The Jingleby Lecture.

ON

THE BLOOD TRAIL.

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BY

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WHEN men and women are impatient in relation to the discovery of causes and means for the cure of dangerous diseases it is useful to remind them of the Blood Trail as a remedy for their impatience.

Knowledge of the blood and its circulation has been acquired by slow and uncertain stages. Our interest in it begins in childhood. The colour and clotting of blood when it escapes from a living animal are among earliest experiences of what was called Animal Economy.

It is 300 years since Harvey discovered the circulation of the blood by observation and inference. Malpighi, at Bologna (1661), discovered the capillaries which link up the arterial and venous systems. He also saw the globules now familiar as red corpuscles. Leeuwenhoek (1673) with a simple lens saw the circulating blood in the tail of a tadpole and the web of a frog's foot. An astute observer—John Hunter—expressed this opinion in regard to the globules: The early observers probably imagined more than they saw because they used magnifying glasses!

One hundred years ago there were men who believed the earth to be flat; and there was much argument concerning the red corpuscles of the blood—were they globules or flat discs? In 1827 J. J. Lister, a wine merchant interested in optics, improved the compound lens and enabled observers to determine with certainty that the red corpuscles are circular biconcave discs. In 1862 Hoppe (Hoppe-Seyler) detected the haemoglobin of the red corpuscles. Sir George Stokes, two years later with the aid of a spectroscope, discovered the astonishing part played by haemoglobin in respiration. To-day, even with new methods of research, it is not known how long a red corpuscle lives fetching and carrying oxygen.

An expert—Dr. W. E. Cooke—recently describing in great detail the structure of the human erythrocyte, expresses the opinion that a volume could be written on its peculiar nature and character.¹

Leucocytes.

The white corpuscles—leucocytes—were discovered by Hewson (1774). Seventy years later Wharton Jones detected their amoeboid movements (1846). Their curious power of flowing through the walls of the capillaries without breach—diapedesis—was observed by Cohnheim (1867).

In 1883 leucocytes came prominently into notice, in consequence of the dramatic discovery by the Russian biologist Metchnikoff that they had the power of ingesting and digesting organic particles in the blood, especially microbes. Metchnikoff died in 1916. His Life, written by his wife, contains an account of the simple way in which the Phagocyte Theory was born. Metchnikoff was at Messina in 1882, and had been watching the mobile cells in the body of a transparent starfish larva, and the idea occurred to him that similar cells might serve in the defence of the organism against intruders. To test this idea he took some thorns from a rose tree and introduced them at night under the skin of some beautiful starfish larvae; these larvae are as transparent as water. In the morning the thorns were surrounded by mobile cells, as is to be observed in a man who runs a splinter in his finger. This simple experiment laid the foundation of Phagocytosis, to which Metchnikoff devoted twenty-five years of his life.

The Clotting of Blood.

Although coagulation of blood has been studied from early times and keen physiologists have given it attention, no one has found a satisfactory answer to the question: Why does blood clot when it leaves the body of an animal?

There is an aspect of it which concerns surgeons deeply—blood sometimes clots in blood vessels, especially veins,

during life, and leads not infrequently to such a disaster as sudden death. Clotting of blood in veins during life has been recognized for centuries, and it is associated with the condition called phlebitis—simply, inflammation of a vein. Physicians, when making examination of the bodies of persons who died suddenly, occasionally found a large blood clot firmly plugging the pulmonary artery. In the middle of the nineteenth century it occurred to an observer that the fatal clot was not formed in the artery where it was found after death, but in some remote vessel, and becoming loose was conveyed by the blood stream to the pulmonary artery, which it plugged so completely as to cause death in a few minutes. A clot of this kind is sometimes rammed in the vessel as tightly as a pellet in a popgun!

It was Virchow who opened our eyes to such sequences and made physicians and surgeons realize their intellectual blindness.

