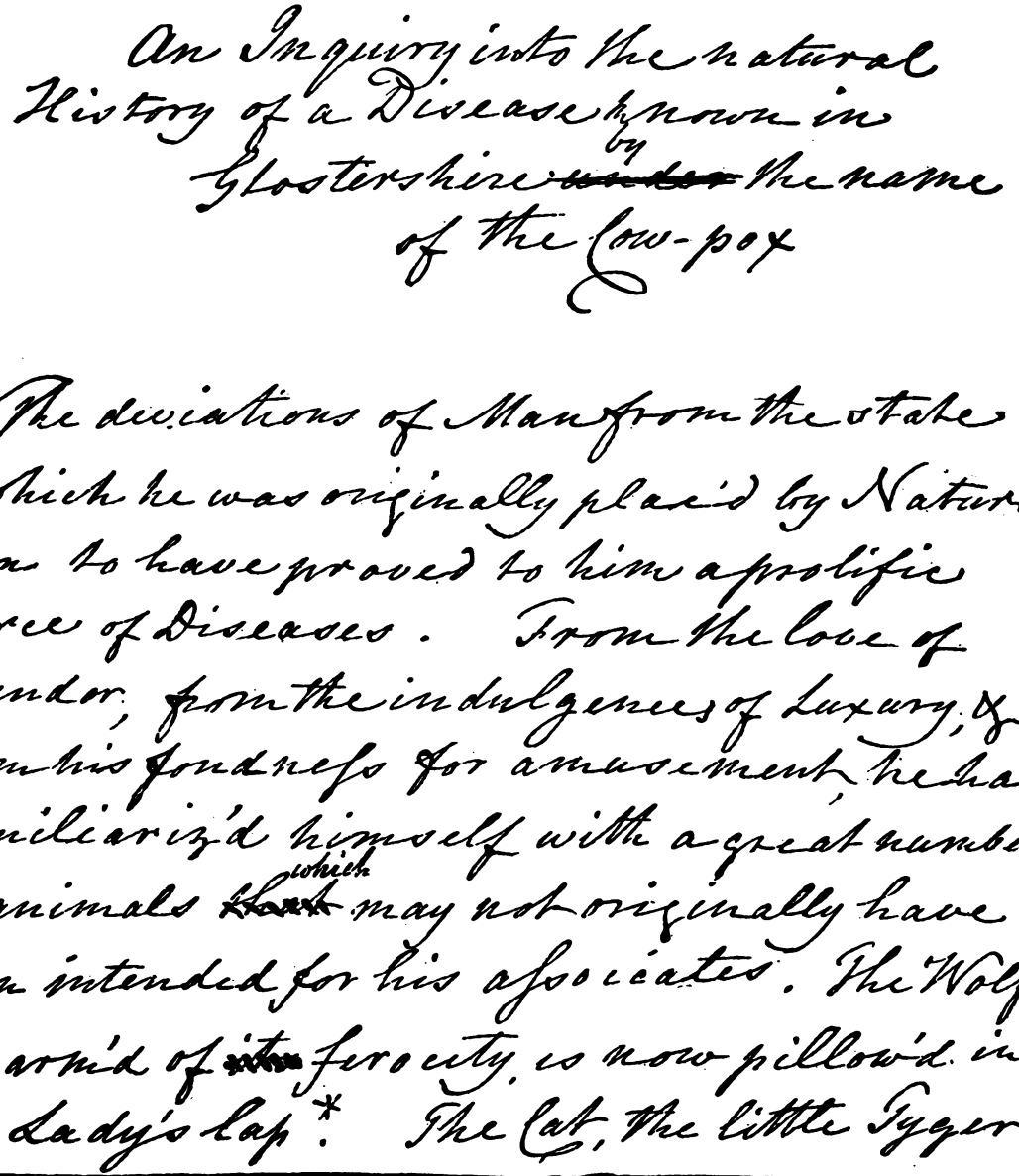
David Gruby, the father of medical mycology and discoverer of the cause of favus, was in 1835 an undergraduate protégé of Carl Rokitansky, the celebrated teacher and pathologist at the University of Vienna. Gruby wrote his first paper on "The Morphology of Pathological Fluids." His study concerned the cell forms in pus from different diseases. The story of the hardships faced and overcome by this remarkable spirit are well-nigh unbelievable. He acquired his early schooling by listening outside a classroom from which he was barred on religious grounds. He was apprenticed to a lens grinder, and as a result he was able to make his own microscope when he entered medical school. Despite the fact that he earned his passage through medicine by tutoring, he nevertheless found time for research under Berres and Rokitansky, the latter permitting him to use his "best microscope" for it. Once again does Rokitansky, the teacher of pathology, enter upon our stage.

