1977

Hermann Lebert's Contributions To The Understanding Of Cancer And Cancer Genetics.

Anne J. Krush
Johns Hopkins Hospital

HERMANN LEBERT'S CONTRIBUTIONS TO THE UNDERSTANDING OF CANCER AND CANCER GENETICS

ANNE J. KRUSH

Moore Clinic, Johns Hopkins Hospital
Baltimore, Maryland 21205

Hermann Lebert (1813-1878) was born in Breslau, Germany (now Poland). His medical studies took place in Berlin and later in Zürich, Switzerland. In 1836 he studied in Paris under Dupuytren and Louis. In 1838 he began the practice of medicine at Bex, Switzerland, followed by work in Berlin, Paris, Zürich, and Bex again, and finally, Breslau. He wrote prolifically in both German and French and is best known as one of the first anatomists of the 19th century to use the microscope for pathology studies. Among his many research efforts, he distinguished between tuberculosis and cancer, which until that time had often been confused as the same disease. In Paris from 1857-1861, he produced an atlas of pathologic anatomy entitled, *Traité D'Anatomie Pathologique, Générale et Spéciale,* in which he may have been one of the first to describe premalignant polyps of the colon, rectum, and stomach. Cancers of all sites were described grossly and microscopically. He believed that only 7% of cancers were hereditary, citing Napoleon's family history of gastric cancer as one example.

† † †

INTRODUCTION

Hermann Lebert was born on June 9, 1813 in Breslau, Germany. He studied medicine in Berlin, later in Zürich, Switzerland, under Schonlein, where he received his doctor's degree at the University of Zürich in 1834. He also studied botany in Switzerland. Then, from 1834-1836 he studied in Paris with Dupytren and Louis. There, he came to know and work with Velpeau, Charcot, Laennec, Broca, and others. He went into private practice in Bex, Switzerland in 1838. After a short stay in Berlin during the winter of 1845-1846, he returned to Paris, received permission to practice medicine, and remained there until 1853 when he was appointed Professor of Medicine at the University in Zürich. In 1859 he returned to Breslau as Professor of Clinical Medicine where he remained until 1874 at which time he returned to Bex. He died August 1, 1878.

Lebert is noted for his numerous anatomical writings, keen observations, and accurate descriptions in pathologic anatomy. One of his best known publications was entitled *Physiologie Pathologique,* published with an atlas in 1845 and for which he received a prize from the French Academy of Sciences in 1848. In Paris, at the invitation of the French government, he and Professor Charles Robin made anatomical preparations for a new medical museum. In 1849 he published *Traité Pratique des Maladies Scrofuleuses et Tuberculeuses* for which he received the Portal Prize of the French Academy of Medicine. In 1851 he published *Traité des Maladies Cancereuses* for which he also received a prize. In 1854 the first volume (a huge tome about 2 feet long, 1 foot wide, and 2-3 inches thick) entitled *Traité d'Anatomie Pathologique Générale et Spéciale* was published. The entire series, which was comprised of a second volume of text and two volumes of atlas, was not completed until 1862. Lebert's earlier writings were in French; his later ones were in German and included *Handbuch der allgemeinen Pathologie and Therapie,* second edition, published in 1875, and *Die Krankheiten des Magens* in 1878.

Lebert was one of the first to use the microscope for pathology studies. Therefore, his descriptions were of gross as well as microscopic aspects of diseased organs, tissues, and cells. He made special studies of tuberculosis, carcinoma, tumors of the uterus, and aneurysms, and was one of the first to differentiate clearly tuberculosis from cancer of the lungs and other organs (Lebert, 1845). Honors which he received included Chevalier de la Legion d'Honneur, Monthyon Prize, Laureat de l'Institut de France et de l'Academie Impériale de Médécine, Member of Anatomical, Biological, Surgery, médicale d'emulation, médical d'observation Societies of Paris. He was a member of the Society of Natural History of Switzerland, Zürich, Berne, Geneva, Lausanne, Neuchatel, Wurzburg, Dresden, Leipzig, and other cities.

