

In regard to Dr. Meltzer's question, I may say that I am not trying to solve the problem of life. I am studying the material of which the colon bacillus is composed. The question of the origin of life is too big for me to undertake to discuss. I imagine that life is something more than matter, and, as stated before, I am simply discussing the material out of which the cell is built. I have used the term hemolysis, not in a biologic but in a chemical sense, and exactly as I understand it has been largely used by Ehrlich and all others working on this subject. I can precipitate the hemolysin, wash it free from other substances, put it into the blood and study its action. I have certain reasons for believing that there is a toxoid group in the colon cell. This point I have not gone into in the paper but hope to do so in a later communication. I have formulated the theory which I have offered because some theory is necessary in order to do systematic and scientific work.

DR. WINFIELD S. HALL, Chicago—I have been very deeply impressed with the character of this work which Dr. Vaughan and his associates in his department have been doing for a number of years, and I feel that this Section is very highly favored in receiving from Dr. Vaughan so clear a statement of the work that he has done and of the hypothesis on which he is working for future results. I can not help feeling that in this work he is really laying the foundation of a broad, scientific basis for the whole subject of toxins and of immunity and immunization. I believe that the discovery of diphtheria antitoxin was a chance discovery. Several of these discoveries have been made, but the relation of these individual toxins and antitoxins, the one to the other, has been purely hypothetical. I believe that the work of Professor Vaughan and his associates will result in clearing up this whole subject, now only hypothetical, and in giving to the world a science of immunization. I wish to offer a resolution, not of thanks, but of appreciation. Dr. Vaughan is not working for thanks; but appreciation helps along a little occasionally, and I move a vote of appreciation to Dr. Vaughan and his department for this epoch-making work that he is doing.

[The resolution was adopted by a unanimous vote.]

## PRIMARY MALIGNANT ENDOTRACHEAL TUMOR.

### PRELIMINARY REPORT.\*

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This case is of interest from not less than three standpoints: First, that of the physician, because of the importance and extreme difficulty of diagnosis; second, that of the surgeon, because the treatment is purely operative, and third, that of the pathologist, not only because of the rarity of malignant growths in this situation, but because of the histologic structure of this tumor. This paper is directed especially to the pathology.

Primary tumor of the trachea is exceedingly rare, and, according to Scheuer,<sup>1</sup> but 22 per cent. of these are primary malignant growths.

Sir Morell Mackenzie,<sup>2</sup> after sixteen years of experience, saw but four cases of tracheal tumor, and it is probable that but one or two of these were primary and malignant.

Only twenty-eight cases of this disease are reported, most of which were discovered at autopsy in Germany or Austria.

In 1882 Delafield<sup>3</sup> reported a case of primary carcinoma of the bronchi, which invaded the trachea to a very slight extent. A number of cases of secondary invasion of the trachea by laryngeal carcinoma have been reported. A careful search through American medical literature failed to disclose a case of primary malignant endotracheal tumor.

*History.*—The patient, a woman, aged 34, married, living in a malarial district, had always enjoyed good health until the present trouble began, although her husband, a physician, observed that she had been rather pale during the past year or two.

In the summer of 1903 a slight cough began, uninfluenced by treatment, and in August dyspnea and expectoration were superadded. The sputum was thick, tenacious, blood-stained and mucopurulent, reaction neutral, and showed, microscopically, squamous epithelium, blood, diplococci, staphylococci, streptococci, but no pneumococci, tubercle bacilli nor yellow elastic tissue. A second examination gave similar results and the quantity for twenty-four hours was 400 c.c. There was no fever and these symptoms gradually increased in severity until Nov. 27, 1903, when she was seen for the first time.

*General Examination.*—The dyspnea was extreme, of the inspiratory type like that observed in laryngeal obstruction. Each inspiration was prolonged, labored and accompanied by insinking of the supraclavicular and infraclavicular fossæ and retraction of the base of the thorax. The rate of respiration and pulse was usually about normal.

The constant struggle for breath, interrupted by frequent paroxysms of coughing, caused sleeplessness and exhaustion. A few bronchitic râles were heard over both lungs, otherwise the examination of thoracic and abdominal contents and urine was negative.

