An Address ON THE HABITS (ECOLOGY) OF TUMOURS.

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WRITINGS which attempt to define the term "tumour" make a big literary rubbish heap. The name though undefinable is applied to a hotch-potch of morbid conditions. A mouse is a mammal, so is an elephant—they have features in common. Many morbid conditions called tumours have sufficient features in common which permit them to be classified for descriptive purposes, for clinical study, and for treatment, but in size and habits they vary as much as mice and elephants.

Tumours are of importance to surgeons because of their harmfulness to the individuals on whom they grow. Nearly all make life uncomfortable; many shorten life. Surgeons do their best to get rid of them and study their habits (ecology) in order to acquire increased proficiency in this respect.

The microscope taught us that the tissues of tumours do not differ from those normal to the body, and with the assistance of embryology the investigation of tumours has become for many an attractive study. Embryology has provided the key to many pathological riddles. I vainly imagined that it would help to solve the problem of the origin of tumours, and a large part of my leisure for many years was devoted to this quest.

I shall endeavour to show how the life history of a tumour corresponds with that of the parent organ. Tumours pass through a period of growth, attain maturity and in some instances exercise the same function as the parent organ; and this exercise by increasing their bulk leads to their discovery. The statement that tumours exercise no function is grossly erroneous.

The tissues of tumours do not differ in their habits (ecology) from the normal tissues of the body.

Take, for example, hyaline cartilage. When this tissue assumes the form of a tumour its naked-eye and microscopic characters are identical with normal cartilage. It often calcifies, and becomes converted into bone. Like cartilage covering the articular end of a bone, it may be smooth and glistening; if submitted to friction a synovial membrane forms over it, constituting a gliding capsule; the space enclosed by the capsule may become distended with synovial fluid. Many instances are known in which a bursa of this kind, formed over an exostosis, has contained loose bodies in every respect resembling the familiar joint-mice of normal articular cavities. Exostoses of long bones repeat the phases of development common to such bones, and during growth are capped with cartilage which behaves like an epiphysis; the growth of the exostosis ceases with that of the skeleton.

Tumours not only agree in structure with the tissues of the organs in which they arise, but they conform to the habits of the parent organ.

Composite odontomes are tumours derived from the germs of teeth and conform to the ecology of teeth. Ensnconed in the jaw an odontome grows in silence. In due time this quiescence is disturbed and the tumour manifests its relationship to teeth by erupting. The chief signs are swelling of the gum and pain such as accompanies the cutting of teeth. These troubles lead to its discovery, which usually ends in its extraction. Some superstitious persons will not submit to its extraction; even then the natural process is triumphant, for the tumour may fall out spontaneously, or, in spite, the patient spits it out! In a few instances an odontome has erupted and taken its place in line with normal teeth and been used in mastication. This has happened to men and horses.

Tumours in hollow viscera can excite them to action.

A tumour growing from the walls and projecting into the cavity of a hollow muscular organ can excite its muscular tissue to contract. A fibroid, a lipoma, or a cluster of warts growing in the gastro-intestinal tract stimulates propulsive movements leading to invagination of the intestine. Many astounding examples have been recorded. A submucous fibroid growing in the gastric wall near the oesophageal opening has been propelled through the pylorus into the duodenum, invaginating the parts with fatal consequences. Invagination of the small intestine is often caused by a sessile tumour. The persistent propulsive action of the muscular tissue converts sessile into stalked tumours. The contractions of the gut excited by a polypus are declared by painful sensations called cramps.

An old woman had a tumour, the size of a walnut, protruding at the anus. A surgeon of experience cut it off and was surprised to see the vermiform appendix. The tumour in this case arose on the margin of the ileo-caecal valve and induced invagination of the whole colon.

The efforts of the uterus to extrude a submucous fibroid may be so vigorous that the organ inverts. A pregnant uterus in its endeavours to expel the placenta sometimes turns inside out. The ovaries and Fallopian tubes occupy the peritoneal pouch formed by the inversion.

A tumour can initiate functional activity in an organ.