POLYPS–COLON AND OTHERS

A hereditary pre-cancerous disease, familial polyposis coli (hereditary polyps of the large intestine) was first described by Cripps in England in 1882 (Cripps, 1882). Though Lebert did not describe the hereditary nature, nor the fact that these polyps are pre-cancerous, he made accurate observations and descriptions of both nasal and intestinal polyps (Fig. 1). He described four kinds of polyps. These were: 1) protruding epithelial polyps which become vascularized and grow quite large; 2) hypertrophy of the glandular layer, particularly in the nasal and intestinal fossae. He described such polyps in the rectum as "large numbers of polyps, each the

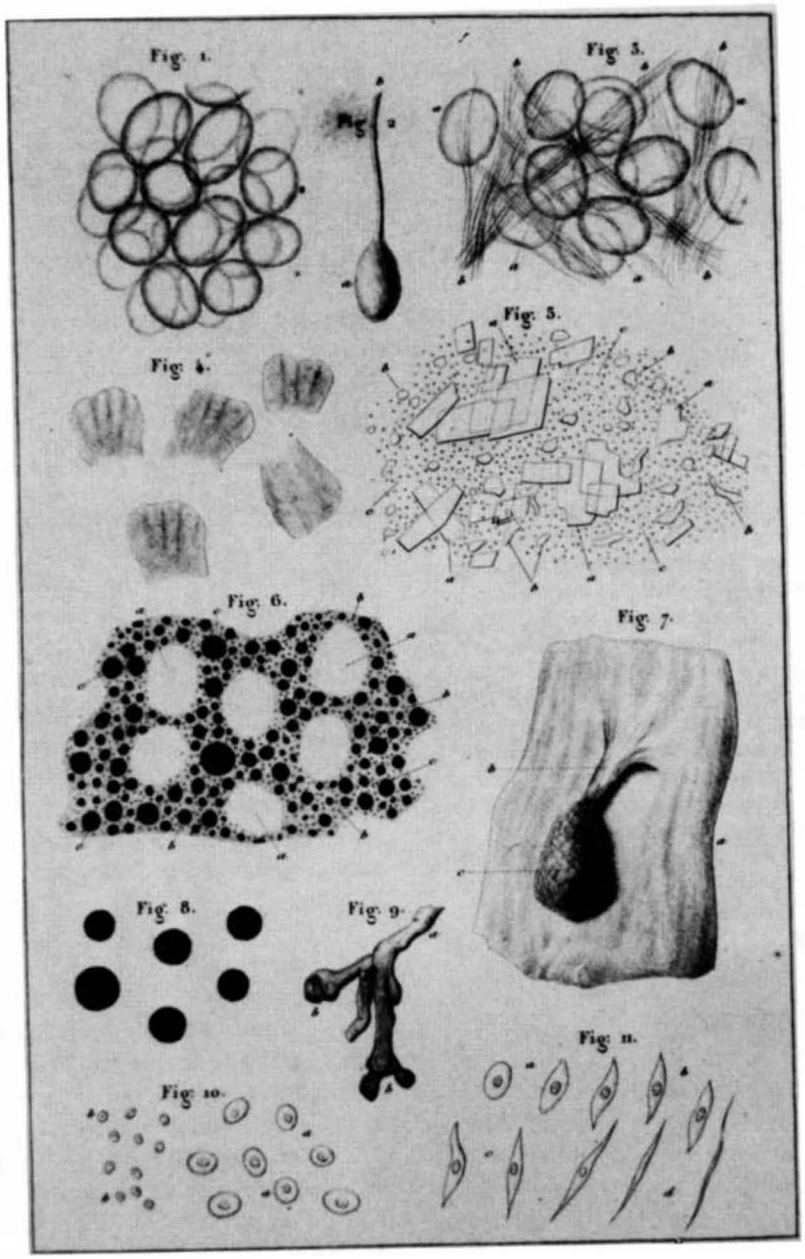

Figure 1. Copies of Hermann Lebert's original drawings of eleven types of cells, fibers and polyps found in the human digestive tract.

size of a hazel-nut, composed of elongated small glandules" (Lebert, 1857-61:266); 3) in the nasal fossae more often than in the intestines and bladder, he described polyps smaller in size than two above–the size of a pea or bean, composed entirely of hypertrophied mucous membrane. These polyps were gelatinous, semitransparent, and elastic; 4) sub-mucous polyps found in the nasal fossae and the digestive tract, of large dimensions and composed of connective tissue interposed with an amorphous gelatinous substance. He felt that these four kinds of polyps were not really distinct, but since one could find among polyps all kinds of intermediate degrees and fibrous tumors seemed to be related to the sub-mucous number four type of polyps, they might all be variations of the same thing (Lebert, 1857-61).

Lebert noted that polyps tended to be multiple in the stomach, intestines, and bladder, but that they were usually small in these locations–the size of a hazel-nut or a walnut. On the surface they were rounded and pedunculated at their point of attachment to the mucous membrane (Lebert, 1857-61:265).