When a mere boy I read in a medical journal (which I casually found among a parcel of stale papers) a lecture with a strange title—Thrombosis and Embolism. These odd Greek words attracted my attention; in plain English the title may be rendered "Clots thrown from a distance."

Ten years later, when making a post-mortem examination, that lecture came forcibly to my mind. I read with vivid interest Virchow's writings on Thrombosis and Embolism, which was deepened when I began to remove the uterus for fibroids, and came face to face with the part played by sepsis in causing coagulation of blood in the living body. Blood may be regarded as a fluid tissue, of which the plasma is the matrix, erythrocytes and leucocytes the cell elements. This question must occur to many: Why does blood remain fluid in the vessels of living animals? It remains unanswered.

Obstetricians and gynaecologists are specially concerned with thrombosis because blood is very apt to clot in the big pelvic veins of lying-in women, and of men and women who have been subject to operations on the pelvic organs. In such conditions the iliac, ovarian, and spermatic veins are liable to become reservoirs of blood clot; an entire clot, or a fragment, may be detached and swept by the blood current to the heart. Embolic clots are forcibly ejected into the pulmonary artery, and, when big, plug this vessel and kill the patient.

Post-operative pulmonary embolism occurring as a sequel to abdominal hysterectomy caused me grave concern. When I began to perform abdominal operations I soon realized that the peritoneum would not tolerate carbolic acid, neither in solution nor as a spray. When I restricted antiseptic treatment to the patient's skin and mucous membrane, my operative results immediately improved. The mortality after hysterectomy for fibroids fell to 1 per cent. This 1 per cent. was due to pulmonary embolism.

Gradually gynaecologists realized that post-operative embolism very rarely happened after vaginal hysterectomy. It is now admitted that post-operative thrombosis of blood in the iliac veins is a sequel of infection of the abdominal wound. The channels of infection are the deep epigastric veins; the iliac veins serve as reservoirs for the big clots which plug the pulmonary artery and lead to surgical tragedies. For example, a stout midwife had a large fibroid which I easily removed, and I secured the abdominal incision with thicker sutures than usual in order to obtain a sound scar in view of her occupation. On the eighth day after operation, at the usual ward visit I noticed that her temperature had suddenly risen to 103°, and said to the house-surgeon: "This forebodes thrombosis of the iliac veins. Pulmonary embolism is impending." She died suddenly a few hours after the visit.

I gave instructions for the pulmonary vessels to be carefully examined. The pathologist, knowing my interest in the matter, removed the thoracic organs entire. We examined them and found a big embolus plugging the pulmonary artery like a cork. It furnished an abundant growth of the colon bacillus.

In addition to big clots which plug with immediately fatal effect, there are smaller clots which readily traverse the large pulmonary arteries and become arrested in small vessels near the periphery of the lungs. Embolic clots of this kind are troublesome and retard convalescence. Pathologists remind us that every clot found in a pulmonary artery is not embolic. The clot may have been formed

in situ. This is true, and does not disturb the fact that venous blood is more prone to thrombose than arterial blood. The blood in the pulmonary artery is venous in character.

Facts accumulated since 1900 make it clear that the naked hands of surgeons are the chief infecting agents which patients risk when they submit to operations; this indictment includes midwifery manipulations.

The chief cause of post-operative thrombosis and embolism is sepsis, and its incidence has diminished enormously since surgeons adopted the habit of wearing sterilized rubber gloves when operating.

Cysts and Menstruating Tumours.

Menstruation—the rhythmical uterine bleeding of women—heralds the attainment of sexual maturity, and occurs monthly in healthy women. The cause, significance, and utility of menstruation are obscure; the blood is furnished by the peculiar tissue of the uterus known as the endo-

FIG. 1.—Uterus in section with a large patch of adenomyoma on its posterior wall. The new growth has permeated the peritoneal surface of the uterus. (From *Tumours*.)

metrium. Menstruation is dominated by the ovaries; and their artificial removal is followed by sterility and enduring amenorrhoea.

