# THE LYMPHATIC SYSTEM

## (WITH SPECIAL EMPHASIS ON ITS IMPORTANCE IN GYNAECOLOGY)

HERMAN A. VAN COEVERDEN DE GROOT, M.B., CH.B. (CAPE TOWN), *Registrar, Division of Obstetrics and Gynaecology, University of Cape Town and Cape Provincial Administration*

The lymphatic system is all-important as a generalized structure with fine ramifications, collecting fluid throughout the body, sifting the contents in its manifold nodes, and passing the purified material, via a large duct, back into the blood stream. The importance of this system has gradually dawned upon medical men. In gynaecology attention is usually focused upon it once genital cancer is diagnosed. It was therefore deemed necessary to study the literature in its broadest aspects and to review the subject, ranging from basic sciences to clinical concepts. A clear understanding of problems as they affect the modern gynaecologist can only be attained by a thorough understanding of embryology, anatomy, physiology and pathology.

### EMBRYOLOGY

Three theories are current regarding the origin of the lymphatic system.

1. Sabin[37] was the first (1902) to study the development of the mammalian lymphatic system. He maintained that lymphatics arise as capillary offshoots from the endothelial lining of veins at special points. Lewis[27] agreed, but stated that these outgrowths occurred at many points in the venous system. The lymphatic capillaries coalesce into plexuses, which later lose connection with the venous system. The plexuses become confluent to form the lymph sacs.

2. Huntington and McClure [17] and others suggested that lymphatic spaces occur as clefts in the primitive mesenchyme. The lining cells of the clefts take on the characteristics of endothelium. These spaces form plexuses which become confluent as lymph sacs. Connections with the venous system occur as a secondary phenomenon only. The balance of evidence seems to favour this theory.

3. Clark[6] concluded that lymphatics and mesenchymal cells grew independently and that there was no conversion from mesenchyme to lymphatic endothelium.

Kampmeier[21] demonstrated valves in the main lymphatic trunks of the human embryo by the end of the second month, indicating that lymphatic circulation is already functional by that time. Lymphatics are easily identified in embryos of 2 - 4 months as thin-walled vessels.

Yoffey and Courtice[40] stated that growth of embryonic lymphatics is by endothelial budding in a centrifugal fashion.

The lymph sacs are 6 in number (Sabin mentioned 5 sacs). There are 2 paired and 2 unpaired sacs. The paired jugular sacs appear at 7 weeks, lateral to the internal jugular veins. The paired posterior lymph sacs arise in the region of the common iliac veins at the end of the second month. The unpaired retroperitoneal sac develops at the root of the mesentery near the adrenal glands at about 2 months, and at the same time the other unpaired sac, the cisterna chyli, arises opposite the third and fourth lumbar vertebrae.

From these sacs lymph vessels bud out along the paths of the embryonic blood vessels. Whether or not lymphatics arise *de novo* to link with existing vessels is not completely clear. Sabin stated that the thoracic duct is formed by anastomosing outgrowths from the jugular sac and the cisterna chyli. All the sacs except for the upper part of the cisterna chyli are later divided up by connective tissue bridges and are invaded by lymphocytes. They break up into chains of lymph nodes with the lymph sinuses representing portions of the original sac cavity. Gulland,[12] quoted by Reiffenstuhl,[36] maintained that lymph nodes develop from connective tissue condensations around capillaries. Lymphocytes are trapped in the meshes, and the displaced connective tissue forms the capsule of the node.

Hellman[13] divided lymph nodes into primary and secondary groups. The primary nodes appear during the third month of foetal life as the lymph sacs break down. Secondary nodes develop later along the paths of the lymphatics arising from these primary centres. Gilmour[9] demonstrated lymphocytes in the blood and lymphocyte formation in connective tissue as early as the eighth week. After the development of the lymph nodes and spleen they become much more abundant.

### ANATOMY

The lymphatic system is only found in the higher mammals. It developed when the increasing arterial pressure resulted in fluid being forced out of the capillaries, necessitating an additional system besides the veins to carry this fluid away.

Herophilus (300 - 250 BC) was one of the first to describe the small nodules 'along the course of the large blood vessels'. The name 'gland' was attacked by Toldt (1895) at a meeting of the German Anatomical Society. He suggested the term 'lymph node', but even today the two names are used concomitantly.

Towards the end of the last century most of the pelvic nodes were described. In 1904 Toldt and Kroemer added the sacral and parametrial nodes.

Basically the lymph drainage of the pelvis is in 3 directions. A *vertical chain* connects the superficial inguinal with the lateral aortic nodes. A *horizontal chain* runs from the pelvic organs in the midline of the body laterally on either side to join the vertical chain. A *posterior chain* runs towards the sacral nodes and thence upwards to the lateral aortic group (Fig. 1).

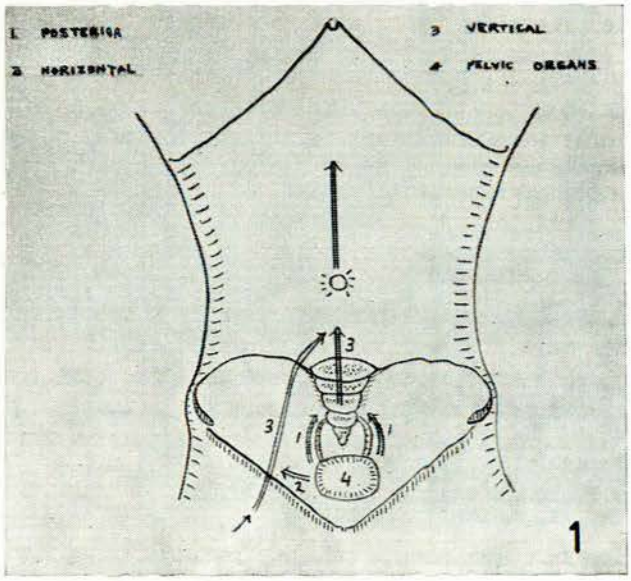


*Fig. 1.* Basic lymph drainage of pelvic organs.

