Carcinoma of the Cervix Uteri

A Clinical Study.

Thesis for M. D. Degree

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Introduction.

An apology is almost necessary for choosing such a hackneyed subject as Carcinoma of the Cervix Uteri, for a Thesis. It has been thrashed out over and over again, and I fear I will not be able to bring forward much new matter. The subject has been specially brought under my notice on account of several cases of this dread disease occurring in my own private practice, and although to the Gynaecologist and the Pathologist, the subject may seem thrashed out, and its very mention excite a feeling of weariness, yet to the patients afflicted with this disease, it possesses a terrible interest — an interest that does not end till life is extinct. As yet unfortunately little can

be done in the way of cure, the most one can do being simply to soothe the rugged pathway to the grave. For reasons already stated Carcinoma of the Cervix possesses very great interest to myself and hence I have been led to select it as the subject of this Thesis, and this also must be my excuse for bringing it under your notice. Should anything be said in the following pages that would either directly or indirectly suggest any means of alleviation or point to any possibility of cure, the writer will be more than rewarded.

Before passing on to the Study of Carcinoma of the Cervix in general, I will briefly narrate the histories of the Cases seen by me in practice:—

Case I.
Mrs J. Aet 31 Married.
was first seen by me on 21st Sept. 88, when she came to have her infant, 6 months old, Vaccinated.
Complaining casually of "too much unwellness" & volunteering the opinion that she "was sure she had Cancer", I proceeded to examine her, hoping to relieve her mind, when I was surprised to find unmistakeable "Cauliflower Excrescence". I therefore recommended her for Admission to the Buchanan ward, Royal Edinburgh Infirmary, where she was admitted next day.
Notes by Dr Fraser Wright
History. In January 1886 while weaning her fourth Child, her illness commenced with a discharge of blood about a week after her first menstrual

period. This Metrorrhagia continued till she became pregnant with her 5th child, when it got somewhat better, but again got much worse after the Child was born. For the last two months, she has had Leucorrhoea, but without any bad smell. In June 1886 she was examined by Dr. R. and treated with Ergot, which somewhat improved it. She has not lost much flesh since this illness began.

Family history. Previous history good.

Pregnancies. 5 in number. 1st 9 years ago and last 6 months ago. Labours all easy. No Miscarriages.

Menstruation commenced at 14. Always regular & normal

Menorrhagia, Metrorrhagia & Leucorrhoea as described above.

Physical Examination. The Cervix is enlarged and indurated and is infiltrated with a dense Cauliflower-like growth, which is situated more on the Anterior lip and invades the

Vaginal roof in the Anterior & left lateral fornices. Uterine body normal. Slight pain on pressing Cervix. Examining finger tinged with blood.

Termination:— As Professor Simpson thought this was a case in which the disease was too advanced for Operative interference, she left the Infirmary on Octr 20th 1884.

During the next few months she continued the use of the hot douche with Corrosive Sublimate and the internal administration of Iron & Ergot.

Unfortunately I was prevented watching the progress of the Case, owing to my being laid aside with Scarlet Fever, but on

16th Febry 1885, I found her in the last stages of the disease. Cachectic and Anaemic to a profound degree & Complaining of Constant headache. She was losing a great deal of discharge Nothing further could be done, than

relieve symptoms with Morphia hypodermically &c
She gradually sank and died on 22nd Febry 1888 the duration of the entire illness being slightly over two years.

Case II

Notes by Dr A. Routh, London-

March 12th 1888.

Mrs W. Aet. 53. Widow 21 years. One child 20 years ago.

Catamenia commenced at 11½. Regular till 48 (1883) when slightly irregular with Metrorrhagia for 3 months. Then regular for a few months. Then Amenorrhoea 12 months. Then regular. Amenorrhoea 11 months 1886 and most of 1884.

For the last 9 months slight "threats of blood" on exertion with watery inoffensive discharge in the intervals and bearing down in the groins. No emaciation. Health good.

Brings note from Dr. Ronaldson stating

nature of the case Vs.
Physical Exam". Cauliflower Cancer of the Cervix, involving posterior vaginal wall and Douglas' pouch, and infiltration of both Broad Ligaments nearly to Pelvic Wall, (felt per Rectum)
Rectum slightly adherent.
Uterus (Body) not enlarged nor fixed.
= | Gland in Obturator foramen enlarged on both sides.
Treatment;- Curetted and followed with Bromine Solution (1 part to 4 of Spirit) packing neighbouring parts with rags soaked in Saturated Solution of Na_2CO_3.
April 10th 1888. Dr Thomas Keith saw her in Consultation in Nursing Home at the desire of her friends.
Prognosis 6 months.
Had to be plugged twice in London.
Soon afterwards went to Scotland"

I am indebted to Dr. A. Routh of London for the foregoing notes of Case II, who came under my care on July 31st 1888 in Dr. Ronaldson's absence in the Country.