A submucous fibroid can imitate pregnancy so successfully as to deceive experienced practitioners. When an oöperm embeds itself in the endometrium the uterus, in the course of a few months, is converted from an organ weighing 2 to 3 oz. to one weighing 2 to 3 lb., with a capacity of one gallon. At the end of 280 days the slow rhythmic contractions of the uterus, stimulated by the growing foetus, ultimately become so powerful that they expel the foetus, the placenta, and the membranes which contain the foetal excrementitious products. When pregnancy occurs in the rudimentary horn of an imperfect uterus, or in a Fallopian tube, the foetus cannot escape from its mother and is mummified; in course of time it becomes converted by the deposit of lime salts into a lithopaedion.

After a successful pregnancy the uterine tissue undergoes an autolytic change (which means it is transformed into soluble nitrogenous extractives) and slowly shrinks to nearly the same size and weight of an unimpregnated uterus. Similar changes may be observed in a uterus occupied by a submucous fibroid. As the tumour grows the uterus enlarges uniformly and as it rises in the hypogastrium becomes easily obvious on examination. When the tumour is soft and grows rapidly a murmur is audible on auscultation. The uterus persistently endeavours to expel the tumour and sometimes succeeds in forcing it into the vagina. This success is accompanied with painful spasms and bleeding so like a miscarriage as to sometimes deceive the medical attendant or a midwife. As a rule, the uterus fails to expel the fibroid and it slowly enlarges year by year, then ceases to grow, slowly dies and is mummified, and in many cases calcified. Large calcified fibroids and lithopaedia may be found in pathological museums and in disused graveyards.

Submucous fibroids, especially when complicated with pregnancy, undergo autolysis, and this process will reduce a submucous fibroid the size of a fist to the consistence of soft soap in two weeks. The comparison between the ecology of a submucous fibroid and normal pregnancy is emphasized when the fibroid stimulates a large corpus luteum to form in the ovary and mucous fluid exudes from the nipples.

EROSIVE ACTION OF VILLI IN RELATION TO TUMOURS.

Villi of various kinds play a part in our lives usually for good; sometimes for evil. Embryologists and pathologists were surprised to learn that the delicate villi of the chorion embed themselves in the endometrium to form the foetal part of the placenta. Occasionally their erosive power enables them to pierce the uterine wall and peer into the peritoneal cavity. It was a greater surprise to learn that

such delicate structures sometimes acquire malignant power and penetrate blood vessels. Fragments detached from such villi become emboli, and lodge in distant organs, embed themselves, and establish new tumour colonies. This disease of the villi, now well recognized, is described as chorionic cancer.

Arachnoid Villi.

It is well known that the pits in the cranial vault, familiar to students of human osteology as the foramina for the Pacchionian bodies, are due to the erosive action of arachnoid tufts; but it is a recent discovery that these villous bodies sometimes grow luxuriantly, overrun the adjacent bones, and produce in them extraordinary changes.

In 1885 Sir William Stokes described the skull of a male Cingalese (Fig. 1), and on the vault of this skull there is a mass of bone resembling a crown of loosely compacted coral. The tissue of this crown is intimately incorporated with the vault of the skull, and the whole mass is permeated with neat vertical pits. Each "pit" is really a tunnel, and as neat as a Pacchionian pit. These tunnels are exaggerated Pacchionian pits produced by pathological arachnoid tufts. Professor S. G. Shattock has made a thin transparent section of the crown, and the tunnels can be seen traversing it completely. There are hundreds of tunnels in this crown, and they recall holes in ship-timber bored by the teredo or those in limestone made by whelks (Pholas).

In recent and unmacrated hyperostoses of this kind arachnoid villi can be demonstrated in the tunnels. In the head of the patient there was a layer of gelatinous material over the bone, between it and the scalp; it also filled the tunnels. The dura adhered to the bone and to the surface of the brain.

When this extraordinary specimen was described by Stokes no one had the least suspicion that such a change could be produced by arachnoid villi. Dr. W. G. Penfield, in 1921, began a careful study of the intracranial tumours preserved in the museum of the National Hospital for the Paralyzed and Epileptic, Queen Square, London. He has proved that the soft tissue of the tumour arises within the cranium, pierces the dura, and involves the overlying bone. The action of the tumour elements leads to complete rearrangement of the osseous tissue between the tumour and the scalp. It is a singular clinical feature, in many of the

patients, that the presence of the hard sessile boss of bone was the first sign of disturbance. In some the first symptom is intense pain beneath the bony boss. In such patients epileptic seizures are common. In a few instances the tumour has been attributed to an intensive local injury, such as a blow upon the head.