The generalized and remarkable anastomoses between the different lymphatic systems in the pelvis almost defy description of pathways of drainage for the different organs. To add to the confusion, certain nodes may be by-

passed and the lymph may drain to nodes higher up along the chain. Where lymph nodes are blocked, such as in metastatic carcinoma, retrograde spread results in bizarre patterns of lymph-node involvement.

*The Vulva*

Parry-Jones[33] has shown by injection studies before operation that a superficial and a deep lymphatic network are present which communicate freely. The networks are very diffuse covering the whole vulva except the lateral aspect of the labia majora. Here the collecting trunks form. Those from the posterior parts of the vulva run transversely to the superficial inguinal nodes. From the anterior part they run upwards onto the mons veneris and then laterally to the same group of nodes.

The lymph from the vulva does not reach the thigh even when the lymphatics are blocked.

A direct link exists between the clitoris and Cloquet's node in the deep femoral group.

There are 12 - 20 *superficial inguinal nodes*. They lie along and slightly below the inguinal ligament. They anastomose freely with the *subinguinal* or *superficial femoral group* which are clustered around the long saphenous vein just before it passes through the fossa ovalis. The efferent vessels of these two groups pass with the femoral vessels to the *deep femoral group* supposedly consisting of 3 nodes. Way,[39] in over 200 dissections, found only 1 lymph node at the upper end of the femoral canal — the node of Cloquet or Rosenmuller. Its upper pole projects under the inguinal ligament into the pelvis.

Anatomists describe this node at the bottom of the femoral canal, presumably owing to the fact that the tissues of the cadaver have shrivelled up in the process of preservation. Cloquet's node is the central point to which all the lymphatics of the lower limb and most of those from the vulva drain.

From here the drainage is to the *external iliac group*, consisting of 8 - 10 nodes. These are arranged in 3 groups, the most important of which is the medial one. The *medial group* consists of a single chain of up to 6 very large nodes lying inferomedial to the external iliac vein. In surgical removal the vein has therefore to be lifted up before these nodes are exposed. The external iliac nodes receive drainage from the inguinal nodes, the lower abdominal wall, the clitoris, the fundus of the bladder, the cervix, and the upper vagina.

The next step is to the important *bifurcation* or *inter-iliac* nodes at the bifurcation of the common iliac artery.

From here drainage is mostly underneath the common iliac vein to the *common iliac nodes*, which are 4 - 6 in number, lying behind and on the sides of the common iliac artery. The efferent vessels drain to the *lateral aortic* or *para-aortic nodes* along the abdominal aorta. The efferents from the lateral aortic nodes anastomose around the aorta with the *pre-* and *retro-aortic* groups. On either side of the aorta they also form the *lumbar lymphatic trunk* which empties into the *cisterna chyli*. From the cisterna chyli the *thoracic duct* runs up into the chest and neck to enter the venous system at the junction of the left internal jugular vein and the left subclavian vein (Fig. 2).

*The Vagina*

The part below the hymen has the same drainage as the vulva. The rest of the vaginal lymphatics drain to the same nodes as the cervix and will be described below. There is free anastomosis with the lymphatics of the rectum, cervix and vulva, as well as between the upper and lower portions of the vagina (Fig. 3).

*The Cervix*

Javer[20] divides the cervix into an upper and a lower portion by a transverse line drawn through the middle of the cervix at the attachment of the vagina. This line is only anatomically of any use since no such demarcation exists physiologically or pathologically, owing to the extremely rich anastomoses of the lymph vessels.

The upper part drains into a vertical trunk on each side of the uterus—*la voie principale*—of Leveuf and Godard.[26] Each trunk continues along the ureter and the uterine artery to *la ganglion principale* or the inter-iliac node of Leitch.[24] The lower part, after anastomosing with vessels from the upper vagina, drains along the utero-sacral ligaments to the *lateral sacral nodes*.[32]

Accessory channels lead from the upper cervix to the so-called *hypogastric chain* — the *ureteral, parametrial,*

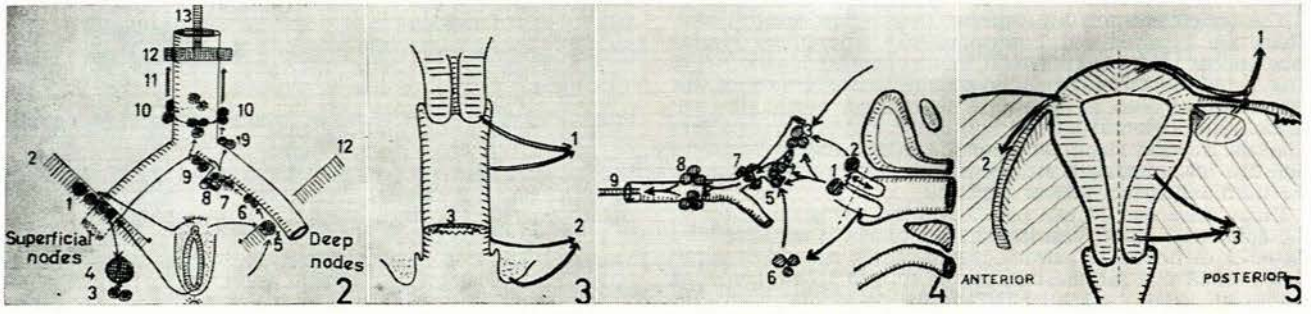


*Fig. 2.* Lymph drainage of vulva. 1=Superficial inguinal nodes. 2=Inguinal ligament. 3=Subinguinal nodes. 4=Fossa ovalis. 5=Deep femoral nodes. 6=External iliac nodes. 7=Interiliac nodes. 8=Hypogastric nodes. 9=Common iliac nodes. 10=Para-aortic nodes. 11=Lumbar lymphatic trunk. 12=Cisterna chyli. 13=Thoracic duct.
*Fig. 3.* Lymph drainage of vagina. 1=Drainage with cervical lymphatics. 2=Drainage with vulval lymphatics. 3=Hymen.
*Fig. 4.* Sagittal section of cervical lymph drainage. 1=Ureteral node. 2=Parametrial nodes. 3=External iliac nodes. 4=Interiliac nodes. 5=Hypogastric nodes. 6=Lateral sacral nodes. 7=Common iliac nodes. 8=Para-aortic nodes. 9=Cisterna chyli and thoracic duct.
*Fig. 5.* Lymph drainage of uterus. 1=Drainage with ovarian lymphatics. 2=Drainage with round ligament lymphatics. 3=Drainage with cervical ligaments.