Dr. Routh saw her in consultation with me on August 13th, by which time, the disease had made rapid progress. What she now suffered most from was incessant retching and vomiting, and Dr. Routh, being of opinion, that from interference with the ureters, a modified Uraemia existed, prescribed Nitroglycerin (one drop of a 1% solution in ℥i of water) when required. This had a markedly beneficial effect, almost invariably arresting the Nausea & Vomiting.

Amongst other remedies that had been previously tried for the same symptoms with little or no effect were:— Cocain, Sulphonal, Bismuth Subnit. and dilute Hydrocyanic Acid.

We found that the administration of Raw Meat Juice was more easily borne

by the Stomach than anything else.
Augt 18th 1888. Everything that is swallowed now is immediately rejected— Chian Turpentine, which the patient had been taking for some months very regularly had now to be stopped, much against her wish. Its marked effect in keeping down the offensiveness of the discharge was well seen, for during the few days it was not taken (owing to the sickness) the foetor became much more pronounced.
Augt 19th Patient now very restless and gradually losing strength. Scarcely able for douching out with the dilute Iodine Solution, she is accustomed to.
At night considerable Haemorrhage took place— several large clots being passed. 10 grains of Gallic Acid taken every two hours, having no effect on the bleeding, it was found necessary to plug the Vagina with a saturated solution of Perchloride of Iron & Glycerine.

Augt 20th Dr Routh saw the patient with me again in consultation

Great pain is now experienced during Micturition, which is frequent; also during Defaecation, which she describes as "even worse than Labour".

21st Can take nothing by the mouth now, except Iced champagne.

Stimulant and food given by Enemata.

22nd Hypodermic injections of Morphia and Ether necessary.

23rd Severe Haemorrhage - Plugged.

24th Great exhaustion. Evidences of Uraemic Coma approaching (Odour of Breath &c)

25th Gradually increasing Coma - from which patient cannot be roused

26th Death.

Case III

Mrs McV. Aet 34. Widow.

This case came under my charge on Sept. 4th 1889.

Although she had suffered from irregular haemorrhages for about 18 months, it was only in the preceding April that she consulted a medical man.

I am indebted to Dr Halliday Croom for the following notes of the condition he found on local examination:—

"P.V. Advanced Epithelioma of cervix breaking down, involving para-vesical cellular tissue, and slightly the back wall of the bladder".

History. For about 18 months, she had suffered from an almost constant bloody discharge, accompanied by dragging pains in the pelvis and down the thighs. In the beginning of 1889 she was troubled with great irritability of

the bladder and frequency of micturition, and the discharge began to have a most unpleasant odour.

Previous health was always good.

Family History:- Mother alive and well. Father died of "Creeping Paralysis." Husband (a Minister) died suddenly from the bursting of a Thoracic Aneurism. One of five sisters had her breast amputated a year ago. She stated that an Aunt had died of "Cancer of the Womb" but recovered.

Menstruation was normal & regular until Menorrhagia & Metrorrhagia as above described commenced

Pregnancies:- She has three Children aged 16, 14, and 9 years respectively. Her first Labour was a difficult one & prolonged. Living at that time some distance from a Medical Man, only the Nurse was present at the birth of the Child. The other two labours were easy.

Further progress and termination.

When she came under my care she was using hot injections with Boracic Acid and Alum. Also Sulphonal in XXX gr. doses for Sleeplessness.

Sept. 10th 1889. She was seized with Haemorrhage which we succeeded in checking with Hot Douche and Hagaline injections. On examination I found that the disease was in an advanced stage, involving the Vaginal roof and walls. Ulceration and Sloughing appeared to be going on to a considerable extent and there was great local tenderness. Up to this time she had been able to move about a little and even go out, but was now ofcourse obliged to keep her bed.

Sept. 12th The haemorrhage recurred to a slight extent. Sickness which had been present for some time now became more & more frequent so that she rapidly became emaciated.

Food of the lightest kind could only be given and that in small quantities.

Sept. 18th. Haemorrhage again occurred and this time an artery seemed to have been ulcerated into. Plugging with Iron & Glycerin resorted to.

19th. & 20th. Had again to be plugged.

21st. To try the effect of checking the foetid discharge Chian Turpentine was prescribed in pill, as follows:—

℞ Sulph. Sublimat grs II
Terebinth. Chio grs III
f. pil. Sig. Two to be taken every 6 hours.

For the Vomiting— Brandy & Iced Champagne were given— Also Raw Meat Juice.

22nd. Considerable irritation of the Bladder. Micturition takes place every 2 hours.

24th. The Sickness & Retching continuing, I prescribed Nitro Glycerin as in Case II.

26th. Becomes more & more irritable. The Sickness is checked by the Nitroglycerin, which allows more food to be taken.

27 The Bowels move naturally every 2nd

day – sometimes aided by Cascara Sagrada.

Oct. 1st Sickness again more troublesome & recourse is necessary to Pancreatized Milk & Egg Enemata. Also Beef Suppositories.

2nd Complains of noises in the head. Dialysed Iron was prescribed for the Anaemia to which they were probably due.

3rd Morphia subcutaneously now given twice daily for lancinating pains. Antipyrin also proved useful in X grain doses.

