Table 4. Complete protection rate for 7 days of each treatment

Complete protection	GRN alone (n = 42)		CMB therapy (n = 27)		CCT therapy (n = 69)	
	n	%	n	%	n	%
Day 1						
0–6 h	40	95.2	26	96.3	69	100
6–12 h	34	81	27	100	67	97.1
12–18 h	28	66.7	19	70.4	63	91.3
18–24 h	27	64.3	19	70.4	62	89.9
Day 2	16	38.1	15	55.6	50	72.5
Day 3	17	40.5	14	51.9	50	72.5
Day 4	27	64.3	16	59.3	54	78.3
Day 5	36	85.7	18	66.7	60	87
Day 6	37	88.1	22	81.5	63	91.3
Day 7	39	92.9	24	88.9	65	94.2

Table 5. Adverse events (days 1–3)

Adverse event	Patients		
	GRN alone (n = 42)	CMB therapy (n = 27)	CCT therapy (n = 69)
Headache	3		2
Vertigo	1		
Hot flushes	2		3
Nervousness			8
Elevated aminotransferase value convulsion		1	
Other			1
Total	6	1	15

When the overall data for days 1–7 were considered, the CCT therapy provided complete protection from nausea in more patients (20%) than GRN alone or CMB, especially for days 1–5.

During days 1-7, complete protection from both nausea and vomiting was also compared between therapies (table 4). On days 2 and 3, the lowest protection rates were observed in 16 of the 42 patients receiving GRN alone (38.1%), in 14 of the 27 patients in the CMB group (51.9%), and in 50 of the 69 patients in the CCT group (72.5%, fig. 1).

Adverse Events

No severe or unexpected adverse events were reported. Table 5 shows the data for days 1–3. Headache, vertigo and hot flushes were slightly increased in patients receiving GRN alone or CCT therapy. The most important adverse event was nervousness just on day 1 or 2, due to the combination of DRP in patients receiving CCT therapy.

Discussion

Very recently, a taxol/carboplatin regimen only for ovarian cancer has been introduced primarily in Japan, so the requirement of strong antiemetic regimens is not frequent. Oral $5HT_3$ antagonists are routinely used. However, one of the key drugs for gynecologic cancer is the platinum compound, such as CDDP or CBDCA. In contrast to CBDCA, CDDP is still included as primary or secondary chemotherapy regimen for uterine and ovarian cancer in Japan.

The randomized crossover study compared the combination of a 5-HT_3 antagonist and MPD with DRP as the third drug in the prevention of acute and delayed emesis in patients receiving CDDP-based chemotherapy for gynecologic malignancies. The combination of GRN plus MPD and DRP as a CCT therapy was shown to be more effective than GRN alone or GRN plus MPD during the first 24 h after chemotherapy. The higher incidence of complete protection from acute nausea, vomiting, or both with CCT therapy as well as the lower occurrence of adverse events are clinically relevant. Fewer patients had protection from nausea than protection from vomiting, a finding also reported in other studies on GRN and DEX [12]. However, in this study, the CCT therapy had the same efficacy regarding both nausea and vomiting during the acute phase of emesis.

Protection against delayed nausea and vomiting is very important for patients subjected to chemotherapy. Delayed emesis (starting 24 h after the administration of chemotherapy) persists for at least 48 h, and patients may thus require antiemetic therapy for several days. In the present study, it is noteworthy that about 73% of the patients treated with the CCT therapy did not vomit during days 2–7. Prophylactic CCT therapy with DRP is superior to the use of GRN alone or CMB therapy. On the other hand, only about 50% of the patients treated with CMB therapy had delayed nausea. Furthermore, almost 60% of the patients treated with GRN alone suffered from delayed emesis. Thus, the control of delayed emesis is a critical consideration. Our results show that compared with other treatments the CCT therapy including DRP provided the best protection for delayed emesis on days 2–3. This finding is significant in its potential for control-

ling delayed emesis resulting from clinical treatment with cisplatin-based chemotherapy.

The mechanism of onset of delayed emesis remains unknown. Combination therapy with steroids to control delayed-type vomiting is thought to be effective [2] because of impaired function of the digestive tract, cytolysis products resulting from the administration of a chemotherapeutic agent and inflammation caused by these products, for example [13].

We conducted an animal study to examine the mechanism of the effect of steroids on delayed-onset vomiting [9]. We administered CDDP intraperitoneally at a dose of 5 mg/kg to ferrets, and compared the emesis among three groups, i.e. the group without any antiemetic (the control group), the group given GRN alone (GRN group), and the group given DEX combined with GRN (DEX/GRN group). A remarkable suppressive effect on emesis was noted in the GRN group both in the acute phase (0–24 h) and in the delayed phase (24–72 h) compared with the control group. The antiemetic effect was strengthened in the DEX/GRN group by the combination with DEX. In comparison to the concentrations of 5-HT and its metabolite 5-HIAA in the intestine and in the area postrema, the increase in 5-HT due to CDDP was not suppressed in the GRN group or in the DEX/GRN group. We hypothesized that combination therapy with GRN plus DEX may be useful to suppress delayed emesis, but that the increased 5-HT concentration in the tissue may not contribute to the occurrence of delayed emesis.