Oroya Fever

Daniel Carrion is probably the only medical student in history to have a medical school and several hospitals named after him. Separated as we are by a period of 70 years from his death from Oroya fever, administered to him in the course of his student research project, it is hard for us to realize the impression which his death made on Latin American medical and scientific circles. As early as 1858, a medical student named Tomas Salazar wrote in his graduation thesis, "Historia de las Verrugas," that this disease was waterborne. Since the Conquest it had been regarded as the equal of the "pest," and in the year 1870 alone had taken the lives of 7,000 workmen completing the trans-Andean railroad into Oroya, Peru. Carrion became interested in the problem and during vacations sought out cases and plotted them on a map of the area. Only near Oroya was the disease endemic. The clinical picture of high fever, profound weakness, joint pains, anemia, and leukocytosis was well known, but the cause was still a mystery. Some called it acute pernicious anemia, some atypical malaria, while others said it originated from the hot springs. On August 27, 1885, Carrion, against all advice, received an inoculation of blood from a 14-year-old boy suffering from the typical verruga peruana skin eruption. He was going to prove, once for all, the connection between Oroya fever and verruga peruana. After 3 weeks of excellent health he suffered muscular pains and prostration, with severe anemia. The post mortem was an important contribution to an understanding of the disease. The Peruvian student had answered the question of the connection between the two diseases.

Patrick Playfair Laidlaw as a Cambridge undergraduate, at the turn of the century, carried on an important investigation on hemoglobin derivatives in the biochemical laboratory of Sir Frederick Gowland Hopkins. This set the stage for his postgraduate work on histamine with Sir Henry Dale and for his lifelong researches into distemper and influenza. Hopkins must be listed among those who most encouraged young investigators.

William George MacCallum entered Johns Hopkins Medical School in 1894 bearing a gold medal from the University of Toronto for an important contribution on worm parasites. In his final year as a student at Johns Hopkins he reported on his studies of malarial parasites in birds. He supplied the missing link in the life cycle of the parasite, showing the flagellated form to be the sperm cell. Sir Ronald Ross, who had interpreted it as a flagellated spore escaping from a female cell, wrote years later: "I have ever since felt disgraced as a man of science!" MacCallum's later discovery of the role of the islet cells of the pancreas in diabetes became the springboard for Banting's revolutionary work, aided by the youthful Charles Best. In fact, as we shall see, the islet cells had been discovered by a medical student, Paul Langerhans.



An Inquiry into the natural
History of a Disease known in
Gloustershire ~~under~~ by the name
of the Cow-pox

The deviations of Man from the state
in which he was originally plac'd by Nature
seem to have proved to him a prolific
source of Diseases. From the love of
Splendor, from the indulgences of Luxury, &
from his fondness for amusement, he has
familiariz'd himself with a great number
of animals ~~which~~ which may not originally have
been intended for his associates. The Wolf,
disarm'd of ~~its~~ ferocity, is now pillow'd in
the Lady's lap*. The Cat, the little Tyger of

* The late Mr John Hunter proved by experiments
that the Dog is the Wolf in a degenerated state.

Reproduced above is the first page of William Jenner's classic which he presented to the Royal Society in 1798—three decades after he had noted the comment of a Gloucestershire milkmaid that she once had cowpox and therefore could not get smallpox. The Royal Society reprimanded him for this "incredible" paper, "so much at variance with established knowledge."

Chemotherapy

The father of modern chemotherapy, Paul Ehrlich, stated his great side-chain theory as a medical student. Encouraged by one of his teachers, Waldeyer, at Strassburg, Ehrlich began in 1877, by testing the staining qualities of many of the aniline dyes just coming into commercial use in Germany. After transferring to the University of Breslau he had the opportunity of working in the laboratories of Conheim and Heidenhain. While still an undergraduate Ehrlich described, in the *Archives of Microscopic Anatomy*, his experiments on histological staining which brought him to the "idea of a chemical binding of heterogeneous substances to the protoplasm." The rest of Ehrlich's life was spent in developing this great generalization in the fields of immunity, bacteriology, and chemotherapy. The key to Ehrlich's research lay in the aniline dyes, the first of which was synthesized by an 18-year-old English chemistry student William Henry Perkin. Two years later Archibald Scott Couper, as a student in Paris, proposed a valency of four for carbon and showed that it formed long-chain compounds. It took the genius of Ehrlich, a chemist with great stereovisual powers and interest in tissues, to bring together into a fundamental concept all that had gone before.

