TUMOURS OF THE HEART: HISTOPATHOLOGICAL AND CLINICAL STUDY*

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TUMOURS of the heart are a pathological rarity. Some produce characteristic clinical manifestations, but are rarely recognized by the clinician. The clinical picture of cardiac tumour so often simulates that of more common cardiac lesions that the physician rarely suspects that such a condition may be present. Secondary tumour of the heart has been diagnosed clinically, and on rare occasions primary tumour has been suspected. Since early in the eighteenth century a vast literature concerning this relatively uncommon condition has accumulated. The publications of Farber and of Yater are accompanied by comprehensive bibliographies of this subject.

From 1915 to 1931, inclusive, 52 cases of secondary and 4 cases of primary tumour of the heart were discovered at necropsy in 8,550 subjects at the Mayo Clinic. The distribution of these tumours was as follows: of secondary tumours, 36 were carcinomas, 16 were sarcomas, and 6 malignant melanomas; of primary tumours, 2 were myxomas, 1 a rhabdomyoma and 1 an angioma.

PRIMARY TUMOURS

CASE 1

Myxoma of the left auricle.—This case has been adequately reported by Barnes and Yater[1] and by Yater,[4] and consequently need not be reported here. The patient was a woman aged 23.

CASE 2

Myxoma of the left auricle.—A woman, aged 34, came to the clinic April 22, 1928, complaining of having had pains in the right lower part of the abdomen for three weeks, and chills and fever for one day. The patient had missed a menstrual period which had been due about the first of April. Then she had begun to experience sharp pains in the lower part of the abdomen. These had lasted for about a week, when she had inserted a rubber catheter up the vagina, hoping to obtain relief. There had been a slight bloody discharge, but the pain continued. April 21, she had passed a blood clot and an hour or so later she had had a chill which had lasted for five or ten minutes. The day of admission she had three severe chills and her temperature rose to 103° F. The patient had five living children, and had had four miscarriages and two still-births. Since 1917 she had been at the clinic several times on account of pregnancy, and for the following operations: excision of a small cyst-like mass on the outer aspect of the proximal phalanx of the fourth finger, which was diagnosed a giant-cell tumour; excision of a small fibroma molluscum from the skin of the right scapular region; trachelorrhaphy and excision of a small cyst of the cervix, perineorrhaphy and appendectomy. Since 1925 she had noticed increasing dyspnœa on exertion. There was nothing in her history suggestive of heart trouble.

The patient was fairly well developed and well nourished. The skin was moist and the face flushed. The heart and lungs were negative. The blood pressure in millimetres of mercury was 102 systolic and 88 diastolic. The pulse rate was 100. The uterus was enlarged to about twice its normal size, and marked tenderness was elicited to the right of the fundus. On April 23, 1928, the patient passed several blood clots, among which was found a hairpin. Following this she became very weak with rapid, thready pulse; cyanosis of the lips and laboured respirations were observed. She failed to respond to intravenous treatment and death ensued a few hours later.

The clinical diagnosis was septicæmia and attempt at self-induced abortion.

At necropsy a moderate amount of blood-tinged fluid in the peritoneal cavity, passive congestion of the lungs, and slight congestion of the liver were noted. There was evidence of chronic interstitial pancreatitis with a moderate amount of fat replacement of the pancreas. The uterus revealed endometritis, and there were a few small leiomyomas in its wall. Culture of the peritoneal fluid demonstrated the presence of hœmolytic streptococci, but culture of the heart's blood gave negative results.