4th Great "Itchiness" of whole body complained of, for which sponging with Menthol was tried.

℞ Menthol ℥ss
Spt. Vini Meth. ℥iii
Aquae ℥vi

6th Pilocarpine subcutaneously seems to give relief to the irritation of the Skin.

8th Vomiting quantities of bilious matter today. Rapidly sinking.

9th Inability to swallow anything.

10th Described her feeling as if the lower part of her body were "riddled through & through".

11th Very weak & prostrate.
No longer able to be douched.
The patient gradually sank into a Semicomatose condition and died on Monday 14th Oct 1889.

The usual symptoms of Carcinoma of the Cervix (Haemorrhage, Pain, Discharges & Wasting and in some Cases Urinary irritation) I need not refer to, as unfortunately they are too well known to need description.
I would briefly however allude to the following points:—

(1). In Case II
An enlarged gland in the Obturator Foramen was felt on both sides. This fact is of considerable diagnostic importance, and I mention it the

more especially, as it does not seem to be commonly referred to in Books.

(2) In Cases II & III

in all probability the Utero-Sacral folds were infiltrated with the disease and the Ureters, being compressed produced a mild form of Uraemic poisoning. As a result of this there was incessant Vomiting and Retching, which did not yield to the ordinary treatment. Here I would therefore point out the value in such cases of Nitroglycerin, as suggested to me by Dr A. Routh, London. Under its influence, the Vomiting as a rule was at once checked & the patient, therefore able to retain food.

In the Brit. Med. Journal Vol I 1883 p 811, there is a reference to the usefulness of this drug in Uraemic Asthma. Its Modus Operandi is difficult to explain.

(3) Chian Turpentine proved useful more especially in Case II, both in relieving pain and keeping down the foetor of the discharge. So far as I could see, it otherwise had no effect in checking the progress of the disease.

Note in reference to the Normal Anatomy of the Cervix.

In order to make this paper as complete as possible I will briefly recapitulate the normal Anatomy of the Cervix, more especially as looked at from a pathological standpoint.

It is usual to describe the Cervix Uteri as consisting of <u>two</u> portions:— (1). The portio Vaginalis,
(2). The Cervical Canal.
It is true that Schroeder has divided the Cervix into <u>three</u> portions, viz: 1 Infravaginal
2 Intermediate
3 Supravaginal;
but this is looking at it more from an Anatomical, than a pathological standpoint. I will therefore adhere to the former division.

(1). The portio Vaginalis.

This is the part of the Cervix that presents in the Vagina, and extends from or a little above the external orifice of the os uteri to a line drawn through the point where the Cervix is inserted into the Vagina.
The limit between the two portions is indicated in the healthy cervix by the change from Squamous to Columnar epithelium.
The portio Vaginalis has very few glands as a rule and those present are simple mucous crypts. Dr John Williams thus describes the portio Vaginalis:-
"The portio Vaginalis is really a "cup of stratified epithelium, re- "sembling a tailor's thimble, which "fits on the lower end of the "cervix proper" (Harveian Lectures 1886).

Between the squamous & columnar epithelium the same author also describes an area covered by transitional epithelium, though in many cases this transitional epithelium disappears and is replaced by an "erosion" which is covered by columnar epithelium, and thus the columnar epithelium meets the squamous, without the interposition of the transitional, and may even extend over a part usually covered by squamous epithelium. The importance of these "erosions" will be seen later on.

(2). <u>The cervix proper.</u>

The second part is the cervix proper. It is limited below by the vaginal portion and above by a plane drawn transversely through the inner orifice. It is covered by columnar epi-

thelium and contains a very large number of glands. Not only are these glands very numerous but they are very complex, being in fact racemose glands. In connection with this portion of the cervix, and with these glands more especially, we will have to notice hereafter two very important pathological conditions, viz:- the so called ulcerations or "erosions", and Carcinoma, together with their possible connection with each other. Both these conditions are intimately associated with, and probably take origin in, the glands of this part of the Cervix.

Now at the very outset the question at once presents itself:-

Why is Carcinoma of the Cervix of the Uterus - or for that matter of any part of the Uterus - so very common?

It is a strange fact that though Uterine Cancer is so exceedingly common in the Human female, it is hardly ever found in other Mammals, and is almost unknown to Veterinary Surgeons. Why then is Carcinoma so common in the Human female as compared with other Mammals? There must be some reason or reasons for this frequency not accounted for by any difference in structure in the Cervix of the lower Mammals as compared with that of the human female.

Among such reasons I believe we have

(1). The erect posture in the human female. This predisposes to

congestions of the uterus simply from the effect of gravity; this fact alone tends to keep up inflammatory affections of the cervix especially and sends a large amount of blood to the uterus. Both of these as we shall see more particularly later tend very markedly to predispose to Carcinoma from:-

(a.) the continuous inflammatory irritation
(b.) the excessive blood supply, as Carcinomata during their growth require a very large supply of blood.

(2.) The effect of Flexions.