In a recent study, the combination of a $5HT_3$ receptor antagonist with a steroid was also found to be effective in patients with delayed emesis [14]. Various mechanisms have been proposed concerning the efficacy of these combinations, including stimulation of the cerebral cortex, inhibition of the synthesis of prostaglandins, reinforcement of the blood-brain barrier, stabilization of the cell membrane, anti-inflammatory action, and acceleration of the metabolism of the drug in the liver and of its excretion into urine [15]. However, some problems have been pointed out, such as the possible adverse effects of steroids and problems from the viewpoint of health insurance and medical expenses [16].

In the past, before the development of $5HT_3$ receptor antagonists, administration of a steroid such as DEX or MPD [17], or of a psychotropic agent such as DRP [18], or an antihistamine agent such as diphenhydramine [19] had been attempted to increase the effect of metoclopramide with relatively good results. The primary effect of the psychotropic agent DRP is suppression of the central nervous system [20, 21]. The agent is administered for tranquilization and sedation so that the quality of life of the patient may be improved, although the patient may become somnolent during therapy. It remains unknown whether the somnolence is due to an inappropriate dose or to an individual condition, but we believe that our CCT therapy including DRP is generally well tolerated by many patients.

Regarding the control of delayed emesis, it has been recently reported that a tachykinin NK1 receptor antagonist seems to be a promising countermeasure for delayed-onset vomiting and is being actively developed mainly in Western countries [22]. The NK1 receptor of substance P and the $5HT_3$ receptor of serotonin seem to hold the passkey to the common action site in the pathway of the vomiting center of the vagus nerve [23]. Preliminary clinical trials have already been performed in the US [24], and have shown that delayed emesis can be better controlled by administration of CP122721, an NK1 receptor antagonist, rather than by administration of a $5HT_3$ receptor antagonist combined with a steroid. Thus, the NK1 receptor antagonist is expected to be effective for delayed emesis. The association of substance P or NK1 with DRP also looks promising in the control of delayed emesis.

In the acute phase within 6 h after chemotherapy, $5HT_3$ receptor antagonists are the most effective. Even the current combination of a $5HT_3$ receptor antagonist with a steroid does not completely control delayed emesis. Women with gynecologic malignancies are especially prone to anticipating factors during chemotherapy. For this reason, DRP may have the highest potential for controlling delayed and anticipatory emesis in gynecological patients undergoing chemotherapy. A prospective randomized study is warranted to compare various treatment modalities combined with steroids, with or without DRP.

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SPECIAL ARTICLE

Committee on Classification of Regional Lymph Nodes of Japan Society of Clinical Oncology

Classification of Regional Lymph Nodes in Japan

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Foreword

The first classification of regional lymph nodes was proposed in the "General Rules for Reporting on Clinical Oncology, Part V," in 1991, to integrate the nomenclature and coding based on individual General Rules for cancer research (in Japanese). However, the proposal became problematic because new codes in the proposal differed from traditional codes in the individual General Rules for cancer research.

During the following decade, much revision of the General Rules for cancer research took place. A new committee on classification of regional lymph nodes was appointed, in November 1997, to establish a new systematic classification by the Japan Society of Clinical Oncology, the core society for the treatment for cancer. The committee members were clinicians from 15 societies that had established the General Rules for cancer research and specialists in anatomy and pathology.

The committee determined that any codes were not employed. The systematic classification of regional lymph nodes was determined to be divided into four parts: 1) the neck, axillae, chest wall, and upper extremities; 2) the thorax; 3) the abdominal cavity (1 & 2); and 4) the pelvis, inguinal region, and lower extremities.

First, the committee discussed anatomically appropriate entries of regional lymph nodes for the systematic classification. These entries were considered to integrate clinical consistency in diagnosis and treatment of regional lymph nodes. Clinically rare lymph nodes, although having anatomically appropriate entries, were omitted, and some subclassifications that were meaningless clinically were not employed. Then, new illustrations were employed in the present classification. Because it is difficult to represent three-dimensional images on a two-dimensional plane, these new illustrations were produced to be used in practice.

All editorial members, as well as the chief of the committee on classification of regional lymph nodes, Ryuichi Kudo, M.D., Ph.D., sincerely hope that this classification will be widely accepted, and that appropriate entries of regional lymph nodes in the systematic classification, such a common word, will be used in aspects of continuing cancer research and in practice in the diagnosis and treatment of cancer.

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Classification of Regional Lymph Nodes

I. Lymph nodes in the neck, axillae, chest wall, and upper extremities

1. Parotid lymph nodes

Parotid lymph nodes can be classified into the following two groups according to their positional relationship to the parotid fascia.

a. Superficial parotid nodes

Superficial parotid nodes are located on the superficial lobe of the parotid gland and anterior to the auricula.

b. Deep parotid nodes

Deep parotid nodes can be subclassified as follows:

- Infra-auricular parotid nodes

Infra-auricular parotid nodes are located on the surface of the lowest area of the parotid gland, which is surrounded by the anterior margin of the sternocleidomastoid muscle, the masseter muscle, and the cervical fascia.

•Intraglandular parotid nodes

Intraglandular parotid nodes are located within the loose connective tissue between the superficial and deep lobes of the parotid gland.