The heart weighed 367 g. There was an egg-shaped, yellowish-white, elastic tumour in the left auricle, measuring 6 cm. in length, 3.7 cm. in width, and 4.4 cm. in its anteroposterior diameter (Fig. 1A). It was attached by a broad base to the interauricular septum, directly over the site of the fossa ovalis; it practically filled the left auricle, and extended for a short distance through the mitral orifice. There were a few small, bright red, hæmorrhagic areas beneath its surface. To the right of the point of its attachment to the auricular wall was an area of thrombus formation, and adhesions had formed between the tumour and the wall of the auricle. The cut surface of the tumour was yellowish white, and there were a few small, hæmorrhagic areas near its upper pole. There were a few small subepicardial hæmorrhages on the left auricle and on the right ventricle. The ventricles were dilated, especially the left, and the wall of the latter chamber was thinned. The heart muscle appeared to be in good condition. An ante-mortem thrombus, measuring 2 by 0.9 by 0.7 cm. in diameter, was caught on the edge of a small, fenestrated Eustachian valve. The tricuspid orifice was considerably dilated. The foramen ovale was closed. Only a slight amount of coronary sclerosis was present.

Histological examination of sections of the tumour, stained by hæmatoxylin and eosin, revealed a palely eosinophilic staining, fibrinous matrix, among which was a fine, granular substance (Fig. 1B). There were numer-

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ous oval or elongated cells of endothelial type, the majority of which were in cord-like formation, and others in groups. These cells were in general placed with their long axes in the same direction. The cytoplasm assumed a pale eosinophilic stain. The nuclei were basophilic, oval or elongated, and slightly granular. They were fairly large, and there were several nuclei in a single cell. A few delicate blood vessels were scattered throughout the sections. They seemed to be in the same stage of development, and were congested with blood. One vessel contained an organizing thrombus. There were a few lymphocytes and polymorphonuclear leukocytes scattered throughout the sections. A few cells, which appeared to be plasma cells, and an occasional eosinophilic leukocyte could also be seen. Sections revealed a considerable quantity of mucin, which was evenly distributed. The van Gieson stain demonstrated the presence of a moderate amount of fine fibrous connective tissue throughout the sections and beginning hyaline degeneration of the capsule. Elastic tissue was also present, as demonstrated by the Weigert stain.

The pathological diagnosis of the tumour was fibromyxoma.

CASE 3

Lymphangioma of the right auricle.—A boy, aged ten months, was brought to the clinic on August 10, 1925, because of a tumour of the left side of the neck, which had been present since birth. It extended from the submental region to the post-auricular region, and from the level of the eye down on to the neck. The mass had fluctuated in size, and the child occasionally had slight fever. There had always been noticeable wheezing with respiration, but no particular discomfort was shown until May, 1925, when the tumour began rapidly to increase in size. The area over the swelling became reddened and the temperature rose to 102° F. The child began to experience difficulty in swallowing liquids, and the respirations became more laboured. A considerable amount of weight had been lost since June, 1925, and he had become pale.

The child appeared anæmic, poorly nourished, and held his head to the right. A large, movable, cystic tumour on the left side of the neck extended from the left submental region backward over the jaw and neck, and into the posterior cervical region. There was slight bulging of the pharyngeal wall on the left side. The heart and lungs were negative, but other abnormal findings were not noted. A roentgenogram of the thorax revealed a slight increase in the width of the mediastinal shadow, which was considered to be due to enlargement of the lymph nodes. Erythrocytes numbered 3,270,000 and leukocytes 15,000 in each cubic millimetre of blood, and the concentration of hæmoglobin (Dare) was 48 per cent.

A course of radium therapy failed to prove of benefit. The temperature rose to 104° F., and the dysphagia and dyspnœa became more pronounced. Feedings were given by tube and rectum, but the child became progressively weaker and died on September 6, 1925, twenty-seven days after admission.

The clinical diagnosis was cystic hygroma of the neck.

At necropsy partial atelectasis of both lungs was noted. There was a large, cystic, encapsulated mass