Public Health

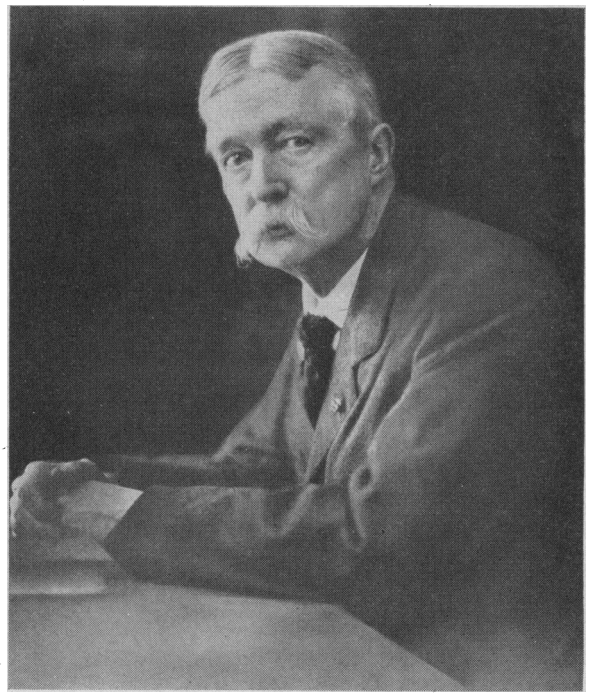
John Shaw Billings has been described as America's greatest contributor to scientific medicine. He was a born inquirer rather than the product of famous teachers. As a student, writing an essay on the surgical treatment of epilepsy, he came to realize the utter lack of any index to the world's medical literature. He lived to remedy this, through the Index Catalogue and its successors in the library of the Surgeon General of the United States Army.

However, our interest in Billings here stems from his campaigns in the fields of sanitation and hospitalization. As an impoverished student at the Medical College of Ohio in Cincinnati from 1858 to 1860, Billings paid his way by serving as caretaker of the dissecting rooms and by "living in" at one of the city's hospitals. This latter appointment caused him to think more about the organization of hospitals—or possibly lack of it—than did contemporary administrators. He found out where things could "go wrong" in institutions and he developed a keen sense of smell with regard to these matters.

It is little wonder that on his first Army posting in the Civil War Billings excoriated Cliffburne General Hospital in Washington, D. C., as being "in an extremely filthy and dilapidated condition—no drainage whatever, . . . no sinks, no water within half a mile." He was later to describe the United States Army as "the best fed and the worst housed" in the world. His suggestions for reorganizing the marine hospitals and his sanitation reports on Army military posts were blunt and forceful. One of his interests was vital statistics, and in 1880 he suggested to the Government that the data compiled from the census "might be recorded on a single card or slip by punching small holes in it, and that these cards might then be sorted and counted by mechanical means according to any selected group of these perforations."

Billings' stimulating influence was to be felt in his work as director of the laboratory of hygiene at the University of Pennsylvania, as designer of the Johns Hopkins and Peter Bent Brigham Hospitals, and in medical education and libraries. When asked how he accomplished so much he replied: "There is nothing really difficult if you only begin. Some people contemplate a task until it looms so big it seems impossible. But I just begin and it gets done somehow. There would be no coral islands if the first bug sat down and began to wonder how the job was to be done."

Thomas "Phenomenon" Young, that many-sided genius who discovered in his first days at medical school that the lens of the eye varies its shape in accommodation was an early constructor of life expectancy tables and of insurance formulas. His first was published in 1826 as "A Formula for Expressing Decrement of Human Life." In his theory of color vision—rediscovered years later by Helmholtz—in his accurate measurements of the size of red and white cells of the blood, in the deciphering of the Rosetta stone, in developing the modulus of elasticity, in setting out a phonetic alphabet for all languages, in standardizing the imperial gallon, and in his writings on gaslighting,



"There is nothing really difficult if you only begin. . . . There would be no coral islands if the first bug sat down and began to wonder how the job was to be done."—Billings.