*hypogastric* (or *internal iliac*) and *obturator nodes*. The ureteral node lies above the uterine artery where it crosses the ureter. Occasionally there are 2 nodes. The internal iliac nodes number 6 - 8 and lie along the internal iliac vein near its junction with the external iliac vein. The obturator node of Leveuf lies near the hypogastric group. Herman *et al.*[15] have shown by lymphography that the obturator node is the middle one of the medial group of the external iliac chain, lying between the external iliac vein and the obturator nerve in the 'obturator fossa'. It must not be confused with the obturator node of the anatomists, which lies in the obturator canal much lower down. The internal iliac nodes receive afferents from all pelvic viscera and the deeper parts of the perineum.

The parametrial and ureteral nodes are seldom involved in Stage 2 carcinoma of the cervix, yet the parametria frequently appear clinically affected. Parametrial oedema occurs early, but actual involvement by carcinoma takes place after the higher nodes have become involved by retrograde spread aided by gravity drainage in the erect posture.

The common iliac and obturator nodes are called *sentinel nodes* by Javert. They are most commonly affected in metastases from cancer of the cervix. Brunschwig[3] found nodal involvement in 33% of 426 cases at operation. The nodes most commonly affected were the obturator, the external iliac and the internal iliac groups, in that order. He also found the ureteral and parametrial nodes least often involved.

Meigs,[30] Javert,[20] Henriksen,[14] and many others have stressed the discrepancy between the clinical staging of cervical carcinoma and the actual findings at operation. Some surgeons perform 'selective lymphadenectomy' for biopsy purposes, selecting the sentinel nodes. This is of value in prognosis.

Posteriorly, the cervical lymphatics do not cross the rectovaginal fascia, but bypass the rectum to the lateral sacral nodes, the posterior component of the internal iliac group. Hence rectal involvement in carcinoma of the cervix is uncommon. Leitch found rectal invasion in 25% of nearly 1,000 postmortem examinations in cases of cancer of the cervix, and recto-vaginal fistulae in 16%.

Anteriorly, lymph channels connect the cervix with the base of the bladder, and direct extension occurs also to the vesico-vaginal septum. Javert noted bladder involvement in 53% of 106 cases of cancer of the cervix at operation. Leitch recorded an incidence of 66% with vesico-vaginal fistulae in 44% in his postmortem series (Fig. 4).

Crichton[7] found inguinal lymph-node involvement in patients suffering from cervical cancer.

*The Uterus*

The lymphatics of the body drain with those of the cervix.[28] The fundal vessels run with those of the ovary. Along the round ligament drainage occurs towards the *deep inguinal nodes* in the inguinal canal (Fig. 5). Free communication exists between these systems. The importance of lymph-node involvement in endometrial cancer has been stressed by Louw.[28] The lymph drainage does not seem to depend upon the site of the cancer.

*The Ovary and the Fallopian Tube*

Since the ovary develops in the region of the kidney, it drains to the para-aortic nodes in the region of the renal artery, following the course of the ovarian vessels. There is free anastomosis with the iliac and obturator nodes via the broad ligament and along the round ligament with the nodes in the groin. Lastly, by means of the tubal lymphatics, communication exists with the fundus uteri and the opposite tube and ovary.

The Fallopian tube drains to the lateral aortic nodes (Fig. 6).

*The Bladder, the Ureter and the Urethra*

Nesselrod[32] and others injected newborns at autopsy and showed that the lymph drainage of the bladder was essentially the same as for the cervix. There are no lymphatics in the bladder mucosa. This accounts for the rarity with which metastases are seen through the cystoscope. Bullous oedema suggests involvement by embolic occlusion of lymphatics in the deeper layers of the bladder wall. 'Gray',[10] however, mentions 3 plexuses in the bladder wall — a mucous, an intramuscular and an extramuscular one. The lymphatics run along the ureteral, vesical and uterine arteries to the external and internal iliac nodes.

The upper part of the ureter drains to the lateral aortic nodes, the middle part to the common iliac group, and the lower part to the common, external or internal iliac nodes.

The urethra drains mainly to the hypogastric nodes. A few vessels go to the external iliac group (Figs. 7 and 8).

*The Rectum*

Gerota[8] was the first to study the lymphatic drainage of the rectum. He described 6 - 7 *pararectal nodes* along the rectum on either side. They drain along the course of the superior haemorrhoidal artery to the *inferior mesenteric* and then to the lower para-aortic nodes.

Bacon and Nesselrod divide the lymph-drainage into upper and lower portions, divided by the dentate line. The superior portion drains to the pararectal nodes of Gerota. The inferior group drains to the inguinal nodes. Again free communication exists between the 2 systems.

'Gray'[10] states that the upper half or more of the rectum drains along the superior rectal veins to the pararectal nodes. From the lower half of the rectum and the anal canal above the muco-cutaneous junction, the lymph flows upwards along the middle rectal vessels to the internal iliac nodes. Below the muco-cutaneous junction the lymph drainage is to the anal margin and then laterally to the most medial of the superficial inguinal nodes.

Anastomoses occur along the columns of Morgagni. Parker has described a communication between the inguinal and the sacral nodes. Hence two possible pathways exist for metastases from the rectum to reach the inguinal nodes, viz.,

1. From the rectum via the pararectal nodes to the sacral nodes and thence to the inguinal nodes,
2. From the rectum via the anal canal to the inguinal nodes (Fig. 9).