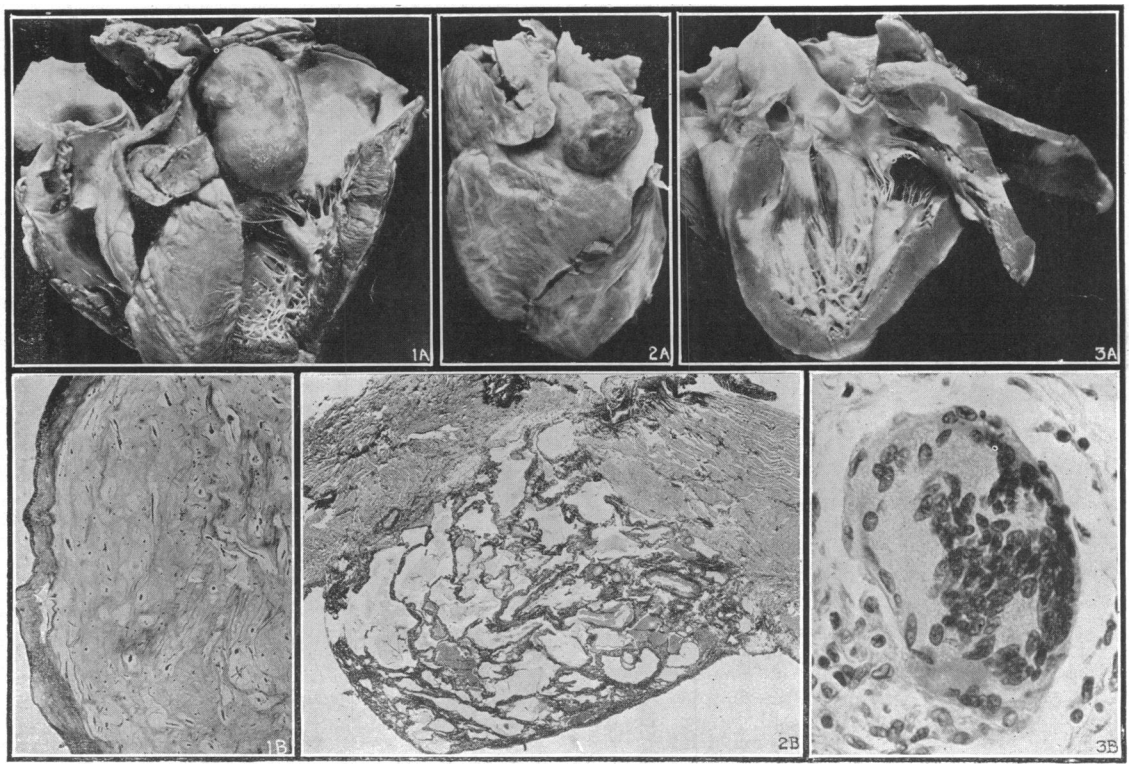

FIG. 1A. (Case 2).—Fibromyxoma of the left auricle.

FIG. 1B. (Case 2).—Photomicrograph of myxoma, demonstrating the fine fibrous connective-tissue stroma, and the beginning hyaline degeneration of the capsule (x75).

FIG. 2A. (Case 3).—Lymphangioma of the right auricle.

FIG. 2B. (Case 3).—Photomicrograph of lymphangioma through the pedicle. The connective-tissue of the tumour is continuous with that of the surface of the auricle (x7¾).

FIG. 3A. (Case 4).—Rhabdomyoma of the heart; the tumour nodules in the left ventricle and myocardium may be noted.

FIG. 3B. (Case 4).—Photomicrograph of rhabdomyoma cell, demonstrating the granular character of the cytoplasm. The cross striations are not clearly seen (x660).

on the left side of the neck which contained many multilocular cysts. Some were clear vesicles, and others were reddish. The mass extended from the parotid gland above to the clavicle below, and to the trapezius muscle posteriorly. It also extended mesially to surround the trachea and larynx. The left jugular vein and its branches were incorporated in the mass, which was densely adherent to adjacent structures. The tumour encroached on the left side of the larynx and involved the false vocal cords, thereby causing partial obliteration of the lumen of the air passages. Numerous encysted regions containing purulent-appearing material were encountered. Situated laterally to and below the left tonsil, and laterally to and slightly above the epiglottis, was a fairly large retropharyngeal abscess in the substance of the growth. On section this mass was seen to be composed of a large number of cysts which varied considerably in size. Some contained a clear, light, yellow fluid, and in others the content appeared hæmorrhagic. One large cyst contained a reddish, degenerating mass which appeared to be old blood. The general appearance of the stroma was that of fibrous tissues.