In addition to the skull of the Cingalese the museum of the Royal College of Surgeons contains a similar and equally remarkable example obtained from a miner, who died in the General Infirmary, Leeds, 1904. Eleven years previously he fell backwards and bruised his head. The bruise did not subside and continued to increase. The man complained of headache and occasional diplopia. With the hope of arresting the growth of the tumour the left external carotid artery was tied, but death followed the operation in ten days. The hyperostosis involves the left parietal, adjacent parts of the occipital, and the squamous portion of the temporal. For the most part the normal tissue has been replaced by exceedingly dense bone, and a plaque-like por-

tion extends within the skull. The dura adhered to this part of the tumour (Fig. 2).

Skulls changed in this way could not escape the observations of pathologists. Some examples have been described by French writers as hemispheric. The frontal is the bone of preference, but the parietal and squamosal are often involved. The relationship of cranial hyperostosis to meningeal tumours has also been considered by American surgeons — Spiller and Cushing among others.

The relationship of an arachnoid tumour to the osseous elements is well shown in a specimen preserved in the museum of St. Bartholomew's Hospital (Fig. 3). The patient was under the care of Sir James Paget. A section prepared for the microscope, contained in the museum cabinet, shows well the villous nature of the tumour.

The merit of Penfield's excellent essay is his demonstration of the soft tissues which fill the tunnels in the cranial hyperostosis, and I enjoyed the privilege of examining the specimens

FIG. 1.—Skull of a male Cingalese, aged 20. The vault of the skull resembles a crown of loosely compacted coral. The mass is traversed by hundreds of tunnels—exaggerated Pacchionian pits—which open on the surface. The orifices are represented, for the sake of emphasis, too big. (Museum, Royal College of Surgeons.)

FIG. 2.—Portion of the base of a skull to the left of the middle line showing, in section, an immense hyperostosis. F, frontal; P, petrosal; O, occipital; F.M., foramen magnum. (Museum, Royal College of Surgeons.)

he prepared for microscopic investigation.

Penfield prefers to use the name "endothelioma" for these tumours; but names are only convenient labels, and in this case matter little if we keep in mind this

important fact: The epithelium, and the associated soft tissues lodged in the tunnels of the osseous bosses, spring from the arachnoid—they are, in fact, abnormal arachnoid villi. When examined in sections these exaggerated villous tufts embedded in osseous tissue resemble fossil ferns in clay or shale. The bony edifice on the skull recalls the huge mounds built by termites in tropical forests.

TUMOURS OF GLANDULAR ORGANS.

Tumours of glandular organs are often functional. Take, for example, an adenoma of the breast. This is a collection of mammary tissue isolated from the main secretory tissue by a firm capsule which cuts it off from the excretory ducts of the breast. Such a tumour in the breast of a pregnant woman takes on its share of lactation in due course, but as there are no ducts permitting the fluid to escape it accumulates in the glandular acini and the pressure of the fluid leads to atrophy of the secreting epithelium, dilatation and coalescence of the distended acini, and the formation of cavities. Such an encapsuled collection of fluid is known as an adenocoele, and when large enough to attract the attention of a surgeon is, as a rule, excised.

A lobe of mammary tissue occasionally becomes detached from the axillary margin of the breast. Such a glandular islet has no excretory duct, but it enlarges during lactation in concert with the main gland and slowly declines when lactation ebbs. These islets are known as accessory breasts, but a similar islet in the substance of the breast would rank as an adenoma or a cyst.

Similar cystic tumours form in the liver in connexion with the minute bile ducts. Paul proved long ago that adenomas of the liver are clumps of encapsuled biliary ducts. The cells of such adenomas are functional and the cystic spaces contain bile. The solitary (non-parasitic) cyst of the liver, though rare, belongs to this set. Some of these cysts have been so large in women as to have been mistaken clinically for ovarian cysts. In such examples as have been examined microscopically the walls of the cyst contained minute bile ducts. I have satisfied myself that these large cysts arise from the dilatation and fusion of the minute biliary ducts unconnected with obstruction to the main bile ducts. It is certain that the parts concerned in the formation of such cysts have continued to exercise their function, for they contain bile.