*Relationships Between Lymphatic and Venous Systems*

Metastases reach the blood stream from the lymphatic system by the following routes:

1. By spread along the thoracic duct.

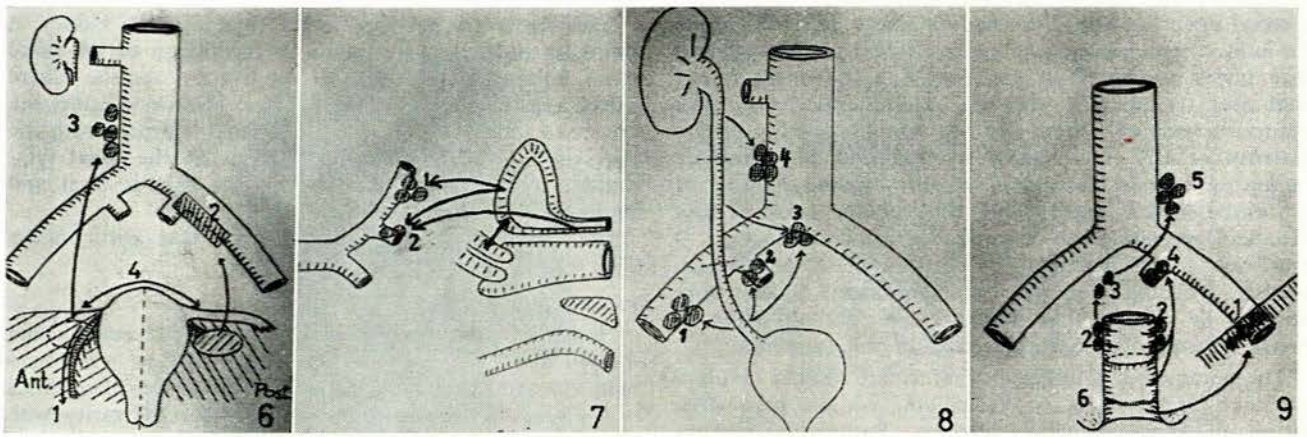


*Fig. 6.* Lymph drainage of ovary and tube. 1=Drainage with round ligament lymphatics. 2=Iliac group of nodes. 3=Para-aortic nodes. 4=Cross-drainage between ovaries. Ant.=Anterior. Post.=posterior.
*Fig. 7.* Lymph drainage of bladder and urethra. 1=External iliac nodes. 2=Hypogastric nodes.
*Fig. 8.* Lymph drainage of ureter. 1=External iliac nodes. 2=Hypogastric nodes. 3=Common iliac nodes. 4=Para-aortic nodes.
*Fig. 9.* Lymph drainage of rectum and anus. 1=Superficial inguinal nodes. 2=Pararectal nodes. 3=Superior mesenteric nodes. 4=Hypogastric nodes. 5=Para-aortic nodes. 6=Dentate line.

2. Some pelvic nodes contain large endothelial-lined blood sinuses which may be invaded from cancer deposits in the node.
3. Pick[34] described direct anastomoses between veins and lymphatics in adults. Pressman[35] demonstrated direct communication between lymph nodes and veins by injection studies.

## PHYSIOLOGY

Physiologically, lymph is the same as interstitial fluid, except for its low protein concentration. In the thoracic duct the protein concentration is 3 - 4 G/100 ml.

The movements of the lymph are governed by Starling's hypothesis. At the arterial end of the capillary the hydrostatic pressure of the blood is greater than that of the tissue fluid. The osmotic pressure of the blood proteins is greater than that of the tissue fluid. The resultant force drives fluid out of the capillary. At the venous end of the capillary there is a slight hydrostatic force outwards, with a greater osmotic force inwards, resulting in a force drawing fluid back into the capillary.[29]

The lymphatic system has the following functions:

1. It represents an *accessory route* by which fluids can flow from the interstitial spaces to the blood. Although the system carries only a fraction of the tissue fluid leaving the arterial end of the capillary, it has the very important property of being able to carry large protein molecules and even particulate matter. These substances cannot be re-absorbed through the endothelium of the venous end of the capillary. The endothelium of the lymphatic capillaries, however, is almost totally permeable and the only limitation as to which substances can be carried away is the size of the lymphatic vessel. Electron-microscopy studies have shown that the lymphatic endothelial cells overlap, with obvious holes through which the larger particles can enter the vessel.

2. It is one of the major channels for the *absorption of fat* from the gastro-intestinal tract. After a fatty meal the lymph in the thoracic duct may contain as much as 1 - 2% of fat.

3. The lymph nodes provide *filters* at strategic sites. The lymph percolating through the node is exposed to the phagocytic action of the reticulo-endothelial cells.

4. In the nodes are made 2 kinds of *blood cells* — lymphocytes and monocytes, as well as plasma cells, which normally do not enter the blood stream. The functions of lymphocytes are not well understood. Certain enzymes, such as some essential in the tricarboxylic acid cycle, have been demonstrated in lymphocytes. It is thought that on disintegration desoxyribonucleic acid is liberated and made available to fast-growing cells in the vicinity. Lymphocytes can become converted into monocytes and macrophages, thus aiding in phagocytosis. In the bone marrow they are converted into multipotential cells. It has for long been thought that lymphocytes produce antibodies. Electron-microscopy studies, however, showed a cytoplasmic architecture most unlikely in cells engaged in protein synthesis. They may well carry antibodies on their surfaces. There is also a possibility that somewhere along their evolution they may become converted into plasma cells.

Electron-microscopy studies have proved that plasma cells produce antibodies which are specific for a single antigen. The so-called rheumatoid factors are present in plasma cells of nodes and synovial membranes.

5. Lever[25] demonstrated *renin* in renal lymph. This was not present in lymph from other organs. Stenosis of the renal artery was usually followed by an increased output of renin from the ischaemic kidney. In the blood renin is so diluted that its detection is very difficult.