*Laryngoscopic Examination.*—This examination, which was rendered extremely difficult by the dyspnea and paralysis of the right vocal cord, showed a swelling in the lower portion of the trachea, the surface of which was the same color as the tracheal mucous membrane. This swelling was erroneously interpreted as indicating external pressure on the walls of the windpipe. Two fluoroscopic and skiagraphic examinations gave negative results. As an absolute diagnosis was impossible, a probable diagnosis was made of a tumor, possibly aneurismal, pressing on the trachea in the region of the innominate artery. An exploratory operation was advised, but was declined by the patient. (The autopsy demonstrated that this probable diagnosis was erroneous.) The prognosis was absolutely unfavorable.

*Death.*—A few weeks later aspiration bronchopneumonia occurred, accompanied by a fever ranging from 101.2 to 103.8 degrees F., which disappeared on the ninth day. Suffocation and exhaustion, preceded by deep cyanosis, caused death on Jan. 1, 1904, seven months after the onset of the first symptoms.

*Autopsy.*—The autopsy was performed ten hours after death. The brain and spinal cord were not examined, and there was no thoracic aneurism nor tumor. With the exception of a tracheal bronchitis, the examination of the thoracic and abdominal contents revealed nothing of importance.

At or about the lower third of the anterior wall of the trachea was a papillomatous tumor about the size of the distal phalanx of an adult finger, which extended almost to the bifurcation of the trachea and measuring 5x3½ cm. This tumor caused extreme stenosis and occupied more than three-fourths of the lumen of the tube.

Immediately beneath this growth were a few moderately enlarged glands about the size of a marrowfat pea, which were firmly adherent to the outer wall of the windpipe. This region corresponds to the place where the innominate artery

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1. Ueber tracheal Tumoren. Inaug. Diss., Muenchen, 1893.

2. H. Crutchley: London Lancet, 1884, vol. II, p. 822.

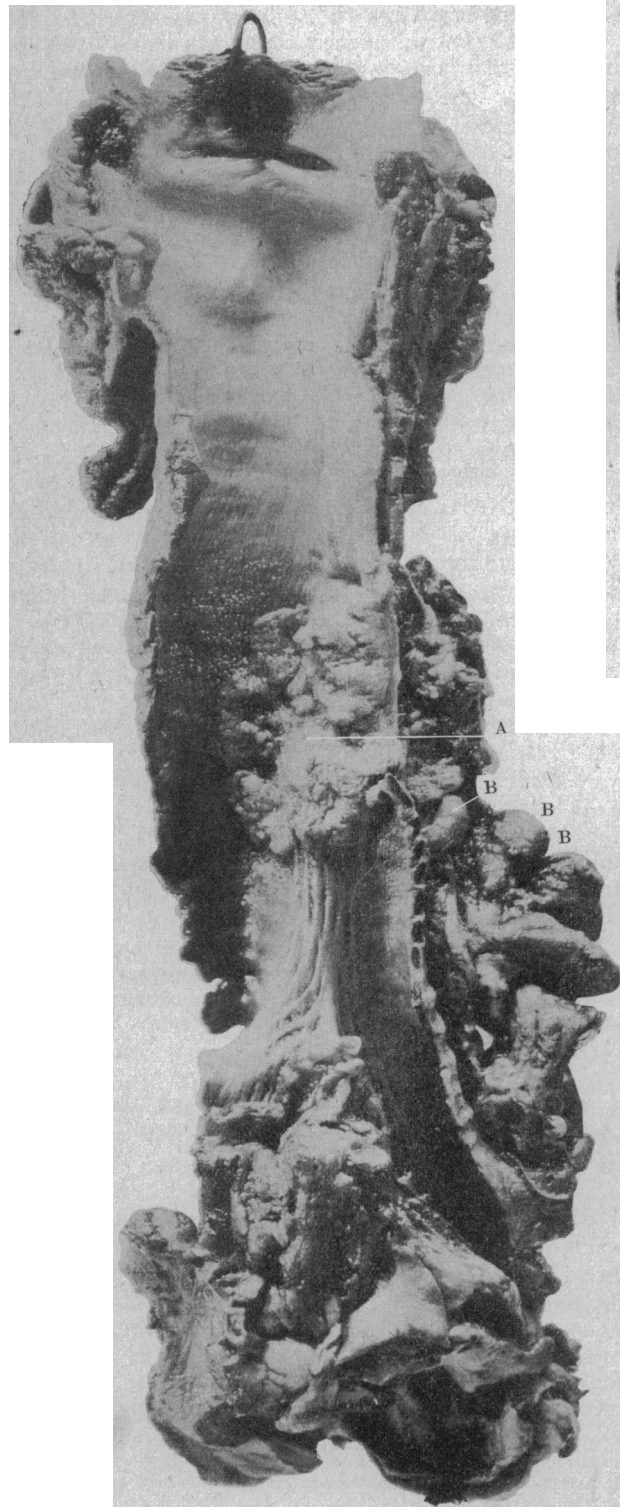
3. New York Med. Jour. and Obst. Rev., 1882, p. 406.