As in the case of the mammary gland, an isolated lobe of liver attached to the liver by a fibrous band is called an accessory lobe of the liver, but a similar islet of hepatic tissue in the substance of the liver

is called an adenoma, and may become a cyst by the accumulation of its own secretion—bile.

We owe to von Eiselsberg an account of a remarkable illustration of this habit of glandular tumours. Billroth in 1886 extirpated a goitrous thyroid from a woman aged 38. The operation was followed by myxoedema. A year

after the removal of the thyroid the patient passed through a normal pregnancy; subsequently a tumour appeared in the upper part of the sternum, and as it increased in size the myxoedema disappeared. In 1892 the sternal tumour was as big as a fist and resembled a sarcoma. As it was incorporated with the bone von Eiselsberg removed it with the aid of a chisel and hammer. In structure it resembled an ossifying columnar-celled carcinoma and contained colloid material. The woman made a good recovery, but the symptoms of myxoedema re-

current in the same order as after the thyroidectomy and persisted.

The thyroid gland, possessing no excretory duct, is very liable to have portions of its secreting tissue isolated, and these, becoming encapsuled and slowly enlarged by the accumulation of colloid material, form thyroid cysts and tumours, some of which attain an astonishing size.

The cell elements of primary and secondary cancer of the pancreas can produce ferments identical with or similar to those furnished by the normal cells of the gland (Waring). The active interest taken by physiologists in the function of the pancreas, especially in relation to glycosuria, has led to some valuable experimental work. In 1892 von Mering and Minkowski succeeded in completely removing the pancreas from living dogs. In man this is an impossible operation on account of its intimate relations with blood vessels and nerves. In dogs complete removal of the pancreas is followed in a day or two by glycosuria. Hédon confirmed the experiments (1892) and succeeded in transferring a piece of the tail of the pancreas into a subcutaneous pouch to one side of the linea alba, but retaining its intra-abdominal connexions. When the graft is well established the remainder of the pancreas is completely removed and glycosuria does not ensue. Later if the graft is excised glycosuria quickly follows. If the intra-abdominal vascular connexions of the graft are obliterated the graft scleroses and disappears; under such conditions glycosuria quickly becomes manifest.

Hédon notes that after the graft is transformed to an artificial subcutaneous pouch, a fistula persists for a time and pancreatic fluid issues from it.

FIG. 3.—Coronal section of the frontal region of the head, showing a soft tumour growing from the arachnoid, permeating the frontal bone. (Museum, St. Bartholomew's Hospital.)

FIG. 4.—Pancreas of a dog, to show its environment. (Hédon.)

The skill and care required to remove completely a dog's pancreas successfully is appreciated by surgeons who have performed operations on the pancreas of man. The intimate connexions of the pancreas with the duodenum in dogs is shown in Fig. 4.

FIG. 5.—Harlequin foetus.

in the course of operations performed on the stomach for the relief of gastric disorders.

When the stomach contains a focus of cancer the cylindrical cells, heavily charged with mucin, permeate its wall, fall into the lesser bag of the peritoneum, engraft themselves, and appear, in the early stages, as small yellow flakes. At this stage microscopic examination shows them to consist of clumps of columnar cells full of mucin. These pathological or secondary foci of cancer act as glands and shed mucus in abundance into the omental fold. Such foci multiply, and being reinforced by cell-showers from the primary focus invade the omentum and convert it into a mass of "colloid" weighing many pounds. Omentum changed in this way sometimes forms such a large mass that it has been mistaken in women for a big ovarian tumour. It is not uncommon when cell-showers of this kind fall from a primary focus in the stomach or the colon for the epithelium to engraft itself on the ovaries and convert them into colloid tumours as big as coco-nuts. Implantation tumours of this kind are by no means rare, and as they are now appreciated by surgeons there is little danger of such enlargements, secondary to primary cancer of the stomach or colon, being mistaken for primary ovarian tumours.

I have considered these conditions especially because, in dealing with the large multilocular glandular tumours of the ovaries, there is a possibility of error unless care is taken in the microscopic examination of the tumour.

Colloid Omentum.