2. Submental lymph nodes and submandibular lymph nodes

a. Submental lymph nodes

Submental lymph nodes are sandwiched between the platysma and mylohyoid muscles, and located in the area surrounded by the mandible, the hyoid bone, and the anterior belly of the digastric muscle.

b. Submandibular lymph nodes

Submandibular lymph nodes are sandwiched between the platysma and mylohyoid muscles, and located in the (triangular) area surrounded by the mandible, and the anterior and posterior bellies of the digastric muscle.

3. Superficial cervical lymph nodes

Superficial cervical lymph nodes are located along the external jugular vein on the surface of the sternocleidomastoid muscle. These nodes can be classified as follows:

a. Anterior superficial cervical nodes

Anterior superficial cervical nodes are located along the anterior jugular vein.

b. Lateral superficial cervical nodes

Lateral superficial cervical nodes are located along the external jugular vein, and can be found on the surface of the upper portion of the sternocleidomastoid muscle.

4. Anterior deep cervical lymph nodes

A. Anterior group

a. Prelaryngeal nodes

Prelaryngeal nodes are located on the surface of the cricothyroid membrane.

b. Thyroid nodes

Thyroid nodes are attached to the thyroid capsule, and can be classified as follows:

•Prethyroid nodes
•Parathyroid nodes

c. Pretracheal nodes

Pretracheal nodes are located in front of the cervical trachea.

d. Cervical paratracheal nodes

Cervical paratracheal nodes are located along the recurrent laryngeal nerve.

B. Posterior group

a. Retropharyngeal nodes

Retropharyngeal nodes are located posterior and lateral to the pharynx.

b. Paraesophageal nodes

Paraesophageal nodes are located along the cervical esophagus.

5. Lateral deep cervical lymph nodes

a. Superior deep cervical nodes (jugulodigastric nodes)

Superior deep cervical nodes are located along the internal jugular vein, at the level of the posterior belly of the digastric muscle.

b. Middle deep cervical nodes (jugulo-omohyoid nodes)

Middle deep cervical nodes are located along the internal jugular vein, at the level of the superior belly of the omohyoid muscle.

c. Inferior deep cervical nodes

Inferior deep cervical nodes are located along the internal jugular vein, at the level of the inferior belly of the omohyoid muscle.

d. Spinal accessory nodes

Spinal accessory nodes are located along the accessory nerve, and anterior to the anterior margin of the trapezius muscle. Because the highest nodes of this group are indistinguishable from the superior deep cervical nodes, they are simply classified as superior deep cervical nodes.

e. Supraclavicular nodes (scalene nodes)

Supraclavicular nodes are located along the transverse cervical vein.

Lymph nodes in the lesser and greater supraclavicular fossae can be classified into medial and lateral groups. The medial group is termed the inferior deep cervical nodes, and the lateral group, the supraclavicular nodes.

6. Axillary lymph nodes

Axillary lymph nodes are classified according to the axillary blood vessels and their branches, as in the classification of lymph nodes in the digestive system.

a. Brachial nodes

Brachial nodes are located along the axillary vein, and distal to the pectoralis minor muscle.

b. Subscapular nodes (scapular nodes)

Subscapular nodes are located along the thoracodorsal blood vessels that are the continuation of the subscapular blood vessels.

c. Pectoral nodes (external mammary nodes)

Pectoral nodes are located along the lateral thoracic blood vessels. These nodes can be classified as upper and lower groups.

The lymph nodes of the upper group (sorgius nodes), deep to the pectoralis major muscle, are located between the second and third ribs. The lymph nodes of the lower group are located between the fourth and sixth ribs, and below the inferior-lateral margin of the pectoralis major muscle.

These nodes were formerly termed the external mammary nodes.

d. Central axillary nodes (superficial axillary nodes)

Central axillary nodes are located near the bottom of the axilla, and are crossed and/or adjacent to the intercostobrachial nerves.

e. Subpectoral nodes

Subpectoral nodes are located along the axillary vein, and posterior to the pectoralis minor muscle.

f. Interpectoral nodes

Interpectoral nodes are located between the pectoralis major and minor muscles, and along the pectoral branches of the thoracoacromial blood vessels, where the pectoral branches extend to the pectoralis major muscle.

g. Infraclavicular nodes (apical nodes)

Infraclavicular nodes are located along the axillary vein between the pectoralis minor muscle and the subclavius muscle, in the medial area where the thoracoacromial vein drains into the axillary vein. These nodes are located at the highest or the most medial margin of the axilla.

7. Parasternal lymph nodes

Parasternal lymph nodes are located along the internal thoracic blood vessels between the first and sixth ribs.

8. Epitrochlear lymph nodes

Epitrochlear lymph nodes are located along the basilic vein, and at the cubital-fossa side above the medial entepicondyle.

II. Lymph nodes in the thorax

1. Supreme mediastinal lymph nodes

Supreme mediastinal lymph nodes are located from the imaginary line connecting the upper margin of the left and right subclavian arteries with the upper margin of the sternum, to the crossing point of the upper margin of the left brachiocephalic vein and the midline of the trachea.

2. Anterior mediastinal lymph nodes

Anterior mediastinal lymph nodes are located between the lowest supreme mediastinal lymph nodes and the diaphragm. Anterior to the trachea, these nodes are located along the aortic arch, superior vena cava, and brachiocephalic veins, and their anterior branches. In the lower boundary area, these nodes are located anterior to the pericardium.