*Lymphatic absorption.* The nature of a substance injected into the skin or subcutaneous tissues determines its mode of absorption. Non-colloidal substances are mainly absorbed by direct diffusion into the blood capillaries, the flow through which is much faster than in the lymphatic system. Proteins, red cells and particulate matter are carried away by the lymphatics. Warming the skin, exercise or massage causes more lymphatics to be opened and the flow through them increases. This was shown by injecting dyes into the skin. Many 'streamers' of intradermal lymphatics radiating from the injection area became visible when the limb was massaged, while keeping the limb dependent inhibited the formation of streamers. In the leg conditions are favourable for the development of oedema, and this is confirmed by the paucity of streamers developing.

Peritoneal absorption of fluid is mainly via the lymphatics, and those of the diaphragm play a major role. It has been suggested that stomata may be present in the peritoneum where that is in close contact with lymphatic plexuses. Through these holes the larger particles could enter the lymphatics.

Ascites occurs most commonly in venous stasis, e.g. cardiac failure. It had always been thought that the back pressure in the portal system caused an accumulation of fluid in the tissues of the gastro-intestinal tract which then leaked into the peritoneal cavity. It has now been shown, however, that ascites is

liver-lymph. This was shown by Freeman and Hyatt and Smith.[18]

These workers constricted the inferior vena cava above the diaphragm. The venous pressure in the liver rose and thus less fluid was re-absorbed from the tissues, causing a flooding of the lymphatics. The excess liver extracellular fluid then literally oozed from the liver capsule. The increased venous pressure, indicative of generalized venous congestion, probably induces a reflex liberation of aldosterone, which, through sodium retention, also plays its part in the formation of oedema fluid.

### LYMPHATIC OBSTRUCTION

The small amount of protein in the tissue fluid can only leave the tissues in the lymph. A blocked lymph drainage results in continuously increased osmotic pressure in the tissues until the latter approximates the osmotic pressure of the blood. The resultant rise in tissue pressure causes rapid and severe oedema.

*Causes*

A. *Filariasis*. The larvae are transmitted by mosquitoes. They leave the capillaries and settle in the lymph nodes. They provoke an inflammatory response and block the lymphatic drainage from that area. Elephantiasis may result.

B. *Following radical surgery*. Lymphatic oedema is sometimes seen following radical mastectomy in the ipsilateral arm. The swelling usually subsides as new channels are formed.

*Histology*. Lymphatic tissue and myeloid tissue are the two subdivisions of the haemopoeietic system.

*Basic Structure*

Lymphatic tissue consists of a delicate network of reticular fibres. In it are dispersed the cells, some attached to the meshes, others lying loose in the network. The meshes are either closely or loosely knit or alternatively coarse or fine.

The mother cell is the (primitive) *reticular cell*. Its progeny forms two lines of cells. The first forms phagocytic cells, the reticulo-endothelial cells or macrophages which are usually attached to the reticular fibres. The second line consists of 'free' cells. The first 'free' cell formed is the haemocytoblast, usually called the lymphoblast. From the lymphoblast are formed lymphocytes, monocytes and plasma cells.

*Basic Unit*

This is called a Malpighian body or primary nodule. It is roughly spherical and from a few hundred microns to more than a millimeter in diameter. It is not encapsulated and from the edge cells are 'shed' into the surrounding tissue. In postnatal life the germinal centre or secondary nodule forms within the primary one. Here active formation of the cells takes place and consequently many mitotic figures are seen. The centre is paler than the periphery, owing to more abundant cytoplasm in the central cells.

Lymphatic tissue in the body is present in 3 arrangements:

1. Designed to filter tissue fluid. This occurs at sites where lymph is formed, and is chiefly seen underneath wet epithelial surfaces which are exposed to contamination from the outside. Hence we find this tissue below the mucosa of the gastro-intestinal tract and to a lesser extent the respiratory and genito-urinary tracts. Tissue fluid percolates through these nodules *en route* to the lymphatics. These nodules produce antibodies to possible antigens entering the body. Good examples are the tonsils and Peyer's patches.

2. Designed to filter lymph: These are, of course, the lymph nodes which are interspersed in the lymphatic channels of the body. They may be round, ovoid or bean-shaped. They vary in size from seeds to almonds. They are encapsulated by firm fibrous tissue, from which trabeculae enter the node, and the space in between the trabeculae is filled with the reticular network already described. Most of this is coarse. In the cortex are rounded areas of fine mesh containing lymphocytes — the primary nodules. From these medullary cords penetrate into the medulla forming an anastomosing pattern. The coarse mesh between the primary nodules and the capsule is called the subcapsular sinus. Afferent lymphatics penetrate the capsule along its convex border and enter the subcapsular sinus. The lymph filters through this sinus, in between the primary nodules and the medullary cords to enter efferent lymphatics which leave the node at the hilus.

Lymphatic nodules are not constant structures. Old ones disappear and others are formed throughout life. Germinal centres are not present at birth, and their presence or absence in later life depends on the state of activity of the node.

*Blood supply*. Arteries and veins enter and leave the node at the hilus. Branches are carried along the trabeculae. Arterioles leave the trabeculae and become ensheathed by condensed reticular tissue. They form capillaries which are especially abundant near the primary nodules. The venules enter the trabeculae and leave the node at the hilus.

3. Designed to filter blood:

A. Haemal nodes or haemal lymph nodes. These structures resemble lymph nodes. They are red or yellow instead of grey. Their mesh is either partly (haemal lymph node) or wholly filled with blood (haemal node).

B. Spleen.

### PATHOLOGY

**1. Congenital**

Kinmonth *et al.*[22] described congenital anomalies of lymphatics. These are: (A) Aplasia; (B) Hypoplasia — here fewer, attenuated lymphatics are found insufficient for drainage; and (C) 'Varicose' lymphatics — here the vessels are tortuous and dilated. Retrograde and lateral flow shows that the lymphatics are incompetent.

These anomalies are the cause of primary non-inflammatory lymphoedema.

Allen,[1] from the Mayo clinic, gave the following classification of lymphoedema:

*(A) Non-inflammatory*

*(i) Primary lymphoedema*, further divided by Kinmonth into (a) lymphoedema congenita; (b) lymphoedema praecox — by far the commonest — the onset of oedema is before the age of 35; and (c) lymphoedema tarda — the onset of the oedema is after the age of 35.