Extraordinary examples of functional activity in cancerous epithelium may be studied in the gastro-intestinal canal. The mucous membrane of this tract contains cells that secrete mucus. In the stomach the cell covering is almost entirely formed of them; in a cell swollen with mucus the nucleus is pushed towards the basement membrane. When the mucous membrane is cancerous, the epithelial cells often furnish large quantities of mucus, which infiltrates the omentum and converts it into a gelatinous mass, commonly called "colloid omentum." The mode in which this change is produced can be explained, and my knowledge of it has been obtained

OVARIAN DERMIODS.

Dermoids have an irresistible attraction for me. They prove that many tumours owe their grossness to the accumulation of retained secretions.

The simplest example is a sequestration dermoid on the face or scalp. This takes the form of a globular tumour with a central cavity lined with skin furnished with dermal elements—epidermis, sweat glands, hair bulbs, sebaceous glands. In such tumours the epidermis is continually shed with hair, sweat, and sebaceous grease into the central cavity. The dermoid slowly enlarges in consequence, and a tumour of this kind, no bigger than a pea or a walnut at birth, may in twenty years be as big as a coco-nut. When such a tumour is opened and the contents cleared away the skin lining its cavity will sweat when the patient sweats, and the fluid can be seen oozing from the sweat ducts. The skin lining the tumour is sensitive to the prick of a pin.

The most impressive examples of functioning tumours arise in the ovary, and the growth of our knowledge concerning these tumours reads like a fairy tale. Fifty years ago dermoids puzzled pathologists, but in the interval much knowledge has been gained concerning them. It is now established that these tumours are the products of ova which have become active and developed into ill conditioned foetuses independent of the stimulus of spermatozoa. An ovarian foetus produced in this way is called an *embryonal rudiment*.

Before dealing with the relation of ovarian embryomas to the products found in their sacs some matters must be considered relating to the activities of a normal uterine foetus.

In the mid-period of gestation the foetus floats freely in a hydrosphere formed by amniotic fluid. There are four sets of organs functional—the placenta on which its life depends, the kidneys, choroid plexuses, and skin with its epitrichium. The urine discharged by the kidneys mingles with the amniotic fluid. If the urine is hindered from

FIG. 6.—Ovarian dermoid. The skin, hair, teeth, and nerve tissue which it contains may be regarded as representing the cephalic end of an ovarian embryoma. From a single woman aged 26. (Museum, Middlesex Hospital.)

escaping the kidneys will become transformed into hydro-nephrotic sacs. The choroid plexuses secrete cerebro-spinal fluid, and if it cannot escape from the fourth ventricle hydrocephalus occurs. This is a common malformation, and museums contain examples by the score. The skin is active,

lanugo grows freely, and the epidermis develops the epitrichium (described by Welcker in 1864) which furnishes the soapy vernix caseosa so conspicuous on the skin of a newborn child. In an embryo the whole of the epidermis consists of a single layer of cells. Later this becomes double and the superficial layer is the epitrichium. About the eighth month the epitrichium is cast off, mixed with grease from the sebaceous glands, and lanugo. Occasionally it persists and forms a collodion-like envelope over the foetus, producing the comic appearance which recalls the harlequin (Fig. 5). The epitrichium persists in aquatic creatures such as frogs and salamanders; it protects them from maceration. The human foetus is an aquatic animal while disporting in the hydrosphere; the epitrichium and the vernix caseosa protect it from maceration.

Normal pregnancy terminates with the expulsion of the foetus and the by-products of its glandular organs. If all goes well it becomes an air-breathing mammal. It sometimes happens that a foetus cannot be expelled. In this event the placenta on which its life depends ceases to act and slowly disappears. The amniotic fluid dries up, the foetus dies, shrinks, mummifies, and eventually its tissues become calcified.

The life of an intrauterine foetus is dominated by the placenta.

THE EMBRYOMA.

An embryoma, the essential element of an ovarian dermoid, may contain nearly every organ required for the equipment of a foetus: skin with its essential glands, hair and teeth, pigment and nerves, limb-buds with cartilage and bone, fat and muscle, brain and spinal cord, nerves and ganglia, an eye, gut, and Auerbach's plexus (Nicholson); trachea and thyroid gland, liver tissue (Warwick).