comes in close relation with the trachea, at which point the recurrent laryngeal nerve was compressed by the enlarged glands and inflammatory exudate.

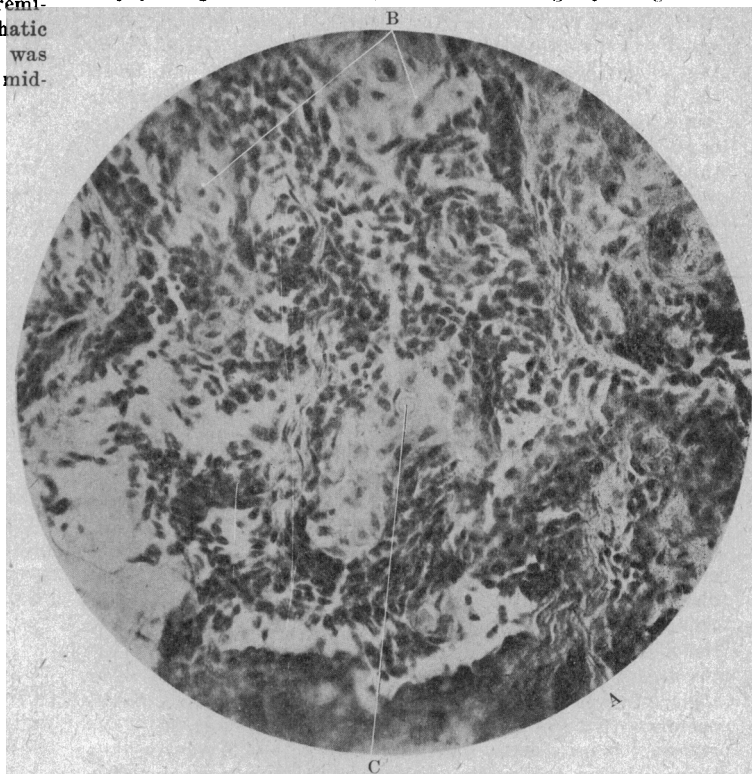
**PATHOLOGIC EXAMINATION BY DR. JOSEPH MCFARLAND.**

**Macroscopic Examination.**—The specimens submitted for examination consisted of the larynx, trachea, the upper extremities of the bronchial tubes, with the adjacent lymphatic glands and tissues of the roots of the lungs. The trachea was opened posteriorly so as to reveal on the anterior wall mid-