Of Kinmonth's 107 cases, 20% were familial and 2 congenital and familial (Milroy's disease). There was a very high (14%) incidence of associated other congenital anomalies. Of these, 50% were vascular, often very mild. The treatment was described by Charles[5] and consists of removal of the skin down to the muscle and full-thickness skin grafting.

*(ii) Secondary lymphoedema*. This is caused by (a) blockage of the lymphatics, and it arises after (b) radical mastectomy in the upper limb.

(*B*) *Inflammatory*

The causes will be given in the appropriate section. Inflammatory disease of the lymph nodes results in blockage of the lymphatic drainage of the area concerned. The lymphatics themselves may become involved in the inflammatory process (lymphangitis).

2. **Traumatic**

Of gynaecological importance are:

*A. X-rays.* These do not cause constant changes. Although fibrosis and hyalinization are seen, these features are also present in nodes outside the area of irradiation effect. The reticular cells are fairly resistant to radiation.

*B. Severing or crushing of the lymphatics.* The effect depends on the state of the collaterals. If these are inadequate, oedema results, e.g. in radical operations.

A very interesting lesion falling in this category is the *lymphocoele*. The first cases were recorded by Kobayashi in 1950.[23] The first American article appeared in 1958 (Gray *et al.*[11]).

This lesion is seen following radical lymphadenectomy. Its incidence varies from no case in 62 operations to 49%.[31] It is generally agreed that the lymphocoele is formed by continued leakage of lymph from lymphatics severed during radical pelvic surgery. The lymph is trapped in the lateral retro-peritoneal space. This accounts for its constant position, between the external iliac vessels and the abdominal wall. There is a slight prominence above and parallel to the inguinal ligament. The lump is not, or very slightly, tender. It is definitely cystic and can easily be felt bimanually to be different from the parametrial induration felt after surgery. There is marked oedema of the surrounding tissues and especially the abdominal muscles. The upper limit seems to be the bifurcation of the aorta. The average cyst contains 300 ml. of a thin, yellow or gray fluid. It has a thin wall, 1 - 2 mm. thick, which is coated with a grey precipitate. Bacteriology reveals mostly contaminants. It develops as a rule about 2 months after the operation. Symptoms vary from none at all to the detection of the lump by the doctor or the patient or oedema of the legs or vulva. More than half of the cases in one series were diagnosed because of urinary infection presumably caused by compression. Large amounts of plasma may be lost, and several workers have given transfusions of plasma, with return of the tachycardia, so often found, to normal. The lesion leaves no permanent disability.

Treatment can be conservative; it is said that all cysts will eventually disappear. If urinary infection supervenes, the cyst has to be drained. In a few cases the lymphocoele extended down into the paravaginal space, where it could be seen and felt. In those cases transvaginal incision and drainage is effective. Many techniques have been developed to prevent this condition, but with little success. Tying all lymphatics at the periphery of the field of operation and leaving the vaginal vault open for drainage are two of the methods suggested. The lymphorrhoea that may be encountered after Basset's operation has the same pathogenesis.

3. **Inflammatory**

1. *Non-specific Inflammations*

A. Acute lymphadenitis. The node is enlarged and tender. The cut surface is pink or grey. The node is full of polymorphs and areas of necrosis, and later abscess formation results if there is no resolution.

B. Chronic lymphadenitis. The node is enlarged and firm. There is hyperplasia of the reticulo-endothelial cells. This is a very common finding, e.g. in the cervical and inguinal nodes.

2. *Specific Inflammations*

A. Tuberculosis.

B. Boeck's sarcoidosis.

C. Leprosy. The inguinal nodes are commonly affected.

D. Infectious mononucleosis (glandular fever). The important point here is that the microscopic picture varies widely in contradistinction to lymphatic leukaemia from which it may have to be differentiated. The characteristic lesion consists of groups of infectious mononucleosis cells and typical and atypical lymphocytes.

E. Typhoid. Extensive necrosis with numerous macrocytic phagocytes is seen.

F. Plague. A haemorrhagic inflammation, necrosis and suppuration are present.

G. Tularaemia.

H. Measles. In the prodromal stage the giant-cells of Warthin-Finkeldey are seen.

I. Infection with nocardia, filiaria, leishmania and toxoplasmosis. In the latter disease the form affecting lymph nodes is the commonest. It occurs as a febrile lymphadenitis or as an almost symptomless condition characterized by lymphadenopathy only.

J. Mycotic infections—coccidiomycosis, blastomycosis, actinomycosis.

K. Brucellosis. Here large mononuclears of reticulo-endothelial origin, giant cells, necrosis and fibrosis are found. This condition may be confused with Hodgkin's disease.

L. Torulosis.

M. Disseminated lupus erythematosus. The nodes here are soft and oedematous, with areas of haemorrhage and necrosis.

N. Dermatopathic lymphadenitis. In certain extensive dermatitides a generalized superficial lymphadenopathy is seen.

O. Syphilis. (*i*) Primary syphilis involves the regional nodes, (*ii*) secondary syphilis causes a generalized lymphadenopathy, and (*iii*) tertiary syphilis causes the extremely rare gumma.

P. Chancroid. 10 - 20 days after the development of the ulcer a painful unilateral or bilateral lymphadenitis occurs.

Q. Granuloma venereum. Here there is rarely gross involvement of the nodes.

R. Lymphogranuloma inguinale. This is primarily a disease of the regional nodes (bubo).

The following two conditions do not really belong in this group:

S. Hashimoto's disease. Here the goitre is infiltrated by lymphocytes.

T. Lymphocytic choriomeningitis. Here a lymphocytic infiltration occurs.

4. **Metabolic**

The nodes are involved in such conditions as Gaucher's disease, Niemann-Pick's disease, Letterer-Siwe's disease, Hans-Schüller-Christian's disease — all examples of primary reticulo-endothelial granulomata. In the first two there is a disturbance of fat metabolism.