For many years pathologists limited their search to the histology of these lumps. Professor S. G. Shattock critically reconstructed some of the sections. For him nervous tissue collected around a central tube is a syringo-myelus. Grey matter enclosed in dura mater is a miniature brain. C. E. Shattock removed an ovarian tumour the size of a bantam's egg from a girl aged 2½ years. The tumour on median section disclosed an embryoma which can be interpreted as an acornus-embryoma; it is trunkless and limbless, consisting only of a hydrocephalic head. The vault is membranous and the base cartilaginous. A piece of hairy scalp is attached to the head and, near it, some tissue consisting of groups of ganglia furnished with large typical nerve cells. This specimen is preserved in the museum of the Royal College of Surgeons.

The importance of interpreting the gross features of embryomas, with the aid of histological details, adds a new interest to these deformed lumps; they seem like misdirected embryologic energy. The ovarian dermoid shown in Fig. 6

is actually the size of a coco-nut and contained the usual mixture of grease and hair. A remnant of the ovary is seen at the lower pole of the tumour and immediately adjacent there is a patch of skin covered with reddish hair resembling a piece of scalp. Two teeth, an incisor and a bicuspid, are fully erupted. The tissue immediately under the skin contains

a collection of nerve tissue with cells like those in grey matter of the brain. The skin, hair, teeth, and nerve tissue may be interpreted as representing the cephalic end of an ovarian embryoma (Warwick). The loose matter filling the cyst is furnished by sebaceous glands, hair, and desquamating epidermis. The cyst wall, to meet requirements, grows in a most accommodating manner.

It is certain that an ovarian embryoma contains active organs, especially skin, which is continually discharging sebum and sweat, and shedding epidermic cells and hair. The embryoma has no time limit like a foetus, not being dependent on a placenta, and though it rarely exceeds the dimensions of a fist the products of its activity accumulate in the bag which encompasses it and may, in the course of years, amount to three litres or more. Occasionally the pressure of the accumulated organic rubbish

bursts the sac and escapes into the peritoneal cavity, which may become so distended that the belly wall pits on pressure like dough. Sometimes the epithelial elements which escape from the sac engraft themselves on the peritoneum. In such circumstances hundreds of little islets of skin bearing tufts of lanugo dot the peritoneal surface of the intestines, liver, and omentum.

After an embryoma ceases to grow, its capsule, like the membranes of an extrauterine foetus, calcify; the museum of the Middlesex Hospital contains a good example, resembling a coco-nut containing a coil of hair, and three teeth on a plate of bone.

So far we have been dealing with ovarian embryomas in which skin played the prominent part in furnishing waste products. We must now consider some parallel conditions in which mucous membrane is the chief factor.

MULTILOCULAR GLANDULAR TUMOURS OF THE OVARY.

These are the biggest tumours which grow in women. Some of the tumours I have removed weighed nearly a hundredweight, and even bigger examples have been recorded. The loculi in such tumours vary in size and their walls are lined with soft tissue covered with a single layer of large columnar cells heavily charged with mucin (Fig. 7). The membrane lining the loculi is

arranged in depressions, bays, and narrower recesses, recalling in their arrangement the simple glands of the large intestine. The amount of mucus furnished by them is often very great; as there are no excretory ducts for the escape of the secretion it accumulates in the loculi, which become enormously distended by the

FIG. 7.—Loculi of an ovarian tumour lined with big mucus-laden epithelium. (Magnified.)

FIG. 8.—Segment of a huge mucigenous ovarian tumour presenting an embryoma, *d*, bedecked with a tuft of lanugo, *h*. (Museum, St. Thomas's Hospital.)

products of the cells. It is a gelatinous substance now called pseudo-mucin. Often the walls of adjacent loculi rupture and allow neighbouring cavities to communicate, and in this way large chambers form. It is not uncommon for a loculus near the periphery of the tumour to burst and allow the contents to escape into the belly. In some of the cases the amount of pseudo-mucin that collects in the belly is almost beyond belief.

A spinster, aged 54, was under my care in 1899 on account of an enlargement of the belly. The physical signs suggested an accumulation of fluid. The pressure was so great as to produce a hernial protrusion as big as a bantam's egg at the navel, and a similar one over the left femoral ring. A tumour could be felt in the pelvis. I removed three gallons of mucin and a mucigenous tumour of the ovary equal in size to a coco-nut. There was a rent in its capsule opening up three loculi, and through this rent the pseudo-mucin secreted by the mucous membrane lining the loculi escaped into the belly. The tumour was easily removed and the patient reported herself in good health five years after the operation.

Un Chiffonnier.