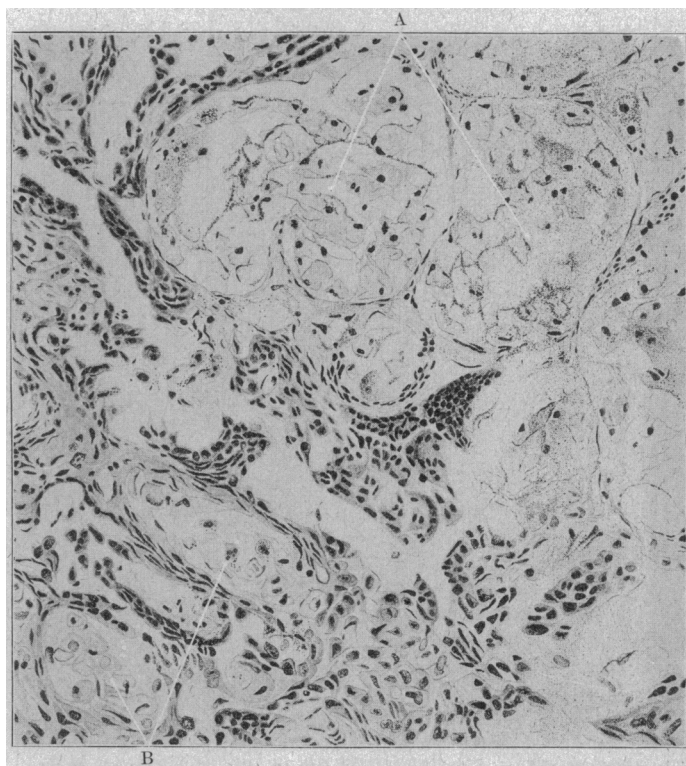
way between the cricoid cartilage and bifurcation a fairly well circumscribed neoplasm. This formed for the most part a somewhat flattened, tabular swelling, whose greatest diameter was about 5 cm. and least diameter about  $3\frac{1}{2}$  cm. The surface appeared villous when the specimen was first examined in physiologic salt solution, but became slightly roughened



Trachea cut open longitudinally, showing the tumor just above the bifurcation. Its originally villous character has been lost through the action of the preserving reagents. The color corresponded exactly with that of the tracheal mucous membrane. (About natural size.) A, The tumor; B, lymphatic nodes of which two were infiltrated.



Section through the superficial portion of the tumor showing the villous connective tissue prolongations (A), the nests of cells (B) and a peculiar cornified cell (C). ( $\times 400$ .)



Section through the base of the tumor showing the disorganizing mucous glands (A) in the upper right-hand half of the drawing, and the squamous epithelium composing the tumor itself in the lower left-hand half of the drawing. ( $\times 500$ .) Nests of squamous cells (B).

after having been placed for exhibition in Zenker's solution.

The tumor had the same pinkish color as the mucous membrane of the trachea. There seemed to be no ulceration, the right half of the tumor, consisting of two fairly good-sized nodes, must have considerably obstructed the lumen of the tube during life. The borders of the growth were, therefore, slightly elevated and differentiated from the normal tissue. When a section of the tumor and tracheal wall was made, it was found that its extension into the substance of the trachea was accompanied by loss of substance, that the cartilage rings of the organ had disappeared and that its wall had been reduced to the layer of connective tissue. The lymphatic nodes about the bifurcation of the tumor were slightly enlarged, and one at least presented small nodes as if from secondary invasion by the tumor, and on microscopic examination this was found to be correct. The nodes thus invaded were immediately beyond the tumor and were adherent to the trachea wall. A portion of the esophagus, fortunately that part underlying the tumor, had been removed together with the trachea, and when opened showed no abnormality. There seemed to be no connection whatever between the neoplasm of the trachea and the tissues of the esophagus.

**Microscopic Examination.**—Examination of the microscopic section with the hand lens showed that the cartilaginous rings of the trachea were not completely destroyed beneath the tumor, but that the tumor invaded the trachea wall between the cartilaginous rings and partly surrounded them. Under the microscope the entire structure of the mucous membrane was disturbed by the neoplasm. In the lower layers of the mass were found mucous glands not showing any marked departure from the normal, but these glands seemed to extend upwards into the tumor mass, and as one followed them in this direction their cells became more and more degenerated until rounded openings devoid of cells were occasionally observed.