Flexions of the Uterus are much more common in the human female, than in the lower mammals, this no doubt being partly due to the erect posture assumed by the human female. Monkeys (Macaques and Baboons) however living in confinement in this country are liable to Uterine flexions.* I am not aware

* See Transactions of Pathological Society. Vol. XXXVI

that these displacements have been demonstrated in any other mammal. The effects of flexions are the same as those described in speaking of the effects of the erect posture, only in an exaggerated degree. The bending of the uterus presses upon the bloodvessels, and in this way the blood is dammed back in the cervix, which is thus kept in a continual state of congestion and inflammatory irritation.

(3). <u>Advanced civilisation.</u>

It would not be difficult to shew that Cancer wherever it occurs is in all likelihood a disease of advanced civilisation. With reference to the uterus we have for example, tight-lacing: this tends to displace and congest the uterus and thus, as shewn in the previous two paragraphs, predisposes to the origin of Cancer. Then again on account of the inanely artificial

emotional and highly strung mode of life at the present time, all the vital powers are lowered and in a general way, the person is less able to resist the inroads of disease. Emotions too without a doubt play a most important part in the production of disease, and its effect in the production of Abdominal Cancer has been frequently remarked.

(4) Menstruation.

This leads to a periodical congestion of the uterus but so far as it itself is concerned, I do not think it has got much to do with the origin of Carcinoma. In combination with other affections however e.g. inflammation of the tissue of the cervix it may help a little. Further it has been shewn* that Macaques and Baboons menstruate after the same fashion as the human female, only not quite so regularly, yet they are

* see Gynaecological Journal Vol. II

not liable to Carcinoma of the Cervix.

(5.) Length of life.

This it is very possible may have something to do with the case, unless it can be shewn that tissue changes occur with greater rapidity in the case of the lower animals, than is the case with the human female.

It is a fact well known to Surgeons, and will be referred to again, that slight but more or less continuous irritation e.g. Chronic Inflammation affecting a tissue or organ for a period varying from 15 to 20 years, is very apt to develop into Cancer. It may take much longer but rarely requires less than 15 years. It is very possible therefore that few of the lower animals would live a sufficiently long time for Cancer to develop even although other things were favourable.

Here the vexed question at once presents itself:-

What is Cancer?

The word itself means but little and I believe has done a great deal of harm both to Pathologists and to the general Public - tying the hands of the one, and frightening the other to death. It would probably therefore be a great advantage were the word expelled from pathological literature.

A Cancer (=Carcinoma) is looked upon as an epithelial growth, possessing the power of invading neighbouring tissues and of reproducing itself in the form of secondary growths in other and distant parts. It thus consists of epithelial cells on the one hand and vascular connective tissue on the other. This connective tissue forms the framework or stroma in which the epithelial cells are embedded.

But what of the Adenomata? for the above description suits in almost every detail an Adenoma as well as a Carcinoma — the build in both cases conforming in histological details to the type of a secreting gland. Where then is the difference? In many cases it is so ill marked that it is impossible for the most experienced pathologist and microscopist to say with certainty whether a given specimen is an "Adenoma" or a "Carcinoma" In malignant tumours of all kinds there is a great broad general principle viz: That the more any given tumour differs from the normal tissues, the more malignant will it be, and conversely, the nearer it approaches in structure normal tissues, the less malignant it will be. As an example of this take Myeloid Sarcoma starting in the cancellated tissue at the extremity of a long bone; of all the Sarcomata it departs least from

the normal type of tissue, and it is a well known fact that it is the least malignant of all the Sarcomata. Take again also Malignant Adenoma of the Intestine: this in many cases probably begins in a Simple Adenoma, and under the microscope it is almost impossible to distinguish the two. It again is by no means a very malignant growth and probably would be a long time in causing death were it not for the fact that it mechanically produces Obstruction of the Bowels. So it is with an Adenoma: the less perfectly it resembles a gland the more likely is it to shew Malignant properties and of course when it does so, it would then be called Carcinoma. Hence the Adenomata and Carcinomata have a common feature in the possession of epithelium, disposed in a more or less definite manner in Alveoli of Vascular Connective

tissue. But in a simple Adenoma the Alveoli are distinct from each other, whereas in Carcinoma, they form an intercommunicating series. Other points of resemblance between Adenomata and Carcinomata consist in the fact, that both arise in parts, where glands are usually present, and that warmth, seclusion and moisture favour their growth and development. For these reasons many pathologists, among whom we may specially mention, Mr. J. Bland Sutton of London, use the term "Carcinoma" as synonymous with "Malignant Adenoma".* This view has much to recommend it especially when dealing with Carcinoma of the Cervix Uteri.

It will be remembered that in the foetus glands are developed from downgrowths of solid rods of epithelium, from the epithelium covering the surface; these rods then become hollow and the peripheral epithelium

* Erasmus Wilson Lectures for 1890.

disposed in a regular manner upon the Vascular Connective Tissue. Carcinomata probably originate in a somewhat similar manner and differ from Adenomata in the fact that the differentiation is not carried to the same extent as in Adenomata — that is in Carcinomata the Acini, instead of being lined by one regular and well disposed layer of cells, may be filled with several rows of ill formed and irregularly and evil-disposed epithelial cells.