CAUSE OF POLYPS

Lebert was as much in the dark concerning the cause of polyps as we are today. He stated that in the past they were attributed to a chronic inflammation of the bowel; but he speculated that they might be caused by something unusual in the diet or nutrition.

Polyps of the stomach were common in Lebert's practice. He described one patient with between 150 and 200 small polyps (the size of a pea) in the pyloric region of the stomach. (He also described one patient who had one large polyp in the cardia of the stomach.) The small pyloric polyps were usually sessile or pedunculated. Patients with gastric polyps were noted only rarely to have any symptoms.

Lebert described a case of multiple polyposis of the large intestine in a woman who died of marasmus following constant diarrhea for a year. All attempts to stop the diarrhea had failed (but surgery, with removal of the colon, was apparently not known at that time). He commented on a case of rectal polyps in a young girl, seventeen years old, and another in a 40-year-old woman (1850) in whose rectum an egg-sized tumor was removed. Previous doctors had made a diagnosis of hemorrhoids. Today we would surmise that both of these women, because of the young age when polyps were discovered, might have the hereditary kind of polyps, either familial polyposis coli or the Gardner syndrome, and we would instigate a family genetic study.

Lebert recognized that sebaceous cysts occurring on the head could be hereditary. He described in detail the appearance and the location of such cysts in a 35-year-old man and in his mother (Lebert, 1845, 2:35-36). It is too bad that he did not look for polyps in the colon in this family, because he might have been the first to describe what is now called the Gardner syndrome which consists of pre-malignant adenomatous polyps of the colon, sebaceous (or epidermoid cysts), osteomas, sometimes desmoid cysts, and other extra-colonic tumors.

Lebert described what is now known as juvenile polyposis in two children. One concerned a child who died of measles. At autopsy he found "a melanotic tumor, with a volume of a pea attached to the intestine by a pedicle 5 millimeters long." He described this polyp in minute detail (Fig. 1; illus. 6) and thought it represented hypertrophied cellular tissue in the sub-mucous layer of the intestine.

The second concerned a polyp in the small intestine of a three-year-old child who died of "tuberculosis" (Fig. 1; illus. 7). He described it as follows: "This black and compact tumor is attached to the small intestine by a pedicle 1 centimeter long, and 4-5 millimeters thick. The polyp is flattened, two centimeters long, 15 millimeters wide at its widest part and 5-7 millimeters wide at its point of insertion. The pedicle is reddish (the color of muscles) . . . is covered by a mucous membrane on which many crystals can be found. The surface of the polyp is covered with many crystals, blood vessels and melanotic cells" (Lebert, 1845, 2:114-115).

CANCER

Lebert thought that cancer differed from benign tumors by the fact that though benign tumors had all the characteristics of the elements or tissues from which they stem, cancer was distinct and "quite different from all the other forms of globules which one finds in the normal state" (Fig. 2). His definition of cancer was: "a near heteromorphic accidental production with a tendency to become generalized (in the body), to become constitutional, and with a tendency to destroy all the tissues it surrounds, whose cells are different from normal cells in the body (Lebert, 1845, 2:211-240). He described a "hard" cancer of the stomach of a woman, age 69. She had been in good health until the age of 67 when she had a short period of dyspepsia which disappeared. She had no other symptoms until 11 months before her death when she began to vomit after meals—coffee ground material with her food. But she had no other symptoms of pain or discomfort in the stomach. At autopsy 11 months later, her stomach was thickened with a large hard tumor in the pylorus (Lebert, 1845, 2:364-365).

Lebert described benign and malignant tumors of cartilage and bone. He noted that sometimes after surgery for a large bony tumor, patients died "because of the production of a large number of tumors in various other internal organs, principally those of the chest cavity" (Lebert, 1845, 2:424-442). This seems to indicate a description of metastasis of sarcoma of the bone to lung.

In discussing possible causes of cancer about which he "confesses insufficient scientific knowledge of this subject" (Lebert, 1851), Lebert suggested a number, including: "external violence (blows and bruises), grief or depression, heredity, influences of age, sex, season of the year, nutrition or diet, economic status, living environment, excessive alcohol intake, state of health, and age at menopause in women (Lebert, 1851:516). For example, in discussing the causes of cancer of the stomach, he noted that cancer of the stomach occurred more frequently among the rich class than among the poor class. In 21 patients with cancer of the stomach in which wealth was noted, 15 were rich and 6 were poor (Lebert, 1851:520). He then concluded that there was actually no known cause at the time he wrote.