The heart weighed 60 g. Just to the left of the right auricular appendage was a soft, cystic, bluish red mass, measuring 2.5 by 1.5 by 1 cm. in various diameters (Fig. 2A). It was attached to the surface of the auricle by a broad base. Section revealed several cysts. The majority contained a clear fluid, but a few were filled with a reddish material, which appeared to be blood. The appearance of the stroma was that of fibrous tissue. Except for the tumour, the heart appeared normal.

Histological examination of sections of the tumour, stained by hæmatoxylin and eosin, revealed many cystic areas. The majority of the cysts contained a clear, homogeneous substance, and a few contained erythrocytes with an occasional lymphocyte and polymorphonuclear leukocyte. The walls of the spaces were lined by flattened endothelial cells, and there was no evidence of muscle tissue. Between the spaces there was a fine, fibrous, connective-tissue stroma, among which could be seen scattered lymphocytes, polymorphonuclear leukocytes, and an occasional plasma cell. Lymph nodes, a few delicate blood vessels, and an occasional nerve bundle were scattered throughout the stroma. The connective-tissue of the tumour was continuous with that of the surface of the auricle (Fig. 2B).

The pathological diagnosis of the tumour was lymphangioma.

The tumour of the heart was not connected with that of the neck and mediastinum. It was considered to be a separate lymphangioma which was probably formed from the lymphatic channels of the auricular surface of the heart.

CASE 4

Rhabdomyoma of the heart.—A woman, aged 45, came to the clinic on December 6, 1929, complaining of repeated "convulsions" over a period of two months. She had felt well until about October 7, 1929, when she suddenly lost consciousness while bending over at work. This was followed by two similar attacks on the same day and one on the following day. The physician who examined her on the day of her first convulsions informed her that the heart rate was 28 beats to the minute. She was then free from attacks until about October 21, 1929, after which she began to have daily "convulsions", sometimes as many as fifteen or twenty in an hour. She stated that the attacks were increasing in severity. Without any apparent warning, she would suddenly lose consciousness, breathe very heavily, and have spasmodic movements of the face and upper extremities. The attacks lasted for an interval of thirty to sixty seconds, and would leave her very weak, extremely exhausted, and with a desire to sleep. She stated that her pulse had been slow since the onset of the trouble. Her past history was of no particular significance.

The patient was well developed, well nourished, and somewhat drowsy. The pulse rate was 32 beats a minute. The blood pressure was 105 systolic and 50 diastolic. Examination of the heart was negative, except for an apex rate of 32 beats each minute. Neurological examination gave negative results. A roentgenogram of the thorax revealed slight enlargement of the heart to the left. The electrocardiogram gave evidence of complete auriculoventricular dissociation, with a ventricular rate of 24 and an auricular rate of 67 beats a minute. There was evidence of left ventricular preponderance, with a notched P wave in leads I and II, and an inverted T wave in lead I. The Wassermann reaction of the blood was negative.

The pulse rate fell to 28 beats a minute. The patient continued to experience frequent convulsive attacks lasting five to sixty seconds. She gradually became weaker and death ensued sixteen days after admission.

The clinical diagnosis was complete heart block with Stokes-Adams' disease.

At necropsy healed pyelonephritis and several diffuse cysts of the mucous membrane of the bladder were observed. The cysts measured about 0.5 cm. in diameter, and were situated at the uretero-vesical juncture. The pericardial sac contained about 100 c.c. of clear, straw-coloured fluid.

The heart weighed 362 g. The muscle was reddish brown and firm. There were multiple, small, whitish nodules on the epicardial surface of the left ventricle. They were irregularly quadrilateral and subepicardial. There was a firm, whitish nodule in the right ventricle, situated just below the cusps of the pulmonary valve. It measured 2 by 1 cm., and projected into the myocardium of the right ventricle for a distance of approximately 0.6 cm. There was a similar nodule in the left ventricle, situated just below the aortic cusps. It measured 3 by 2 cm., and invaded the interventricular septum. There were two nodules in the myocardium of the left ventricle (Fig. 3A). One measured 2 by 1 cm., and involved the interventricular septum. The other measured 1 by 1 cm., and invaded approximately the entire thickness of the ventricular wall near the apex. The cut surface of the tumour was yellowish white and homogeneous. The tumour tissue was sharply demarcated from the surrounding cardiac tissue, but was not encapsulated.