What I wish specially to shew in the foregoing paragraphs, is the close relationship between ~~the~~ Carcinomata and the normal processes of tissue growth and gland development. Now there must be a time when this normal and healthy process just <u>begins</u> to pass into the Cancerous development and the great duty of the Physician or Surgeon is to find out this time, for our

great work should be to oppose the <u>beginnings</u> of disease. It would seem therefore that in examining a Carcinoma with the microscope, there is nothing in the tissue <u>itself</u> that would indicate Malignancy or evil disposition. It consists of ordinary tissues— epithelium and connective tissue and blood Vessels— but the great evil seems to consist in time and place — the growth growing at a time when it should not grow, and the elements being in a place where they should not be.

What forms of Carcinomata attack the Cervix?

I Carcinoma of the portio vaginalis is, as one would naturally have expected from the nature of the surface in which it originates, Squamous epithelioma. This form has been specially investigated by Dr. John Williams in his work on "Cancer of the Uterus" being the Harveian Lectures for 1886. In these lectures he describes eight cases of Cancer of the portio vaginalis out of a total of twenty seven cases of Cancer of the Cervix. Now this proportion though by no means large, yet is far larger than one would have been led to expect from previous investigations on the same subject. Still Carcinoma beginning in this part of the Cervix is not by any means so common as Cancer of the Cervix proper; it is however common enough to find this part involved secondarily to

Cancer of the other part of the cervix, the disease not originating in the portio vaginalis.

The Clinical history and Course of this form of Carcinoma are quite different from that of the form beginning in the Cervix proper. According to Dr. Williams this form does not extend deeply but spreads in a superficial manner and does not invade to any extent the cellular tissue. Hence there may be an absence of any distinct feeling of thickening. Further the lines of growth are not towards the cavity of the uterus nor cervical canal, but outwards and downwards towards the vagina. It creeps along the surface of the vaginal walls, hence as a rule does not cause thickening of the broad ligaments and the Cervix is <u>not fixed</u> to any extent. Again this form of Carcinoma appears much more frequently

during menstrual life than after the menopause. Lastly its duration though doubtful is probably as a rule many years. It does not involve the glands early and seems to kill but very slowly. The fact of its superficial nature and the little tendency it shews to involve deeper structures or produce secondary growths together with this other fact that it tends to grow away from the uterus are points of considerable importance when considering the question of operative interference.

II. Carcinoma of the Cervix proper

is quite different from that of the portio vaginalis. It resembles Columnar epithelioma or Adenoid Cancer and as I have already stated, may be regarded as a true Malignant Adenoma. Its relation to the so called "erosions" will be more fully discussed in the next section.

"The starting-point of Cancer of the "cervix is in, so far as I have seen, "the cervical glands. I have seen "no clear instance in which the disease "originated in the epithelium of the "surface" (Williams).

"The favourite starting-point appears to be the lower half of the cervix (the favourite situation for "erosions"). Occasionally however it begins near the inner orifice. Further it seems to "shew preference for the posterior rather than the anterior lip of the uterus" (Williams)

The growth soon involves the whole

thickness of the lip and also soon invades the cellular tissue around. When once it reaches the peri-uterine cellular tissue, it seems to grow very rapidly: it rarely passes the internal os, and thus but rarely attacks the body of the uterus.
The mode of growth and the direction it takes, make surgical treatment all but impossible and hopeless. It soon involves the whole of the cervical wall in its length and thickness and rapidly infiltrates the peri-uterine tissue.
"So that the lines of growth of Cancer
"of the Cervix are mainly outwards
"and downwards, in such a direction
"as to involve the portio vaginalis,
"and the vesico-vaginal and recto-
"vaginal septa, but respecting the
"mucous membrane of the vagina."
(Williams.)
This form of Carcinoma is most common after the Menopause — or during the ten years, in the course

of which the Menopause generally occurs.

It will be interesting now to contrast the two forms of Cancer attacking the Cervix.

(See Table next page)

Table contrasting
Cancer of the Portio Vaginalis
with that occurring in
the Cervix proper:—

Cancer of the Cervix

	Portio Vaginalis-	Cervix proper.
1. Form of Cancer.	Squamous Epithelioma	Columnar celled Epithelioma- Adenoid Cancer, or True Malignant Adenoma
2. Origin & Spread.	Begins on the surface and does not extend deeply and rarely involves the Cellular tissue.	Begins deeply in the glands of the Cervix, tends to spread deeply into the cellular tissue & also involve the whole thickness of the lip, as well as the peri-uterine tissues.
3. Direction of growth	Not towards the cavity of the Cervical Canal, but outwards & downwards towards the Vagina & creeps along the surface of the Vaginal Walls. Cervix remains movable.	Involves the whole Cervix & peri-uterine tissue; also spreads to the portio vaginalis, the Vesico-vaginal, & recto-vaginal septa, but does not affect the mucous membrane of the Vagina. Cervix soon fixed.
4. Age of patient	Appears much more frequently during Menstrual life	Appears much more frequently after the Menopause
5. Prognosis as to length of life	Comparatively slow growth and patient may live for years.	Usually rapid growth, especially after it spreads to the Cellular tissue, and rapidly fatal.
6. Prospect of Surgical Cure.	Fairly good and hopeful	All but impossible and hopeless.
7. Part affected.	No preference for either lip of cervix, but most often spreads along Anterior Vaginal Wall.	Shews preference for the posterior lip.
8. Frequency.	Comparatively rare.	Very common: more common than at any other part of the uterus.