3. Ligamentum arteriosum lymph node

Ligamentum arteriosum lymph nodes are located along the left margin of the ligamentum arteriosum, and below the aortic arch.

4. Ascending aortic lymph nodes

Ascending aortic lymph nodes are located on the lateral wall of the ascending aorta and the aortic arch, anterior to the vagus nerve.

5. Thoracic paratracheal lymph nodes

Thoracic paratracheal lymph nodes are located between the supreme mediastinal lymph nodes and tracheobronchial nodes. These nodes can be classified according to the areas anterior and lateral to the trachea, and divided into left and right groups.

6. Tracheobronchial lymph nodes

Tracheobronchial lymph nodes are located in the tracheobronchial angle. On the right side, these nodes are located medial to the azygos vein. On the left side, these nodes are located in the space between the aortic arch and left pulmonary artery, and medial to the ligamentum arteriosum. These nodes can be classified as right and left groups.

7. Inferior tracheobronchial lymph nodes (subcarinal lymph nodes)

Inferior tracheobronchial lymph nodes are located in the immediate proximity of the tracheal bifurcation.

8. Bronchopulmonary lymph nodes

Bronchopulmonary lymph nodes are located around the right and left bronchi. These nodes can be classified into the following groups.

•Main bronchus nodes (hilar nodes)

Main bronchus nodes, or hilar nodes, are located around the right and left principal bronchi.

•Interlobar nodes

Interlobar nodes are located along the lobar bronchi.

•Lobar nodes

Lobar nodes are located around the lobar bronchi.

•Segmental nodes

Segmental nodes are located along the segmental bronchi.

•Subsegmental nodes

Subsegmental nodes are located along the subsegmental bronchi, and distal to the subsegments.

9. Paraesophageal lymph nodes

Paraesophageal lymph nodes are located along the thoracic esophagus, and can be classified as upper, middle, and lower thoracic paraesophageal nodes.

10. Supradiaphragmatic lymph nodes

Supradiaphragmatic lymph nodes are located around the esophageal hiatus of the diaphragm, in the midback area of the diaphragm.

11. Posterior mediastinal lymph nodes

Posterior mediastinal lymph nodes are located in the posterior mediastinum below the supreme mediastinal lymph nodes, except for paraesophageal and supradiaphragmatic lymph nodes. These nodes can be classified as follows:

a. Pulmonary ligament nodes

Pulmonary ligament nodes are located within the pulmonary ligament and also posterior to and below the inferior pulmonary vein.

b. Thoracic duct nodes

Thoracic duct nodes are located along the thoracic duct.

c. Thoracic para-aortic nodes

Thoracic para-aortic nodes are located around the descending aorta.

III. Lymph nodes in the abdominal cavity, No. 1

1. Paracardial lymph nodes

Paracardial lymph nodes are located around the cardia of the stomach, and they can be classified as follows:

a. Right paracardial nodes

The boundary, between the right cardial nodes and the lesser curvature lymph nodes, is the first branch of the ascending branch of the left gastric artery that enters the gastric wall. Lymph nodes located along the first branch can be classified as right paracardial nodes.

b. Left paracardial nodes

Left paracardial nodes are located along the cardioesophageal branch of the left inferior phrenic svein.

2. Esophageal hiatus lymph nodes

Esophageal hiatus lymph nodes are located in the esophageal hiatus.

3. Lesser curvature lymph nodes

The boundary, between the lesser curvature lymph nodes and the suprapyloric lymph nodes, is the first branch of the right gastric artery to the lesser curvature. Lymph nodes located along the first branch can be classified as suprapyloric lymph nodes.

4. Greater curvature lymph nodes

The boundary, between the greater curvature lymph nodes and the infrapyloric lymph nodes, is the first branch of the right gastroepiploic artery to the greater curvature. Lymph nodes located along this first branch can be classified as greater curvature lymph nodes.

5. Suprapyloric lymph nodes

Suprapyloric lymph nodes are located along the right gastric artery and its origin.

6. Infrapyloric lymph nodes

The boundary, between the infrapyloric lymph nodes and the superior mesenteric lymph nodes, is the confluence of the right gastroepiploic vein with the anterior inferior pancreaticoduodenal vein. Lymph nodes at the confluence can be classified as infrapyloric lymph nodes.

7. Hepatoduodenal ligament lymph nodes

Hepatoduodenal ligament lymph nodes are located within the hepatoduodenal ligament, which can be classified as follows:

a. Hepatic artery nodes

Hepatic artery nodes are located along the hepatic artery.

b. Bile duct nodes

Bile duct nodes are located along the bile duct.

c. Cystic duct nodes

Cystic duct nodes are located along the cystic duct.

8. Peripancreatic lymph nodes

a. Anterior and posterior pancreaticoduodenal nodes

Anterior and posterior pancreaticoduodenal nodes are located on the anterior and posterior surfaces of the pancreatic head, from the superior mesenteric artery and/or the portal vein to the medial margin of the duodenum. The upper and lower nodes can be divided at the level of the ampulla of Vater.

b. Inferior pancreatic nodes

Inferior pancreatic nodes are located along the inferior margin of the pancreatic body and tail; these nodes do not include the splenic hilum lymph nodes or superior mesenteric lymph nodes.