The endocardium, valves, and chambers of the heart did not present any other lesion worthy of note.

Microscopic examination of the sections taken from the nodules, stained with hæmatoxylin and eosin, gave evidence of replacement of the normal heart tissue by a young type of connective-tissue trabeculæ. Many irregular, clear areas were scattered among the stroma. They varied from round to oval, and gave a sponge-like appearance to the tumour tissue. These areas could best be seen by means of the van Gieson, and Mallory-Heidenhain stains. Delicate blood vessels were observed among the connective-tissue network.

Numerous, large multinucleated cells were scattered irregularly throughout the tumour. They appeared to be giant cells of a granulomatous reaction, but acid-fast bacilli could not be found in sections stained by the Ziehl-Neelsen method. The nuclei of these cells were for the most part situated at the periphery, or grouped in clusters at one pole of the cell. They were oval or fusiform, and each contained a deeply-stained nucleolus. The cytoplasm was granular, and assumed a palely eosinophilic stain with hæmatoxylin and eosin (Fig. 3B). The granular nature of the cytoplasm was demonstrated more clearly by Mallory's phosphotungstic acid-hæmatoxylin stain. Many of these granules were arranged in parallel rows, which gave the appearance of cross striations.

There were clear areas between the giant cells and the connective-tissue. Numerous cells, which appeared to be lymphocytes, were scattered among the stroma. Mitotic figures were not seen.

The first observation of these sections gave the impression that the tumour was granulomatous. Suitable methods of staining, however, demonstrated more clearly the granular cystoplasm of the giant cells, and evidence of cross-striations could be seen in some of the cells studied under high magnification. This observation, together with the general appearance of the tumour tissue, and the inability to demonstrate acid-fast bacilli after repeated attempts with sections from various areas, led to the conclusion that the tumour was probably a rhabdomyoma.

SECONDARY TUMOURS

Thirty-six cases of secondary carcinoma and 16 cases of secondary sarcoma of the heart were found at necropsy at the Mayo Clinic during 1915-1931, inclusive. This gave an incidence of approximately 0.4 per cent for metastatic carcinoma, and approximately 0.2 per cent for metastatic sarcoma among the 8.550 post-mortem examinations made.

TABLE I.

PRIMARY SITE OF MALIGNANCY IN CASES OF SECONDARY TUMOUR OF THE HEART (52 CASES)

Primary Site of Malignancy	*Carcinoma*	*Sarcoma*
Breast	6	
Bladder (urinary)	4	
Stomach	4	
Skin	4*	
Kidney	3	
Pancreas	3	2
Eye	2*	
Lung	2	1
Suprarenal glands	1	
Bronchus	1	
Œsophagus	1	
Gall bladder	1	
Liver	1	
Thyroid Gland	1	
Uterus	1	
Lymph Nodes		7
Bone (femur)		1
Ovary		1
Spleen		1
Toe		1
Thymus		1
Unknown	1*	1
Total	36	16

*Malignant melanoma.

In these cases of secondary tumour of the heart, metastasis had occurred from the various organs of the body in which neoplastic change is commonly found. The relative incidence of the primary sites of malignancy from which metastasis occurred in the heart may be noted in Table I. The majority of the secondary growths in the heart were considered to have metastasized by way of the blood stream. In many cases microscopic examination revealed tumour cells within the lumen of the coronary arteries. In other cases, malignant cells simulating those of the primary neoplasm were observed in the thrombotic masses within the chambers of the heart. In a few cases tumour cells were seen by microscopic examination within the lymphatic channels of the heart. In one case of primary carcinoma of the bronchus the superficial lymph nodes of the heart were dilated with actively growing malignant cells. This condition has been observed by previous authors and termed carcinomatous lymphangitis. The probable modes of metastasis may be noted in Table II.