Young made himself one of the most celebrated scientific contributors of all time. If he were alive today we would find him, doubtless, energizing the Food and Agriculture Organization with reports of his observations on the production of better wool and meat through crossbreeding and of increased food production through irrigation, matters which he studied as a medical student. His drive to understand things was inexhaustible and his capabilities truly Newtonian.

Nutrition

The field of nutrition reveres the name of Sir Frederick Gowland Hopkins for his early researches on "accessory food factors" which we now call vitamins. Before graduation in medicine, Hopkins published a paper on the pigments in the wings of the English brimstone butterfly. He found the pigment to be a derivative of uric acid and, in his typical way, immediately improved the method for the determination of uric acid. This method was the key to his succeeding researches on nitrogenous compounds. As he investigated the effects of artificial diets composed of purified proteins he became aware of "unidentified accessory food factors" and pursued them, with what great success we all know today.

To follow briefly this lead in nutrition one finds the field of carbohydrate metabolism bristling with student contributors. But, it is the disease diabetes which absorbs us as physicians interested in public health problems. Paul Langerhans discovered his famous "islets" in the pancreas 2 years before he graduated in medicine. Virchow had given him encouragement and laboratory space in 1867, and his graduation thesis, completed in 1869, is an historic document. In 31 pages he described his discovery, adding: "There is indeed hardly another organ in which there is such glaring contrast between the brilliant results of physiological research and the complete darkness in the realm of anatomic knowledge."

The deposition of calcium in the teeth and bones of the body was poorly understood until the Swedish medical student, Ivar Sandstrom, in 1877 discovered the parathyroid glands. True, it remained for W. G. MacCallum and others to demonstrate the physiological principles involved, but Sandstrom's investigation as a 25-year-old student at Uppsala was basic to further progress. His paper was returned to him by a German editor as being too long to publish. The fact is that the paper was so thorough that little has been added to the subject since!

At a time when cardiovascular disease is receiving such attention we would do well to review the student work of Jean L. M. Poiseuille. In 1828 he wrote his M. D. thesis in Paris on "Recherches sur la force du coeur aortique" and in it described his revolutionary mercury manometer for registering blood pressure. Using this instrument he was able to show the rise and fall in the recorded blood pressure with each heart beat, and he actually calculated the degree of dilation of the arteries with each systole.

Aviation medicine has had a number of interesting undergraduate devotees. Alphonse Gal, while a medical student in Italy, served in 1872 on a "mother ship" for sponge divers operating off the Turkish coast. He was the first

to describe the itching which goes with "the bends" in deep sea divers. The father of aerial photography, Felix Tournachon, was a medical student. Known as "Nadar," he, like Jenner, was one of the early balloonists. With this reference to the latest specialty we must conclude this account.

Certainly, one thing is clear from this brief review of 2 dozen student contributors of the past: Good seed can be helped greatly by good soil. The determining factor has often been the provision of facilities for a student investigator by a sympathetic teacher. The lesson for us today would seem to be clear. Summer research scholarships in all fields of medicine and its ancillary sciences are likely to repay us handsomely as educators. Encouragement of original work by undergraduates is in the best tradition, as I have tried to show in this paper, and offers one method of offsetting the homogenizing influence of too many specialty boards. Student curiosity can be depended upon to bring to light new facts of major importance, as it has in the past. The shaping of the conditions under which such students will work and grow is a major challenge to all educated people.

Medical Research Fellowships

The Division of Medical Sciences is accepting applications for National Academy of Sciences-National Research Council postdoctoral research fellowships for 1956–57. The following programs, offered only—except as indicated—to American citizens under 35, are available:

Study in all branches of the biological, chemical, and physical sciences, and of clinical investigation applicable to the study of typical or malignant growth; also, exchange fellowships open to American and British scientists for advanced study in specialized fields pertaining to growth. These awards are sponsored by the American Cancer Society.

Fellowships in the basic medical sciences. These awards, also open to Canadian citizens, are supported by the Rockefeller Foundation.

Study in fields related to tuberculosis, supported by the National Tuberculosis Association. Applicants must be graduates of American schools.

Preparation for radiological research. Appointments to this program, sponsored by the James Picker Foundation, are not limited to citizens of the United States.

The closing date for applications is December 1, 1955. Forms may be obtained from the Fellowship Office, National Academy of Sciences-National Research Council, 2101 Constitution Avenue, NW., Washington 25, D. C.