5. **Neoplastic**

*A. Benign*

Lymphangioma. This is a slow-growing and frequently congenital tumour. It is very widespread in the body. A few cases of lymphangioma of the fallopian tube have been seen.

Wegner's classification is as follows:

(*a*) Simple — rare, congenital, slow-growing.
(*b*) Cavernous — mainly on the skin.
(*c*) Cystic hygroma — a true neoplasm, mostly cervical.

*B. Malignant*

(*a*) *Of vessels.* Lymphangiosarcoma. This lesion was first described in 1948. It occurs 6 - 24 years after radical mastectomy in some cases where severe lymphoedema has persisted for that length of time. It has not been described in lymphoedematous areas elsewhere.[38]

(*b*) *Of nodes* — (1) Primary. All primary node tumours are malignant and are (i) composed of lymphocytes and lymphoblasts (lymphosarcoma, giant follicular lymphoma, and lymphatic leukaemia) or (ii) composed of reticulum cells (reticulum cell sarcoma). (2) Secondary. (3) Hodgkin's disease.

## LYMPHOGRAPHY

Direct injection of a dye into palpable lymph nodes (lymphadenography) was introduced by Carvalho in 1931.[4] In 1933 Hudack and McMaster[16] used patent blue violet, a water-soluble dye, for studies on the lymphatics of the human skin. Kinmonth *et al.*[22] injected dye into lymphatics (lymphangiography) to study lymphoedema of the lower limb. This is called visual lymphangiography. Radiological lymphangiography entails the use of radio-opaque dyes.

*Technique*

0·2 ml. of a 10% aqueous solution of patent blue is injected into each webspace of one or both feet. This soon outlines a fair-sized lymphatic trunk on the dorsum of the foot. A 'cut-down' is performed and the oily medium is injected at the rate of 1 ml. every 8 - 10 minutes. A Lund injector, an instrument designed for bilateral injection, can be used for greater stability during the operation. With bilateral filling about 15 ml. of the medium is enough to outline the inguinal, iliac and para-aortic nodes. The vessels remain visible on an X-ray plate for about an hour, but the nodes remain opaque for weeks.

*Radiological appearances*. The lymphatics are seen to parallel the veins throughout the body. The findings in *primary lymphoedema* have been described. In *lymphatic obstruction* 'back-flow' is demonstrated. Here many small collateral vessels become visible in the skin. The lymphatics may be distorted where masses push the vessels aside. The *normal node* has a homogeneous, reticular pattern. In *lymphadenitis* the nodes are greatly enlarged, but they retain their normal architecture. The local lymphatics are dilated. In *carcinoma* there is an increase in the number and the individual sizes of the nodes. Irregular filling defects at the nodal margin give a moth-eaten appearance. In other cases the presence of involved nodes is indicated by distortion of the surrounding lymphatics.

In *lymphomas* the nodes are enlarged and have a foamy appearance. The nodal margin is intact. Herman *et al.*[15] have shown that filling defects may be seen in normal nodes.

*Clinical Applications of Lymphography*

1. It aids in the diagnosis of lymphoedema by demonstrating congenital absence or anomalies of the lymphatics.
2. In obscure oedemas it differentiates lymphatic from venous causes.
3. It aids in the diagnosis of obscure cases of pyrexia, raised erythrocyte sedimentation rate, or splenomegaly, by demonstrating unsuspected malignant disease in lymph nodes.
4. It may show unsuspected metastases, e.g. in carcinoma of the cervix, thus aiding treatment.
5. It aids in the differentiation between the lymphomata, Hodgkin's disease, and metastatic carcinoma. It also outlines the extent of the lymphatic involvement.
6. It shows the efficacy of treatment and shows up residual or recurrent disease.
7. It aids the radiotherapist in pinpointing the sites to be irradiated and aids the surgeon where to operate.
8. An interesting field is the development of endolymphatic radiotherapy. Radioactive colloidal gold has been used in the irradiation of the inguinal nodes in malignant melanoma of the lower limb. As affected nodes are either too high to be reached by the gold or the latter cannot penetrate deeply enough into the mass, its most logical use seems to be prophylactic.[19]

*Dangers and Side-effects*

1. Transient lymphangitis.
2. Sepsis at the site of the cut-down.
3. Extravasation. In the case of $^{198}Au$ this is disastrous.
4. Mild or moderate pyrexia.
5. Iodine sensitivity.
6. One case of pulmonary oedema has been described.
7. Theoretically, tumour emboli may be pushed up further along the lymphatic chain.
8. Aplastic anaemia — in endolymphatic radiotherapy.
9. Pulmonary oil embolism. This is usually a minor problem but in a few cases this may be a serious complication.[2]
10. Experimental work has not shown any subsequent chronic inflammation with the possibility of later lymphatic obstruction.

## CONCLUSION

A detailed survey of the lymphatic system has been given in the form of a review. Much work remains to be done. There are main lymphatic 'flows'. Lymph, however, can find its way in its channel in a proximal or distal direction. Blockage causes a reversal of flow until side or skirting channels are found. This finding and the fact that it is impossible to remove *all* lymph nodes and lymphatics at any operation, together with the thought that these nodes may well be barriers to cancerous penetration, cast doubt on whether gross nodal dissection in the treatment of cancer is really necessary. New methods of studying this system may yield much of the information required in the study of disease processes.

## OPSOMMING

Die verskillende aspekte van die limfatiese stelsel, wat van besondere belang in die ginekologie is, word beskryf.

Die veelvuldige verbindings tussen limfvate en die dikwels onberekenbare dreineringspatrone maak dit prakties onmoontlik om werkelik radikale kankeroperasies te kan uitvoer.

I am indebted to the late Prof. James T. Louw and should like to thank Dr. H. Edelstein for his kind interest and help. My thanks also to my brother, Dr. D. Henk J. van Coeverden de Groot, for the drawings; and to Mr. D. Middleton for the photography.