Another question now naturally arises, viz:-
Why is Cancer of the Cervix so common?

The rough and ready answer will usually be given that it is due to irritation. Very true but the word is such a wide and indefinite one that without further explanation it means nothing.
No doubt irritation, as usually understood does give rise to Cancer; e.g. the irritation of a clay pipe producing Squamous epithelioma of the lip. In the case of the Cervix therefore one would a priori have expected Squamous Epithelioma of the Vaginal portion as a result of irritation. But this form of Malignant disease is the least common form found present in the Cervix.
What then is the irritation that gives rise to Cancer of the Cervix proper, (not including the Portio Vaginalis)?
It is I believe Chronic Inflammation.
Now observe it is not Chronic Inflammation plus irritation but the Chronic inflammation, is itself the irritation,

and this long continued Chronic inflammation is without a doubt the cause of the Cancerous growth. It may seem at first sight that Chronic Inflammation and Cancer can have but little in common, but Clinically the difference is not so great as it seems, as witness the great difficulty in diagnosing between Chronic Inflammation of the Breast near the Menopause and Cancer. Both infiltrate their surroundings; in both the glands are enlarged; both produce a fibrous Stroma, infiltrated with cells, which fibrous stroma tends to contract and both are probably due to the growth of some special form of micro-organism. Again glance for a moment at Tertiary Syphilis of the Tongue. This chronic Syphilitic Inflammation of the tongue is only too well known by Surgeons to have a very intimate association with epithelial Cancer of the same organ. Indeed Cancer

of the tongue is becoming more common just because Syphilis is more common. Now what possible relationship can there be between Chronic syphilitic Inflammation and Cancer? It is simply that the Chronic Inflammation acts as the irritant that leads to the irregular and perverted growth or "open rebellion" of the epithelial cells. Cure Syphilis of the Tongue quickly and there is no fear whatever of its ever passing into Epithelioma. But leave it alone for 10 or 20 years or treat it with irritating and useless applications at various periods and for various lengths of time and it is certain to develop into Cancer.

Again take a Chronic ulcer or a scar in the palm of a working man's hand. Cicatricial tissue is weak, easily breaks down under any rough usage and forms a Chronic ulcer; the patient rests his hand

for a little time, the ulcer heals; then he works again, and again the ulcer forms, and so on for years, till at last an epithelioma forms. The epithelial cells have done their very best to heal the ulcer but at length they lose patience, throw off the controlling influence and strike out on their own account, or as Paget expresses it, break out into open rebellion and spread destruction around them.

Thus it is with the Cervix Uteri. The long continued Chronic Inflammation and Congestion lead on surely to Cancer. This too gains support from the fact that the posterior lip is the part more frequently attacked as from the more common forms of Flexions and Versions this part is more likely to be Chronically Congested and inflamed.

Heredity, according to Dr. Williams, plays no part in the origin of Cancer of the Cervix; nor does he find that lacerations have anything to do with it either, contrary to the usually received opinion — hence the uselessness of Emmet's Operation as a means of preventing the disease. Indeed is it not more likely to cause it from the irritation of the needle punctures and satures, for one often sees new growths start at needle punctures at the edges of wounds.?

We must look for a moment now at the possible influence of "erosions" of the Cervix on the development of Cancer. Many names have been given to this condition e.g. Ulceration, Abrasion or Erosion of the os uteri. As a matter of fact however it is none of these but, according to the researches of Ruge and Veit, is really an

Adenoid growth. There is no loss of tissue and the surface is covered by epithelium, but it is epithelium of the Columnar kind. The Columnar epithelium has encroached upon the territory of the Squamous and displaced it. It is an extension of the mucous membrane of the Cervical Canal with its glands through the external orifice on to the lips of the os. The part that should be covered by stratified Squamous epithelium and contain no glands but only mucous crypts, is now replaced by the Columnar epithelium and racemose glands of the Cervical Canal. The glands in the erosion in fact are much more numerous and more complex than in the ordinary canal of the Cervix. Under the Microscope the resemblance to Cancer is usually very great; the differences being that in Cancer the glands are less perfectly formed and the Acini instead of being lined

with a regular peripheral layer of cells as in the erosion are often filled with rows of cll formed cells — the cells often having several nuclei and vacuoles, or presenting other aberrant forms. The resemblance however to Cancer is very great and still more so when the surrounding Stroma is looked at, for in the erosion, just as in Cancer, it is infiltrated with numerous small round cells and nuclei.