9. Common hepatic artery lymph nodes

Common hepatic artery lymph nodes are located along the common hepatic artery between the origin of the splenic artery and that of the gastroduodenal artery. These nodes can be classified as follows:

a. Anterosuperior group

These nodes are located anterosuperior to the common hepatic artery.

b. Posterior group
These nodes are located posterior to the common hepatic artery.

10. Splenic hilum lymph nodes
The boundary, between the splenic hilum lymph nodes and the splenic artery lymph nodes, is the end of the pancreatic tail.

11. Splenic artery lymph nodes
Splenic artery lymph nodes are located along the splenic artery, and include the nodes posterior to the pancreas. These nodes can be classified as distal and proximal groups, according to the origin of the posterior gastric artery.

12. Left gastric artery lymph nodes
Left gastric artery lymph nodes are located along the left gastric artery, from the origin to the ascending branch of the left gastric artery.

13. Celiac artery lymph nodes
Celiac artery lymph nodes are located around the celiac trunk. These nodes, which are located immediately near the origins of the left gastric artery, the common hepatic artery, and the splenic artery, can be classified as celiac artery lymph nodes.

14. Infradiaphragmatic lymph nodes
Infradiaphragmatic lymph nodes are located on the abdominal surface of the diaphragm.

15. Intestinal mesenteric lymph nodes
Intestinal mesenteric lymph nodes are located in the area of the intestinal mesentery.

16. Epicolic and paracolic lymph nodes
Epicolic lymph nodes are located on the colon wall, from the cecum to the sigmoid colon; those nodes along the marginal arteries can be classified as the paracolic lymph nodes.

17. Ileocolic artery lymph nodes
Ileocolic artery lymph nodes are located along the ileocolic artery.

18. Right colic artery lymph nodes
Right colic artery lymph nodes are located along the right colic artery.

19. Middle colic artery lymph nodes
Middle colic artery lymph nodes are located along the middle colic artery.

20. Superior mesenteric lymph nodes
Superior mesenteric lymph nodes surround the superior mesenteric blood vessels, from the origin of the superior mesenteric artery to that of the middle colic artery.

21. Left colic artery lymph nodes
Left colic artery lymph nodes are located along the left colic artery.

22. Sigmoid artery lymph nodes
Sigmoid artery lymph nodes are located along the first and second sigmoid arteries.

23. Inferior mesenteric artery lymph nodes
Inferior mesenteric artery lymph nodes are located along the inferior mesenteric artery, from the origin of the inferior mesenteric artery to that of the lowest sigmoid artery. These nodes can be classified as follows:

a. Inferior mesenteric trunk nodes
Inferior mesenteric trunk nodes are located along the inferior mesenteric artery, from the origin of the left colic artery to that of the lowest sigmoid artery.

b. Inferior mesenteric root nodes
Inferior mesenteric root nodes are located along the inferior mesenteric artery, from the origin of the inferior mesenteric artery to that of the left colic artery.

III. Lymph nodes in the abdominal cavity, No. 2

1. Abdominal para-aortic lymph nodes
Abdominal para-aortic lymph nodes surround the abdominal aorta and inferior vena cava, which can be classified into the following four groups, from cranial to caudal areas.

•a1 group
Lymph nodes in the a1 group are located in the area of the aortic hiatus (about 4–5 cm in width, surrounded by the medial crus of the diaphragm). These nodes are located within the median arcuate ligament of the diaphragm.

•a2 group
Lymph nodes in the a2 group are located in the area from the uppermost part of the origin of the celiac trunk to the lower margin of the left renal vein.

•b1 group
Lymph nodes in the b1 group are located in the area from the lower margin of the left renal vein to the uppermost part of the origin of the inferior mesenteric artery.

•b2 group
Lymph nodes in the b2 group are located in the area from the upper margin of the origin of the inferior mesenteric artery to the aortic bifurcation.

Lymph nodes in the cross-sectional circumference of the abdominal aorta and the inferior vena cava can be classified as follows:

- Preaortic nodes
- Lateroaortic nodes
- Retroaortic nodes
- Interaorticocaval nodes
- Precaval nodes
- Laterocaval nodes
- Retrocaval nodes

2. Renal lymph nodes

From the point of view of renal cancer, another classification has been employed.

a. Right renal lymph nodes

Right renal lymph nodes are located to the right of the median line of the abdominal aorta, from the origin of the celiac trunk to that of the inferior mesenteric artery.

b. Left renal lymph nodes

Left renal lymph nodes are located to the left of the median line of the abdominal aorta, from the origin of the celiac trunk to that of the inferior mesenteric artery.

IV. Lymph nodes in the pelvis, inguinal region, and lower extremities

1. Subaortic lymph nodes

Subaortic lymph nodes are located immediately below the aortic bifurcation, and in the angle of the right and left common iliac arteries.

2. Median sacral lymph nodes

Median sacral lymph nodes are located along the median sacral artery, and outside the mesorectum.

3. Lateral sacral lymph nodes

Lateral sacral lymph nodes are located along the lateral sacral artery, from the origin of the internal iliac artery to the second or third sacral foramen.