Menstruation is not confined to human beings. I was astonished to discover its occurrence in macaque monkeys and baboons living in the Zoological Gardens, London; and was able to study this curious process on fresh material, but failed to discover the cause. It was suggested that menstruation happens in monkeys living in the Gardens because they are in a country and climate foreign to them. My observations were communicated to the British Gynaecological Society in 1886. In consequence of these observations W. Heape of Cambridge went to Calcutta for the purpose of studying menstruation in the sacred monkey of India—the *Entellus* monkey—and described his research in an elaborate paper in the *Transactions of the Royal Society* (1894). Heape's observations bear out in the main my conclusions, but the cause of menstruation remains obscure. The dominant features are these: menstrual blood is furnished by the endometrium; the superficial layer of epithelium is shed during the process; the shedding extends from the uterine orifice of the Fallopian tubes to the internal orifice of the cervical canal.

The ovaries are often occupied by cysts; many are ripening follicles and others are degenerate corpora lutea. It is not uncommon for an ovary to be converted into a cluster of cysts. Distorted ovaries of this kind are familiar to gynaecologists, and it is not uncommon to find them adherent to the body of the uterus, especially its posterior surface. In the course of operations undertaken for their removal the detachment of such cysts is apt to burst them, and they discharge thick blood resembling chocolate or tar; hence the term "tarry cysts" of the ovary. As a rule, both ovaries are affected, and this cystic condition is often associated with adenomyoma of the uterus.

Adenomyoma of the Uterus.

This tumour disease is the product of overgrowth of the endometrium with a responsive increase of the connective tissue in which the uterine glands are implanted. The increase of the endometrium leads to a corresponding enlargement of the uterus, and in clinical features it resembles a submucous fibroid. Operations are usually performed for an enlarged uterus of this kind under the impression that it contains a fibroid, but after removal its nature is easily appreciated on bisecting the mass, for it is unencapsuled and displays an intimate association with the wall of the uterus (Fig. 1). Occasionally buds of the endometrium appear on the peritoneal aspect of the uterus which to the naked eye resemble subserous fibroids, but on microscopic examination they will be found to contain diffuse tissue resembling the endometrium, and they lack a capsule. In typical examples the appearance of the cut surface of a large adenomatous mass resembles the fabric known as "watered silk." In some examples of this disease the uterus may be as big as a coco-nut and clinically mistaken for a submucous fibroid.

FIG. 2.—Microscopic features of diffuse adenomyoma of the uterus. (From *Tumours*.)

The Endometrium—the Organ of Menstruation.

For the proper understanding of the nature of the endometrium it is necessary to bear in mind that the uterus is a hollow muscular organ in which the embryo is nourished and protected from the time it leaves the Fallopian tube until it is fit to be expelled as an air-breathing child.

Until the advent of puberty—declared by the onset of menstruation—the cavity of the uterus is lined with endometrium which is covered with columnar epithelium, and beset with glands which discharge their secretion into the central cleft. The endometrium and the muscular wall of the uterus insensibly blend.

It is common knowledge that the menstrual fluid—mainly blood—is furnished by the endometrium, and this is the essential organ of menstruation. The blood is effused at intervals of four weeks, mixed with shed epithelium. Occasionally the epithelium is shed as a complete cast—menstrual decidua.

It is established that the tissues of tumours are derived from the normal tissues of the body. Tumours do not differ in their habits (ecology) from normal tissues; this is demonstrated in a curious way by tarry cysts of the ovary. In 1920 J. A. Sampson, an American gynaecologist, discovered that the lining membrane of such cysts is structurally identical with endometrium, and the blood they contain is furnished by it. These cysts actually menstruate!