TABLE II.

MODE OF METASTASIS

	Carcinoma		*Sarcoma*	
	Cases	*Per cent*	*Cases*	*Per cent*
Blood stream	26	72	6	37
Lymphatic structures and blood stream	5	13	2	12
Direct invasion	3	8	8	50
Lymphatic structures	2	5		
Total cases	36		16	

Primary or secondary intrathoracic growths were associated in 32 cases (88 per cent) of metastatic carcinoma of the heart. In 26 of these (72 per cent) the lungs were involved. Fourteen cases (87 per cent) of secondary sarcoma of the heart were associated with malignant growth in other intrathoracic structures, and in 6 of these (42 per cent) the lungs were involved. Metastasis associated with secondary tumours of the heart may be noted in Table III.

Signs of congestive heart failure were commonly found in association with the cardiac malignancy. The most common of these were ascites and pleural effusion. The incidence was as follows. Ascites occurred in 9 cases of carcinoma and in 9 cases of sarcoma; hydrothorax occurred in 9 cases of carcinoma and in 6 cases of sarcoma; hæmothorax occurred in 5 cases of carcinoma and in 1 case of sarcoma; hydropericardium occurred in 5 cases of carcinoma and in 2 cases of sarcoma; and hæmopericardium occurred in 4 cases of carcinoma and in 4 cases of sarcoma.

These secondary cardiac tumours varied in size, shape, and appearance. In some cases small, whitish, firm nodules were scattered dif-

fusely through the myocardium; in other cases there was a single isolated nodule in the myocardium; and in others practically the entire heart was involved in metastatic growth. Thrombotic masses which contained tumour cells, and malignant polyps were also observed. The histological structure of the secondary cardiac tumour simulated the primary lesion and the metastatic growths in other parts of the body.

The incidence of the types was as follows. In 15 of 36 cases (41.6 per cent) the carcinoma

TABLE III.

METASTASIS ASSOCIATED WITH SECONDARY TUMOURS OF THE HEART

Organ Involved	Instances	
	Carcinoma	Sarcoma
Suprarenal glands	16	2
Bile ducts	1	
Bladder	2	1
Bone	13	5
Brain	6	1
Breast	2	
Bronchus	1	
Diaphragm	8	3
Duodenum	3	1
Epididymis	1	
Œsophagus	1	
Gall bladder	3	2
Intestines	12	1
Kidneys	16	5
Liver	24	3
Lungs	26	6
Lymph nodes	29	9
Mesentery	5	
Muscle	2	1
Omentum	7	1
Ovaries	5	1
Pancreas	12	3
Pericardium	16	5
Peritoneum	7	
Pleura	10	3
Prostate gland	1	
Rectum	1	
Spleen	6	1
Stomach	8	3
Thymus	2	2
Thyroid gland	1	2
Trachea	1	1
Ureter	3	
Uterus	1	
Vagina		2

was single; in 13 (36.1 per cent) it was multiple; and in 8 (22.2 per cent) it was diffuse. In 5 (31.2 per cent) of 16 cases the sarcoma was single; in 10 (62.5 per cent) it was multiple; and in 1 (6.2 per cent) it was diffuse.

The distribution of the secondary tumours in the heart was extremely variable, but the right side of the heart was affected slightly more commonly than the left (Table IV).

The clinical picture of the secondary cardiac tumours varied greatly, and in only one case

TABLE IV.

DISTRIBUTION OF SECONDARY TUMOURS IN HEART

Tumour	Left ventricle	Right ventricle	Left auricle	Right auricle	Both auricles	Interventricular septum	Interauricular septum	Diffuse
Carcinoma	13	9	4	9	2	1		8
Sarcoma	5	8	1	4	1		1	1
Total	18	17	5	13	3	1	1	9

was a diagnosis made clinically. This case has been reported by Willius and Amberg,[3] and was an example of sarcoma of the left femur, affecting a girl, aged eight years, who had no former history or clinical evidence of heart disease; evidence of incomplete bundle-branch block developed. The age and incidence by sex, and the duration of symptoms are given in Table V.