## REFERENCES

1. Allen, E. V. (1934): Arch. Intern. Med., **54**, 606.
2. Bron, K. M. *et al.* (1963): Radiology, **80**, 194.
3. Brunschwig, A. and Daniel, W. W. (1962): Amer. J. Obstet. Gynec., **83**, 389.
4. Carvalho, R. *et al.* (1931): Ann. Anat. path., **8**, 193.
5. Charles, H. (1912) *A System of Treatment*. London: Churchill.
6. Clark, E. R. (1912): Amer. J. Anat., **13**, 351.
7. Crichton, D. (1961): *Proceedings of the Third World Congress of the International Federation of Gynaecology & Obstetrics, Vienna,* vol. 3, p. 168.
8. Gerota, D. (1895): Arch. Anat. physiol. Anat. Abt., 240.
9. Gilmour, J. R. (1941): J. Path. Bact., **52**, 25.
10. Davies, D. V. and Davies, F., eds. (1962): *Gray's Anatomy*, 33rd ed. London: Longmans.
11. Gray, M. J. *et al.* (1958): Amer. J. Obstet. Gynec., **75**, 1059.
12. Gulland, G. L. (1894): J. Path. Bact., **2**, 447.
13. Hellman, J. (1930): In *Handbuch der Mikroskopischen Anatomie der Menschen*, Band 6, Teil 1. Berlin: Springer.
14. Henriksen, E. *in* Meigs, J. V., ed. (1954): *Op cit.*[30]
15. Herman, P. G. *et al.* (1963): Radiology, **80**, 182.
16. Hudack, S. S. and McMaster, P. D. (1933): J. Exp. Med., **57**, 751.
17. Huntington, G. S. and McClure, C. F. W. (1907): Amer. J. Anat., **6**, 39.
18. Hyatt, R. E. and Smith, J. R. (1954): Amer. J. Med., **16**, 434.
19. Jantet, G. H. (1962): Brit. J. Radiol., **35**, 692.
20. Javert, C. T. *in* Meigs, J. V., ed. (1954): *Op cit.*[30]
21. Kampmeier, O. F. (1928): Amer. J. Anat., **40**, 413.
22. Kinmonth, J. B. *et al.* (1957): Brit. J. Surg., **45**, 1.
23. Kobayashi, T. and Inoue, S. (1950): Clin. Gynec. Obstet., **4**, 91.
24. Leitch, A. (1910): Trans. Roy. Soc. Med. Lond. (Obstet. Gynaec. Sect.), **4**, 69.
25. Lever, A. F. *et al.* (1962): J. Physiol., **160**, 548.
26. Leveuf, J. and Godard, H. (1923): Rev. Chir. (Paris), **61**, 219.
27. Lewis, F. T. (1906): Amer. J. Anat., **5**, 95.
28. Louw, J. T. (1958): *Proceedings of the 2nd World Congress of the International Federation of Gynaecology & Obstetrics,* Montreal.
29. Mayerson, H. S. (1963): Sci. Amer., **208**, 80.
30. Meigs, J. V., ed. (1954): *Surgical Treatment of Cancer of the Cervix*. New York: Grune & Stratton.
31. Mori, N. (1955): J. Jap. Obstet Gynaec. Soc., **2**, 178.
32. Nesselrod, J. P. (1936): Ann. Surg., **104**, 905.
33. Parry-Jones, E. (1961): J. Obstet. Gynaec. Brit. Emp., **68**, 878.
34. Pick, J. W. *et al.* (1943 - 45): Quart. Bull. Northw. Univ. Med. Sch., **17 - 19**, 307.
35. Pressman, J. J. *et al.* (1961): Surg. Gynec. Obstet., **113**, 537.
36. Reiffenstuhl, G. (1957): *Das Lymphsystem des weiblichen Genitale*. Wien: Urban & Schwarzenberg.
37. Sabin, F. R. (1902): Amer. J. Anat., **1**, 367.
38. Stewart, F. W. and Treves, N. (1948): Cancer (Philad.), **1**, 64.
39. Way, S. (1951): *Malignant Disease of the Female Genital Tract*. London: Churchill.
40. Yoffey, J. M. and Courtice, F. C. (1956): *Lymphatics, Lymph and Lymphoid Tissue*. London: Arnold.

BIBLIOGRAPHY

Anderson, W. A. D. (1961): *Pathology*, 4th ed. St. Louis: Mosby.
Boyd, W. (1961): *Textbook of Pathology*, 7th ed. Philadelphia: Lea & Febiger.
Braunstein, H. *et al.* (1962): Cancer (Philad.), **15**, 130.
Davson, H. and Eggleton, M. G., eds. (1962): *Starling & Lovatt Evans' Principles of Human Physiology*, 13th ed. London: Churchill.
Ditchek, T. *et al.* (1963): Radiology, **80**, 175.
Ferguson, J. H. *et al.* (1961): Amer. J. Obstet. Gynec., **82**, 783.
Fisher, H. W. *et al.* (1961): J. Amer. Med. Assoc., **175**, 327.
Gorton, G. (1953): *Post-irradiative Prophylactic Extra-peritoneal Lymphadenectomy in Carcinoma of the Uterine Cervix*. Lund: Berlingska Boktryckeriet.
Gough, M. H. *et al.* (1963): Brit. Med. J., **1**, 1181.
Guyton, A. C. (1961): *Textbook of Medical Physiology*, 2nd ed. Philadelphia: Saunders.
Ham, A. W. and Leeson, T. S. (1961): *Histology*, 4th ed. Philadelphia: Lippincott.
Kampmeier, O. F. (1912): Amer. J. Anat., **13**, 401.
Mellors, R. C. *et al.* (1961): Amer. J. Path., **39**, 533.
Sabin, F. R. (1912): Anat. Rec., **6**, 335.
Tjernberg, B. (1962): Acta radiol. (Stockh.), suppl. 214.
Wallace, S. *et al.* (1961): Radiology, **76**, 179.
Wintrobe, M. M. (1962): *Clinical Hematology*, 5th ed. Philadelphia: Lea & Febiger.
Wright, S. (1961): *Applied Physiology*, 10th ed. London: Oxford University Press.