I have already pointed out the possible part that Flexions play in the production of Carcinoma. The various stages seem to me to be something like the following:—

1st Stage. Uterus acutely flexed, Cervix becomes congested and inflamed.

2nd Stage. Chronic Inflammation lasting, gives rise to the so called "erosion".

3rd Stage. Chronic erosion passes into Carcinoma of the Cervix (Malignant Adenoma)

Now if this be the case, we ought as soon as possible to put the first stage to rights, for it is the long continuance of the condition that does all the harm.

Here also I think I ought to add a word of warning - If a chronic erosion can or does often pass into Carcinoma (of which there can be little doubt) then the practice of applying irritating applications for the purpose of healing the so called Ulceration ought to be most rigorously condemned. A woman comes perhaps for years to a practitioner, or goes from one to another, who treats the os uteri with various irritating applications according to the special view he takes of the pathology and treatment of the erosions. What is the result? The life-history of the erosion is hurried on to the stage of Cancer by the irritating applications - a

stage it might never have reached, had it not been for these applications, but a stage it must reach provided these irritating applications are persisted in. It would be sad indeed were there any grounds for believing that Carcinoma of the Cervix is so very common just because of this very habit. This question is worthy of most careful consideration.

But we have other examples of simple Adenoma taking on Malignant Action. Take a case of a simple Adenoma of the Breast of a young woman. So apt is it, if allowed to remain, to by and bye take on Malignant action that Surgeons at once advise its removal.

Or again, Simple Adenoma of the Rectum becoming a Columnar celled Epithelioma.

An interesting relation may I think be traced between Cancer of the Breast and Cancer of the Cervix.

In the Breast we meet with Paget's disease of the nipple leading on to Cancer of the Breast, and in the same way we meet with erosions of the Os uteri (or more properly Adenomata) leading on to Cancer of the Cervix. Paget's disease of the nipple probably begins in Chronic Inflammation or Catarrh of the Milk ducts, and corresponds to the growth of erosions on the Os Uteri. It may also assume a papillary or polypoid form just as we often find in Adenomata of the Cervix. Paget's disease will be referred to again.

Why is Carcinoma of the Cervix so rapidly fatal?

Its rapidly fatal character is due I believe to its environment.

The very same conditions that have been found to favour the growth and development of glands in general are found to favour the growth of Cancer, viz:- Seclusion, Warmth and Moisture.

If we take Cancer of the Tongue and Epithelioma of the Lip we see these points well brought out. Cancer of the tongue, if left alone, is rapidly fatal, and the glands become very quickly affected probably because of the heat, the moisture and the movement of the organ. This contrasts very markedly with the slow spread and the late involvement of the glands as seen in Epithelioma of the lip. The lip is not secluded, it is exposed to the cool air, and it is not specially moist.

Why is Carcinoma of the Cervix chiefly found after the Menopause?

But why should Cancer of the Cervix arise so frequently during the course of the ten years in which the Menopause usually occurs?

It is a well known fact that Cancers in their growth require a very large supply of blood and that they always grow towards the chief blood supply. It is possible that during Menstrual life, the blood being used for another purpose, there is not supply enough to start the growth & feed the development of Cancer, but when the Menstrual flow has ceased then all the blood that would have been lost in Menstruation can now be used for the development of the Cancerous growth.

Before closing this clinical study on Carcinoma of the Cervix Uteri I would like to consider for a little the possible Microbic origin of Cancer.

Many objections have been urged to this theory:-

(1). If it has a Microbic origin it is said it ought to be contagious; Well, and very possibly it is. Two examples must suffice. Cases are occasionally met with by the surgeon where the husband has Epithelioma of the Penis and the wife Carcinoma of the Cervix Uteri. This ofcourse may admit of other explanations, but to say the very least, it points very strongly towards the contagious Nature of Cancer.

Again take an Epithelioma of one Labium, and then at the place where the Cancerous spot touches the other Labium, it is by no means uncommon to find a Cancer-

ous growth beginning - the spread not being due to the continuity of tissue for the two growths are and remain quite distinct. This also we think furnishes fairly strong proof of the contagious nature of Cancer.

(2). Another objection urged is that it is entirely the result of local irritation, and that therefore it is not likely to be due to a Microbe. That is quite true but the local irritation may only serve to prepare the soil and fit it as a proper midus for the growth of the micro-organisms.

Take for example Acute Necrosis in a young boy, which is undoubtedly Microbic. The Microbes circulating in the blood are powerless to exert their evil effects till some slight injury such as a blow or a wrench has prepared the soil for them.

The same is true of Ulcerative Endocarditis, the Microbes in the blood are powerless till the inflammation of the Cusps of the Valves of the heart has prepared a fit nidus for them. In both the above examples the patients will die of Pyaemia if the disease be not checked. This form of Pyaemia used to be called "Idiopathic" because we did not know better. Hence we require two things and the one just as much as the other, the fitting soil and the presence of the Micro-organisms.

(3). A third objection to the Microbic theory is — that if it is Microbic in origin, <u>how is it that it is hereditary</u>.