From the connective tissue of the tracheal wall prolongations extended inward, branching so as to have a dendritic appearance. These were covered by layers of epithelial cells of a peculiar flattened spindle shape, the superficial layers of which were in process of active desquamation. In the depths of the tumor this desquamation caused the spaces between the dendritic outgrowths to be filled with a seminecrotic mass of desquamated cells. The interspaces between closely approximated villi not infrequently contained cells massed together in a manner suggestive of the epithelial pearls of the common forms of squamous epithelioma. In these cells various peculiar inclusions may be observed. The cells on the terminal branches of the villi desquamate singly and in masses, so that the surface of the tumor presents a very much frayed appearance.

As has already been suggested, the invasive nature of the tumor was shown by the metastatic growths in the adjacent lymph nodes, in one of which there was a nodule  $\frac{1}{2}$  c. in diameter, distinctly circumscribed and corresponding in all its histologic details with the primary growth. The situation of the tumor, the peculiarity of the cells of which it was composed, the partial cornification of the cells, suggest that the tumor had developed from an inclusion of esophageal epithelium in the wall of the trachea during embryonal life, and we are lead to believe that this is the true explanation of the origin of the growth.

**The Word Neurasthenia.**—The *Lancet*, April 30, begins an editorial article as follows: "Invented by Beard, of America, in the 'sixties' to describe and to include a class of nervous affections more common in America than elsewhere, the term 'neurasthenia' has been used with great elasticity," etc. It is true that we owe much of our knowledge of neurasthenia to the late Dr. Beard, but he did not invent the word, says the (N. Y.) *Medical Record*. Old Ludwig Kraus defined it in his "Kritisch-etymologisches medicinisches Lexikon," the third edition of which was published in Göttingen in 1844, long before Beard dealt with the subject.

## REGENERATIVE CHANGES IN CIRRHOSIS OF THE LIVER.\*

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In the literature and in the text-books of pathology little reference is made to the evidences of regeneration in cirrhosis of the liver. It is true that it is stated that regenerative changes are evident in certain cases leading to the production of adenoma-like nodular masses of liver tissue, and there is in general a tendency to regard the bile duct-like structures which occur in the fibrous bands as newly formed and as representing an effort toward the restitution of the liver to its original bulk. Especial stress is, however, usually laid on the degenerative changes in the liver cells and the anatomic picture presented by a cirrhotic liver is commonly looked on as the expression of a steadily progressive destructive process.

Kretz<sup>1</sup> only, so far as I can see in the literature at my command, has especially emphasized the importance of the regenerative changes in the ordinary type of cirrhosis and the fact that the anatomic condition as found at autopsy is probably the product of numerous attacks of some destructive affection from which the liver has more or less completely recovered. He discusses these changes briefly in a variety of conditions in an earlier paper, and in his later communication speaks particularly of the disturbed anatomic arrangement of the liver tissues in cases of advanced cirrhosis and of the consequent obstruction to the circulation. His attention is particularly attracted to the masses of liver tissue which he thinks are no longer to be regarded as acini since they have lost the typical architecture of the acini and the typical relation to the blood vessels. He states that many of these nodules are without central veins—others have central veins at their edges, while within the nodule the capillaries are so distorted that injections through the portal vein pass more readily to the hepatic veins by way of the fibrous tissue than through their substance, and even that the blood from these masses reaches the central vein by way of the fibrous strands. He regards these isolated masses of liver tissue as largely new formed and defines cirrhosis as essentially a combination of focal or localized recurring chronic degenerative processes with regeneration.

All of the studies of regeneration in cirrhosis are based on the experimental work of Ponfick, Podwyszozi, von Meister and others, and the anatomic observations of Marchand, Meder, Stroebe, Barbacci and others who have investigated the late results of those destructive processes loosely classed under the name "Acute Yellow Atrophy of the Liver," in which conditions for the study of regeneration almost identical with those produced experimentally are presented.

It is well established, as I have also pointed out in a previous paper,<sup>2</sup> that in those cases in which, after extensive destruction of the liver substance, the individual survives for a considerable time, not only is the debris of the necrotic liver substance removed and scar tissue

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1. Kretz: Ueber Lebercirrhose, Wiener klin. Woch., 1900, vol. xlii, p. 271.

2. W. G. MacCallum: Regenerative Changes in the Liver After Acute Yellow Atrophy, Johns Hopkins Hospital Reports, 1903, vol. x.