How do they acquire an endometrium? Sampson explains it in this way: During menstruation blood and shed epithelium escape from the uterine cavity into the Fallopian tubes; leaking from the ostia into the pelvic cavity this fluid comes in contact with the surface of the ovary; the cells engraft themselves on the ovary, flourish, multiply, and originate an endometrial cyst! I venture to submit another explanation: Tarry cysts of the ovary are associated with adenomyomatous uteri. In this disease the

epithelium is apt to permeate the wall of the uterus and bud-like outgrowths may emerge on its peritoneal surface. When an ovary lies in contact with an adenomyomatous uterus its tissues may be implicated by the active epithelium and in this way establish a menstruating cyst. An example of such implication is represented in Fig. 3; in this instance the uterine wall is occupied by a localized patch of adenomyoma situated near the tubal angle; to the naked eye it appeared to be an intramural myoma, but unencapsuled. This raised my suspicions, and a microscopic examination proved it to be a localized patch of adenomyoma. The adherent ovary was cystic and the cavities of the cysts contained tarry blood; the endometrium they contained was derived from the uterine endometrium by permeation.

Although unconvinced by the theory of implantation secondary to retrograde menstruation I was unable to discard it in the face of the following facts.

A woman, aged 29, complaining of dysmenorrhoea, was submitted to the following operation by Bonney. The uterus was withdrawn from the pelvis through a median subumbilical incision,

FIG. 3.—Uterus in section with a patch of adenomyoma and a cystic ovary. From a primipara aged 35. (Tumours.)

its cavity exposed, and the endometrium thoroughly erased. During the operation the margins of the abdominal incision were soiled by blood and endometrial fragments. Two years later the patient returned with a small lump at the lower end of the abdominal scar. This lump swelled during a menstrual period and became painful; it was excised and on microscopic examination displayed the structure characteristic of normal endometrium; there was blood in the stroma and in the lumen of the glands.²

This experience has the value of a reliable experiment. The adventitious vascular lump arose in a fragment erased from the endometrium and accidentally implanted on the raw margin of the abdominal incision made two years previously.

The Endometrium and the Mammary Gland: A Comparison.

The endometrium is liable to the same perversions as a compound secreting gland—for example, the mammary gland—with which its functions are closely correlated in reproduction.

When the functions of the menstrual organs are manifest the mammary glands are quiescent, though they may exhibit what is sometimes poetically called sympathy with them in activity. When the endometrium—so far as menstruation is concerned—is in abeyance—for example, during pregnancy—the mammary glands are active, and when the uterus acquits itself normally their activity is manifest.

The correlation of the breasts and endometrium is obvious in a comparison of their pathological tendencies. The essential gland elements of each are liable to similar morbid changes—adenomas, papillomas, and polypi. The liability of the mammary gland to cancer is perhaps greater than that of the endometrium. This may be due to exceptional facility of observation in the case of the

breast. The very rare cystic adenomas of the breast are parallel to the large adenomyomas of the uterus.

Cancer of the endometrium differs clinically and pathologically from cancer of its neck, and, like mammary cancer, leads to secondary deposits in the lungs.

The leading clinical features of adenomyoma of the uterus are excessive and prolonged menstruation associated with enlargement of the uterus, which simulates the physical signs presented by a submucous fibroid. The tendency of adenomyomatous tissue to permeate adjacent organs explains its occurrence in the round ligaments of the uterus and the wall of the rectum. In patients under my own observation large adenomyomas were accompanied by excessive and prolonged menorrhagia and its sequence—profound anaemia.

The results of subtotal hysterectomy for this disease are admirable. The patients are usually nulliparous—spinsters and barren married women between 30 and 50 years of age.

FIG. 4.—Ovary, Fallopian tube, and a fold of omentum, lying in the omental fold—a mole or apoplectic ovum which was discharged through the rent in the tube. Removed by operation in 1886.

An accurate diagnosis is only possible after removal of the uterus.

Note.—Mr. F. Roques lent me some excellent slides obtained from endometriomas, which have been useful in the preparation of this lecture.

Pelvic Haematocoele.