4. Common iliac lymph nodes

Common iliac lymph nodes are located along the common iliac blood vessels.

5. External iliac lymph nodes

External iliac lymph nodes are located below the origin of the external iliac blood vessels.

6. Suprafemoral lymph nodes

Suprafemoral lymph nodes are located along the external iliac blood vessels, to the area just above the inguinal ligament. These nodes can be classified into the lateral and medial groups relative to the external iliac blood vessels.

7. Internal iliac lymph nodes

Internal iliac lymph nodes are located in the triangular area between the external and internal iliac blood vessels, and along the internal iliac blood vessels.

8. Obturator lymph nodes

Obturator lymph nodes are located dorsal to the external iliac blood vessels. These nodes surround the obturator nerve and blood vessels. Some nodes are also near the internal orifice of the obturator canal.

9. Parametrial lymph nodes

Parametrial lymph nodes are located in and/or around the cardinal ligament.

10. Pararectal lymph nodes

Pararectal lymph nodes are located along the superior rectal artery distal to the origin of the lowest sigmoid artery from the inferior mesenteric artery. These nodes are also located within the rectal fascia, as well as along the middle rectal artery medial to the pelvic plexus.

11. Inferior rectal lymph nodes

Inferior rectal lymph nodes are located along the inferior rectal artery in the ischiorectal fossa.

12. Middle rectal root lymph nodes

Middle rectal root lymph nodes are located along the middle rectal artery, from the origin of the internal iliac artery to the area lateral to the pelvic plexus.

13. Inguinal lymph nodes

Inguinal lymph nodes are located below the inguinal ligament. These nodes can be classified as follows:

a. Superficial inguinal nodes

Superficial inguinal nodes are located on the surface of the fascia lata.

b. Deep inguinal nodes

Deep inguinal nodes are located deep to the fascia lata.

14. Popliteal lymph nodes

Popliteal lymph nodes are located around the popliteal artery, within the rhomboid-shaped area surrounded by the femoral biceps, the semimembranous muscle, and the medial and lateral heads of the gastrocnemius muscle.

Acknowledgment This classification of regional lymph nodes is the result of a number of meetings of the Committee on Classification of Regional Lymph Nodes, and these meetings were organized and supported by representative members of individual cancer societies. Therefore, this classification of lymph nodes was approved by the individual cancer societies. Finally, the classification was recognized by the council meeting and the Board of Directors of the Japan Society of Clinical Oncology. We are also grateful to Mr. T. Kohga, a medical illustrator, for drawing new illustrations under the guidance of Dr. T. Sato.

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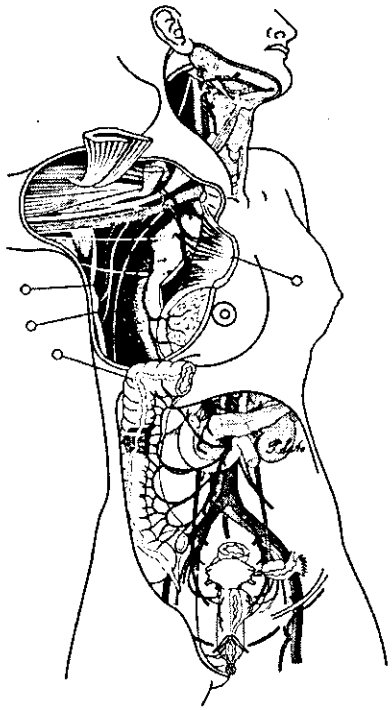

Fig. 1. View of blood vessels and visceral organs (female)

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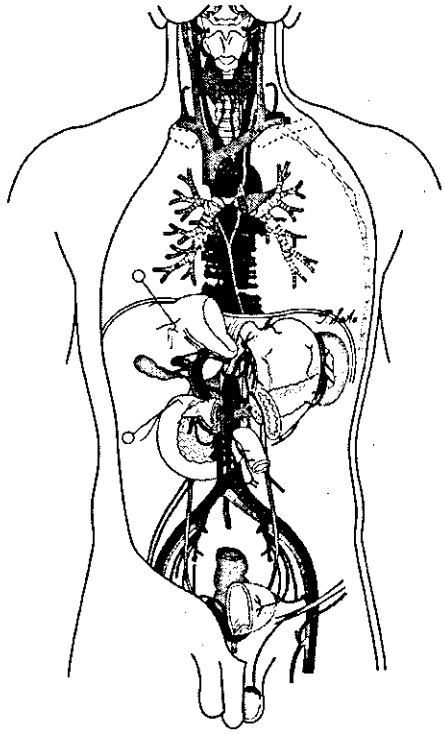

Fig. 2. View of blood vessels and visceral organs (male)

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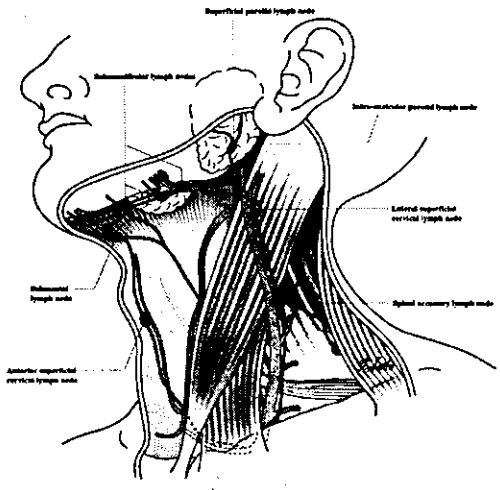