In the first place the Heredity of Cancer is more than doubtful and according to Dr. Williams in Cancer of the Cervix there is no proof submitted in support of its hereditary character.

But grant that it is hereditary, it is not nearly so hereditary as Tubercle or Syphilis and those diseases are by almost universal consent (especially the former) allowed to be due to the growth of micro-organisms. It is not the microbes that are handed down, but only the soil specially fitted for the growth of special forms of micro-organisms. And here let me point out how very easy it is to cure both Tubercle and Syphilis if they be taken in time. Both are very curable and if that be so why should not Cancer also be, if we could only take it in time.

Tubercular disease so easily cured by Rest
Syphilis " " Grey powder

But the corresponding therapeutic agent so far as Cancer is concerned has yet to be found, although Mr Clay believes he has found such an agent in Chian Turpentine.

In support of the Microbic theory let me refer once more to Paget's disease of the nipple. I have already stated that the same relation appears to me to exist between Paget's disease of the nipple and Scirrhus of the Mamma, as that existing between an "erosion" of the Os uteri and Carcinoma of the Cervix.

Paget's disease has more recently received the name of "Malignant Papillary dermatitis," and may form a small raspberry-like projection corresponding to the Papillary growths assumed by some forms of Cancer of the Cervix.

Excerpt from the British Medical Journal
Vol. I 1889. Page 1254.

"M. Darier, from recent observations, has been led to conclude that Paget's disease of the nipple is a new form of Cutaneous Psorospermosis. Paget's disease is distinguished from ordinary

eczema by the fact that it is limited by a well-marked edge, and that the skin becomes parchment-like. The affection is incurable, and is invariably followed by Cancer. M. Darier examined epidermic scales taken from the affected parts, and mixed them with water or potassium iodide, or macerated them in diluted ammonium or bichromate of Ammonium. He detected among the epithelial cells and in their interior round bodies surrounded by a double-edged membrane. The diameter of these bodies was equal to, or greater than, that of the cells; their membrane contained a single mass of protoplasm or globules. They were invariably present in all the sections of the pieces of skin excised, in every layer of the epidermis, and especially in the glandulae of the skin. These bodies were undeniably psorosperniae or conidia. Epithelioma of the nipple contained similar parasites in the beds, and a number of elements,

usually enclosed in other cells. It is well known that the presence of these organisms in an epithelial tissue determines the budding of this tissue. Cases of epithelioma containing Conidia in their buds have more than once been recorded. M. Darier considers it clear that Paget's disease of the nipple is caused by these parasites, which determine the budding of the galactophorous ducts."

The psorospermiae belong to the Protozoa and as seen from the above description usually live in the cells and cause them to proliferate, burst through the basement membrane and spread into the surrounding tissues.

Still more recently Mr. Jonathan Hutchinson Jun. has corroborated the above statements :- (see next page).

Excerpt from the Brit. Med. Journal.
Vol I. 1890 page 664. (Mar. 22nd)

"Mr. J. Hutchinson, Jr., showed (at the Pathological Society of London, Mar. 18th. 1890) specimens illustrating the presence, in what was known as "Paget's disease", or Eczema of the breast, of psoro-sperms or coccidia. The parasites, of oval or rounded shape, and one-thirtieth of a millimètre in length, were found in the thin layer of epithelium which covered the floriid surface of the diseased patch of skin. Each coccidium had a shell which in sections gave it the appearance of a double contour or outline. Often a small knot or aperture at one end, the micropyle could be distinguished. In the interior one, a more granular and globose mass could be seen, and sometimes the psorosperms might be made out. In the Coccidium oviforme of Leuchart, each Coccidium developed four psorosperms inside the shell,

which subsequently became free. Mr. Hutchinson believed that he had detected these amongst the epithelial cells. The case from which the specimens were obtained was a woman, aged 46, who for four years had had a patch of inveterate eczema round the nipple, measuring four inches in diameter. The development of a scirrhous tumour in the breast led to the removal of the latter. M. Darier, who discovered the parasites in cases of Paget's disease in 1889, pointed out that the easiest method of demonstrating them was to scrape the surface, and treat the scraping with iodine solution or bichromate of Potash. The best way, according to Mr. Hutchinson, was to soak the scraped epithelium with liquor potassae, and to mount it in glycerine jelly. By this means the coccidia were differentiated, and their number could be estimated by using a five-eighths inch power; as

many as 100 Coccidia were counted in a single field."

Another point that seems to me to favour the microbic view of the origin of Cancer is the profound Cachexia and the low adynamic febrile condition produced when the disease runs its course unchecked — a condition not at all unlike that we meet with in Chronic forms of Blood poisoning, which are undoubtedly due to the presence of micro-organisms.

The question of the Microbic origin of Cancer is however still in its infancy, but nevertheless these above points are well worthy being kept in mind. If Paget's disease be parasitic it thus seems to be dependent on the growth of an <u>Animal</u> parasite in the superficial layer of the skin —

the parasite belonging to the very lowest group in the Animal Kingdom, whereas most of the as yet known micro-organisms are believed to belong to the Vegetable Kingdom.