Fifty years ago textbooks on diseases peculiar to women contained descriptions of disabling, and occasionally fatal, effusions of blood in the pelvis which occurred in healthy women in the prime of life. Such collections, when the blood was free in the pelvic cavity, were called intrapelvic haematocoeles. When the blood was effused between the layers of the broad ligaments of the uterus it was called a haematoma. Various causes were suggested to account for such effusions. Occasionally they were profuse and caused death. Nothing was known of the cause.

Lawson Tait simplified our knowledge of these things. When operating on women for the relief of chronic disease of the ovaries and Fallopian tubes he occasionally found an abundant collection of fresh blood in the pelvis. His experience led him to announce this bold generalization. *Probably all forms of ectopic pregnancy have their starting place in the Fallopian tube.*

Tait produced no evidence to support his opinion. I was impressed with the brilliant conception and looked out for a sign. It came in an unexpected way.

While the Imlach trial was in progress (1886) I operated on a young and recently married woman at the Middlesex Hospital. The patient had been admitted under the care of the obstetric physician (in those days obstetricians did not perform abdominal operations); the pelvic cavity was flooded with blood, and in a pouch of omentum, associated with a rent in the Fallopian tube, lodged an oval body the size of a chestnut. I removed the tube, ovary, and

fold of omentum with the oval body in one piece, and preserved them for future study.

Three years later (1889) a woman was admitted under my care in the Middlesex Hospital with signs of intra-pelvic bleeding. I promptly operated, and found a movable body as big as a walnut with a smooth cavity at one pole, and at once recognized its similarity to the familiar uterine mole. The effused blood and clot were collected, and the operation completed. I then washed the clot in a glass vessel with a gentle stream of water from a tap. Suddenly I saw the head of an embryo rise to the surface in a gentle swirl. This clinched the evidence—I had found a *tubal mole*! The name soon became current in gynaecological literature.

When no embryo is forthcoming the presence of chorionic villi in the mole is now accepted as evidence of tubal gestation.

This lecture was opened with a recital of the Blood Trail. Let me end by reminding you that men who make original observations are often obdurate in accepting the discoveries of their contemporaries.

Harvey discovered the circulation of the blood, but did not believe in the existence of the lacteals described by Aselli (1622). The discovery of the lymphatic system was second only in importance to that of the circulation of the blood.

Baer found the human ovum, but would not accept the idea that the spermatozoon initiates development in the ovum. We may believe that the tail of the spermatozoon led to the discovery, "since things in motion sooner catch the eye than what not stirs."

Lawson Tait, in his vigorous Ingleby Lecture (1886) on Pelvic Haematocele, insisted that the blood came from the sac of an ectopic pregnancy. He not only ridiculed my discovery of the tubal mole, but warned teachers of midwifery against my transcendental notions relating to tubal abortion.

To-day a tubal mole is as familiar to a gynaecologist as a placenta to a midwife.

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SPONTANEOUS DETACHMENT OF THE RETINA.

BY

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As far as I have been able to ascertain no general account of Professor Gonin's work on the causation and treatment of spontaneous detachment of the retina has up to now appeared in English. His writings have been either in French or in German, and have been directed to explaining various aspects of his views, but there is no comprehensive article dealing with the matter. Having had the good fortune to see Professor Gonin operate, and to have his views explained to me personally, I think it may be of use to my colleagues and to the medical profession generally if I attempt to place on record what I understand to be the pathological conception on which he bases his mode of treatment.

By spontaneous detachment of the retina is meant the condition of retinal detachment found without evidence of any concomitant gross pathological condition, and excludes intraocular growths, definite inflammation, gross traumatism, etc., the detachment being unaccompanied by any of these factors and apparently having occurred spontaneously without any obvious visible cause. It is, however, generally allowed that some degree (not necessarily a high degree) of myopia may be present, or the condition may occur in old people where senile changes exist and without any traumatic history, or only a history of slight jarring, shaking, etc., of the eye or body.