TABLE V.

AGE AND INCIDENCE BY SEX OF HEART DISEASE

Tumour	Age incidence		Sex incidence		Duration of symptoms	
	Years	Average	M.	F.	Months	Average
Carcinoma	32 to 71	53	26	10	¾ to 120	22½
Sarcoma	2½ to 63	29	11	5	1 to 29	13

In the majority of the cases cardiac symptoms were not noted; in others the symptoms were indefinite, and could not be directly attributed to heart disease. The chief signs and symptoms were dyspnœa, cyanosis, tachycardia, cardiac enlargement, congestive signs, auricular fibrillation, extra-systoles and bundle-branch block. In only 5 cases were there any definite cardiac symptoms which may have been suggestive of secondary involvement of the heart.

CONCLUSIONS

1. Primary tumour of the heart occurs in about 0.05 per cent of cases which come to necropsy.

2. The majority of primary cardiac tumours are benign, and about 25 per cent are malignant.

3. The most common primary cardiac tumour is myxoma. Sarcoma and rhabdomyoma range next in frequency. Other primary neoplasms found in the heart are fibroma, lipoma, angioma, and carcinoma. Carcinoma of the heart is probably always secondary.

4. Secondary malignant lesions of the heart are discovered at necropsy in about 0.6 per cent of cases.

5. Metastasis to the heart comes from various organs of the body in which malignant change is commonly found. The incidence of cardiac metastasis is relatively much higher when mediastinal structures are involved.

6. The right side of the heart is more commonly involved by secondary neoplastic growth than the left side. This may be explained on a blood-vascular basis.

7. There are no definite pathognomonic signs or symptoms of heart tumour. Sudden and unexpected onset of cardiac symptoms, which are progressive and regressive, and especially if associated with an evanescent cardiac murmur and with cardiac failure which is not responsive to digitalis, strongly suggests a tumour of the heart. Metastatic tumours of the heart have been diagnosed clinically, and on rare occasions primary cardiac neoplasms have been suspected.

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TUBERCULOSIS OF THE THYROID GLAND WITH REPORT OF A CASE IN A CHILD AGED THREE*

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THE early writers on diseases of the thyroid gland stated that this gland always escapes tuberculous infection. Rokitansky,[24] in 1861, said the gland had some special immunity and was never involved in tuberculosis. Virchow[8] in his early writings stated that there was some antagonistic action between the thyroid gland and the tubercle bacillus. He later discovered 3 cases of tuberculosis of the thyroid gland at post-mortem. These positive statements by such prominent men undoubtedly retarded the progress of study in this subject. During the present century, however, greater strides were made in the study of the condition, both from the experimental and clinical standpoints. During this period, thyroidectomies became more numerous and the histological study of these resected glands increased our knowledge of the subject. The increase in the number of recorded cases during the last decade is probably relative rather than actual.

The first case of tuberculosis of the thyroid gland on record was found at autopsy and reported by Albers[9] in 1847. Bruns,[1] in 1893, was probably the first to report a case diagnosed at operation. Since the report by Albers about 255 cases have been recorded in the literature. From this one can see that the incidence of tuberculosis of the thyroid is very low compared with that of tuberculous lesions in other parts of the body. Of these 255 cases, 125 were discovered during operation or on histological study of the gland following operation. The remaining 130 were found at autopsy, and consist chiefly of cases in which there were miliary tubercles of the thyroid associated with an acute generalized miliary tuberculosis. Rankin and Graham,[7] in 1932, made a careful study of the 125 cases in which tuberculosis of the thyroid was diagnosed at the time of operation or by histological examination of the gland. Of these, 104 were selected from the literature and 21 added from the records of the Mayo Clinic. Rankin's and Graham's 21 cases occurred in 20,758 thyroidectomies at the Mayo Clinic, an incidence of 0.1 per cent. The diagnosis was made either from a clinical

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