Fig. 3. Superficial lymph nodes of the neck

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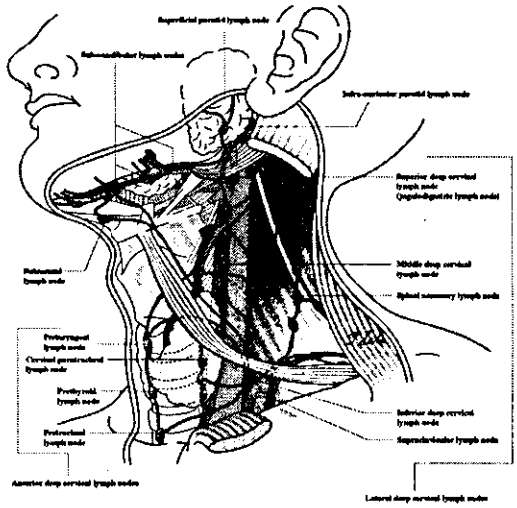

Fig. 4. Deep lymph nodes of the neck

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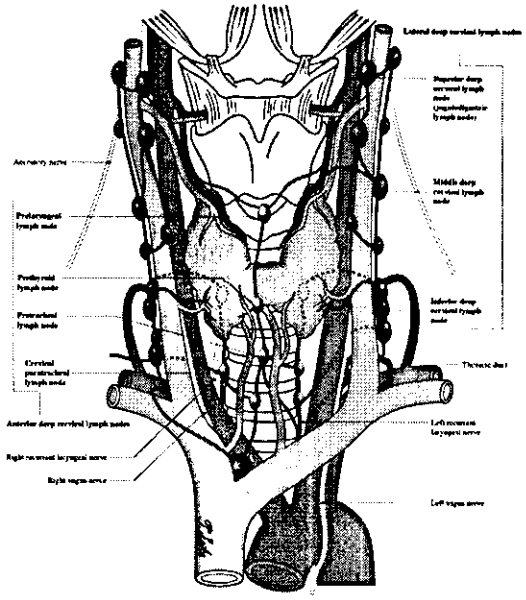

Fig. 5. Lymph nodes around the thyroid gland and cervical trachea

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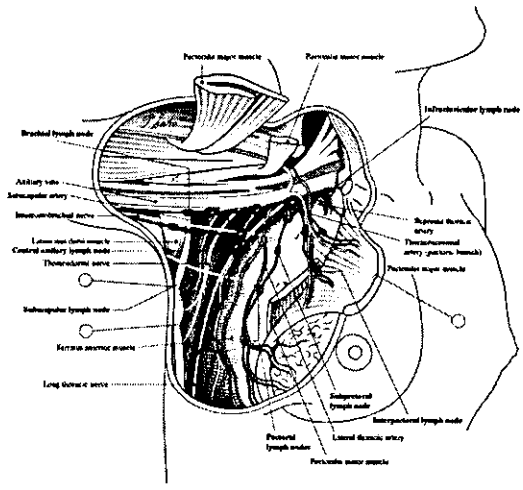

Fig. 6. Lymph nodes in the breast and axilla

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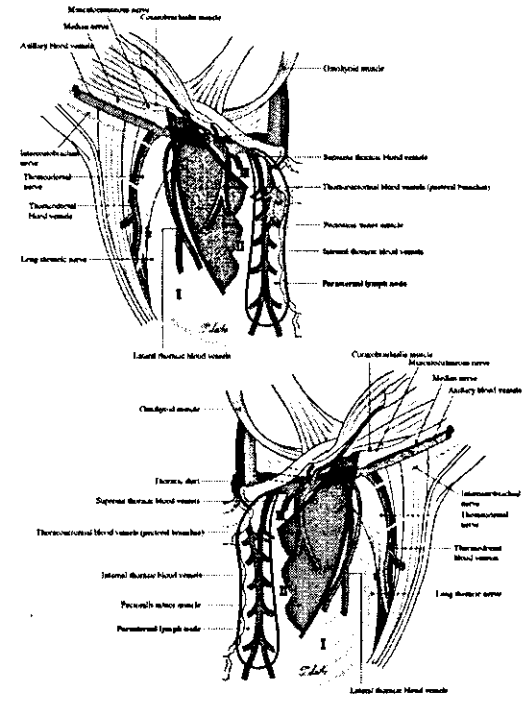

Fig. 7. Levels of the axillary lymph nodes

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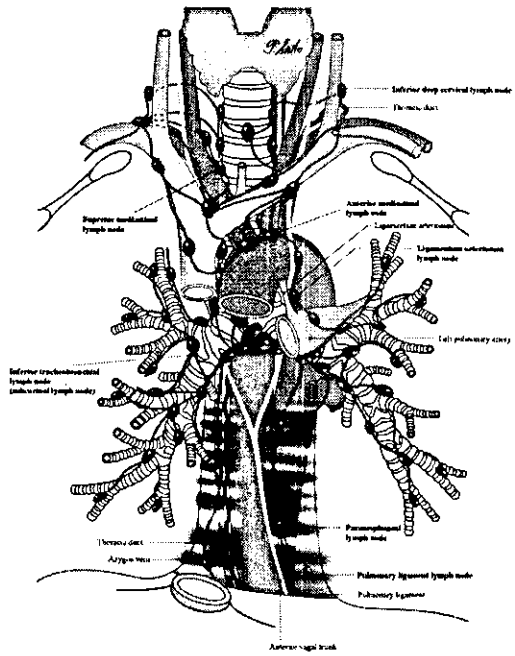