Concerning the influence of heredity, Lebert mentioned that a number of scientists had cited examples of hereditary cancer of the stomach, the most noteworthy being the family of Napoleon. In his own series of cases, Lebert reported that only 5 of 42 instances of stomach cancer appeared to be hereditary. Therefore, he felt that heredity, though sometimes a "cause" of cancer, was more the exception than the rule (Lebert, 1851:521-522).

Finally, Lebert's chief aim in all of his anatomical and pathological studies with the microscope was to "end the suffering and death of cancer victims (Lebert, 1851: XX).

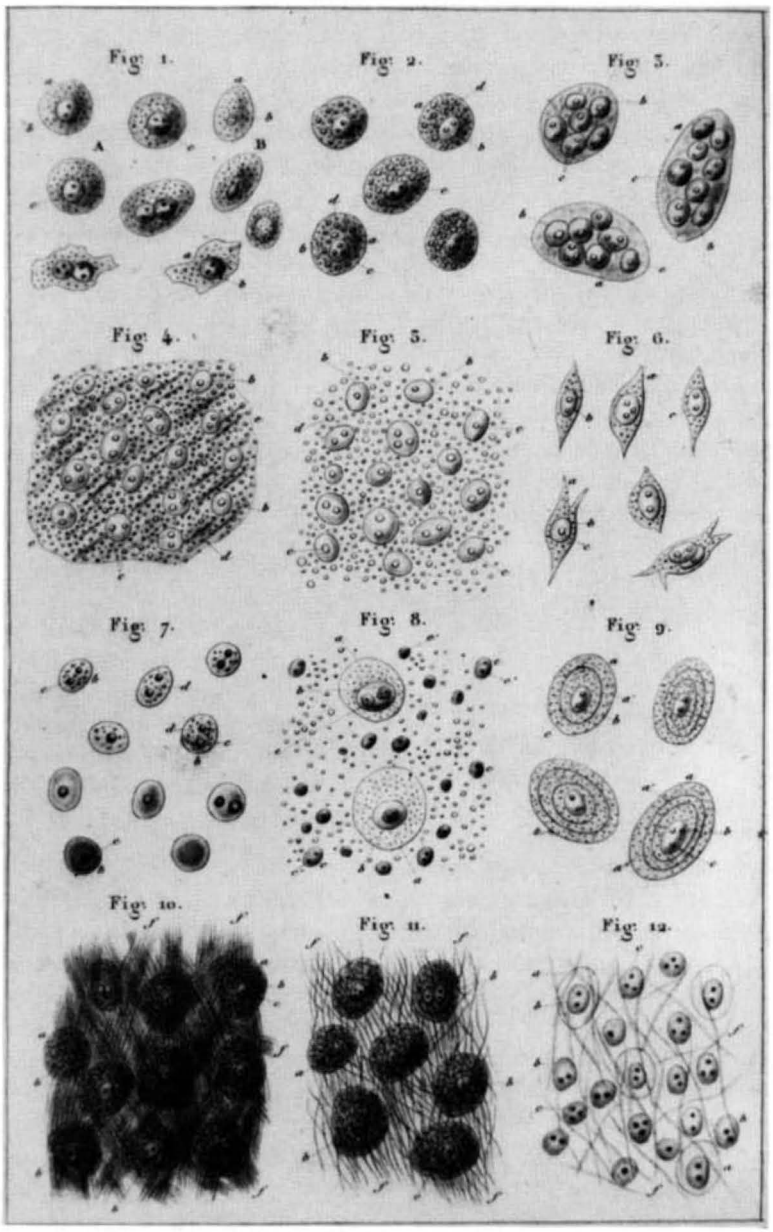

Figure 2. Copies of Hermann Lebert's original drawings of twelve types of cancer globules, cells, and tissue found in cancer of the human digestive tract.

REFERENCES

Cripps, W.H. 1882. Two cases of disseminated polypus of the rectum. Trans. Path. Soc. Lond. 33:165-168.

Lebert, H. 1845. Physiologie Pathologique; ou Recherches Cliniques, experimentals et microscopiques sur l'inflammation, la tuberculization, les tumeurs, la formation du cal, etc. Paris, J.B. Bailliére.

_____. 1845. Physiologie Pathologique. Paris, J.B. Bailliére. 2:35-56.

_____. 1851. Traité Pratique des Maladies Cancéreuses et des Affections Curables Confondus avec le Cancer. Paris, J.B. Bailliére, XXI.

_____. 1857-1861. Traité d'Anatomie pathologique, générale et spéciale; ou Description et Iconographie pathologique des alterations morbides tant liquides que solides observées dans le corps humain. Paris, J.B. Bailliére et fils. 1:264.