Many similar cases have been under my care and observation, but all do not end in this simple way. Occasionally, when a mucigenous tumour bursts, clumps of cells escape from the walls and settle on the peritoneum and act as grafts, and become independent tumours, discharging pseudo-mucin, which helps to increase the general mass. In some women hundreds of these pathological glands grow on the serous membrane, and the amount furnished in this way, after the primary tumour has been removed, is so great that it is necessary to open the abdomen annually for the removal of the pseudo-mucin. In removing this material care should be taken to protect the edges of the abdominal incision; it occasionally happens that the epithelial elements in the pseudo-mucin accidentally implanted will grow in the scar and form independent tumours. I have seen them as large as ripe gooseberries.

Surgeons are familiar with these remarkable tumours, concerning which the following facts may be stated: It is not uncommon to find in a woman one ovary occupied with a dermoid and the other converted into a mucigenous cyst. It is not rare to find an ovary transformed into a bilobed tumour one lobe of which is a typical dermoid and the other mucigenous. The inner walls of isolated cavities are often covered with cylindrical epithelium loaded with mucin and indistinguishable from the large cells found on the surface and recesses of the rectal polypi so common in children. Mucigenous tumours are often so large that it is only by chance the embryoma is detected. Quite by chance I saw one on the cut surface of a huge tumour. The embryoma presented as a patch of skin, less than 2 cm. square, bedecked with a tuft of delicate lanugo (Fig. 8).

I have studied the histology of these tumours in season and out of season, and often asked myself the question, Why is the intestinal tract rarely demonstrable in the ovarian embryoma? Gradually I have realized that the mucin (or pseudo-mucin) of these tumours is produced by the gastro-intestinal epithelium of the embryoma, and this, the active agent in the production of mucin, is masked by the accumulated products of its own activity.

The matter may be briefly expressed in this way: In the common kind of ovarian embryoma the cutaneous elements are conspicuous; the products resulting from the activity of the skin preponderate and make up the bulk of the tumour mass. In mucigenous ovarian tumours the so-called "colloid stuff" is furnished by the gastro-intestinal epithelium of the embryoma.

In dermoid tumours skin prevails.

In mucigenous tumours mucous membrane prevails.

In France the man who picks up rubbish in the streets and collects it in the *hotte* on his back is called a chiffonnier. The membranes of a uterine foetus, or the sac of an ovarian embryoma, serve to remind us of the *hotte* of the chiffonnier. The simile helps to illustrate the thesis set out in the beginning of this lecture: *Many tumours become manifest by the accumulation of the products of their own activity.*

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ARSENICAL PIGMENTATION OF THE MOUTH AND SKIN.

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PIGMENTATION of the skin, varying in depth of colour from a light mottled grey to black-brown, and in extent from a small area to the entire surface of the body, is now well known as one of the occasional effects of the ingestion of arsenic in repeated small doses. It has occurred also very exceptionally and in mild degree after a single large dose.¹ The most detailed account of it has been given by Nielsen,² who in the course of his article makes two statements which have also been made by many other writers, either on his authority or their own. He says:

"A deposit of pigment in the mucous membrane of the mouth seems never to have been seen"; and

"A far more trustworthy symptom, which will serve for the diagnosis between arsenical melanosis and argyria and Addison's disease, is the fact pointed out by several writers that in arsenical melanosis the visible mucous membrane is never pigmented. It is true one case has been reported,²⁰ in which the bulbus oculi had been affected by pigmentation, but no case apparently where the mucous membrane of the mouth had been so affected."

I have, however, now met with two cases in which not only was the skin deeply pigmented, but the mucous membrane of the mouth shared markedly in the discoloration. One of these I reported in 1921.³ It was the case of a woman, aged 49, who had taken liquor arsenicalis daily for six years, and in that time had swallowed about 32,850 minims, equal to 298 grains (19.3 grams), arsenious acid. When I first saw her she had very extensive pigmentation of the skin, and keratosis of the palms and soles. The mucous membrane of the mouth and tongue had a bluish dark tint all over, and on the inner surface of the lower lip there was an irregular deep blue-black patch about the size of a sixpenny piece. She also had cirrhosis of the liver and ascites, but no neuritis.

The second case was that of a man, aged 57, suffering from pernicious anaemia, who developed marked pigmen-