Professor Gonin first visualizes a change in the vitreous, and subsequently in the retina, which may be unobservable to ordinary ophthalmoscopic examination. A partial liquefaction of the vitreous takes place, and a localized

or general thinning of the retina, also giving no definite ophthalmoscopic evidence. The retinal change, however, is often in the region of the ora serrata, and therefore not obvious to ordinary ophthalmoscopic view unless extraordinary means are taken, such as full dilatation of the pupil and pressure deliberately made outside by the finger, in the neighbourhood of the ciliary body.

The primary change in the vitreous is one of partial liquefaction. The evidence for this is the frequent presence of fine floating opacities in myopic and senile eyes, and the occasional presence of a deformation of the details of the papilla, which vary with movements of the ophthalmoscope, presenting a condition similar to that seen when viewing the fundus through an irregularly astigmatic lens or cornea; in addition we can sometimes see a diffuse opacity in the vitreous associated with "floaters" or streaks, but it is allowed that the ophthalmoscopic evidence of a liquefied vitreous may pass unnoticed or give only very equivocal signs. With regard to the retina, Professor Gonin suggests that the retina, like the choroid, may be subject to strain and stress, and may be the subject of thinnings, atrophic areas, holes, and tears. The retina as well as the choroid is more firmly attached at one place than at another. The optic nerve fibres secure the retina firmly at the optic disc, but the attachment at the ora serrata is thinner, more attenuated, and more apt to fail, either as the result of pathological conditions affecting the choroid, or a senile condition associated with the attenuation of the nerve fibres and its parenchyma. On the other hand, the choroid is more firmly attached to the ciliary body and yields in the region of the optic disc and macula.

The partial detachment and retraction of the vitreous turns that body into a heterogeneous system, consisting of (1) non-albuminous watery fluid, and (2) the unaltered or only slightly altered vitreous gel. This condition has an importance, Professor Gonin thinks, in causing an unequal strain on the thinned and degenerated retina, so that any sharp abrupt movements of the eye or body may result in a sudden pull on the friable membrane. Traversing the liquefied vitreous may be strands of vitreous jelly attached at one point more or less firmly to the membrana limitans interna, and any abrupt sharp movement may cause a definite, localized strain or pull at a point in the retina. The presence of any fine adhesion, the result of a small localized inflammation, would fasten the retina at such a point to the underlying choroid and would form an attachment which, as a result of even very slight trauma, would allow a tear to take place if the surrounding area were only supported by a liquid vitreous.

Professor Gonin believes that detachment of the retina only takes place if a tear or hole exists in the retina, and that this hole allows the liquid vitreous to pass through it and so raise the retina from its bed on the pigment epithelium. These retinal tears are usually situated, in recent cases, on the convexity of the detachment, but if and when the fluid shifts further round or down, then the tear may be found at a spot where the detachment has become less raised. Another area where the tears are often found is in the region of the ora serrata, because it is here that the retina is thinnest, most vulnerable, and liable to degenerative and pathological changes either from cystic degeneration or choroido-retinal atrophy. Holes in the area behind the equator are less common, and more often than not are the result of gross traumatism or definite pathological change.

Professor Gonin observes that in macroscopical specimens of spontaneous retinal detachment there is no gelatinous clot behind the retina—that is to say, no coagulable exudate the result of inflammation. The preretinal and subretinal spaces are filled with an identical fluid of a watery nature. The vitreous gel is retracted forward, and is best and most abundantly seen between the equator and the ora serrata, and shows more or less extensive adhesions with the retina. These macroscopical specimens frequently disclose the presence of a hole or tear.

A simple progressive stretching is not sufficient to detach the retina from the choroid, as was originally supposed to be the case in myopic detachment; on the contrary, the retina can adapt itself better than the choroid to a gradual enlargement of the globe; the retina yields only to a sudden tension, and is torn either at the