Fig. 8. Lymph nodes in the mediastinum (superficial view)

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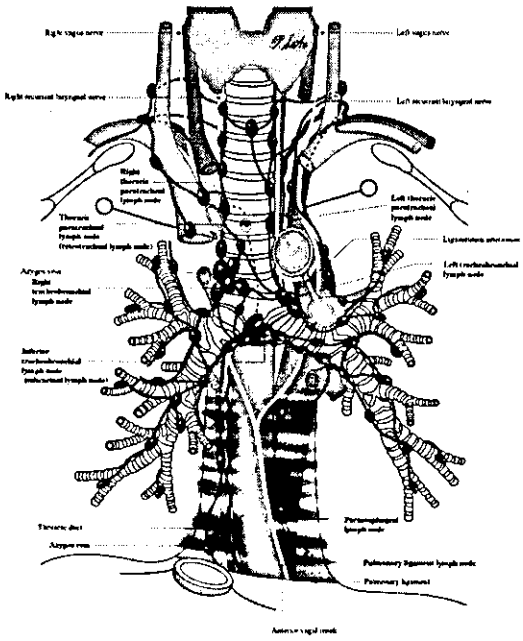

Fig. 9. Lymph nodes in the mediastinum (deep view)

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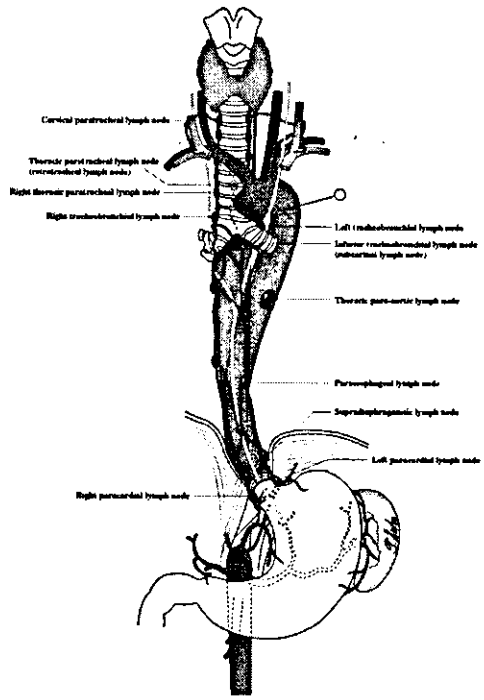

Fig. 10. Lymph nodes around the esophagus

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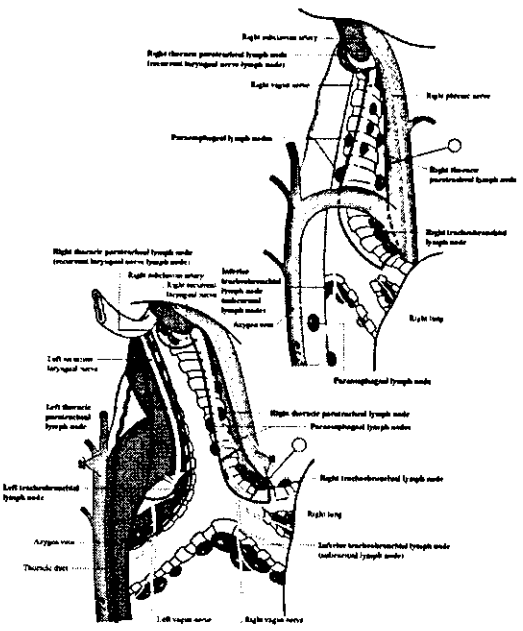

Fig. 11. Groups of lymph nodes around the esophagus

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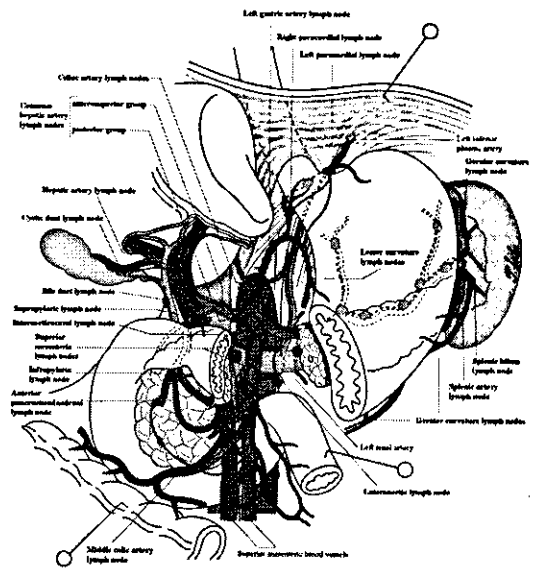

Fig. 12. Lymph nodes around the stomach

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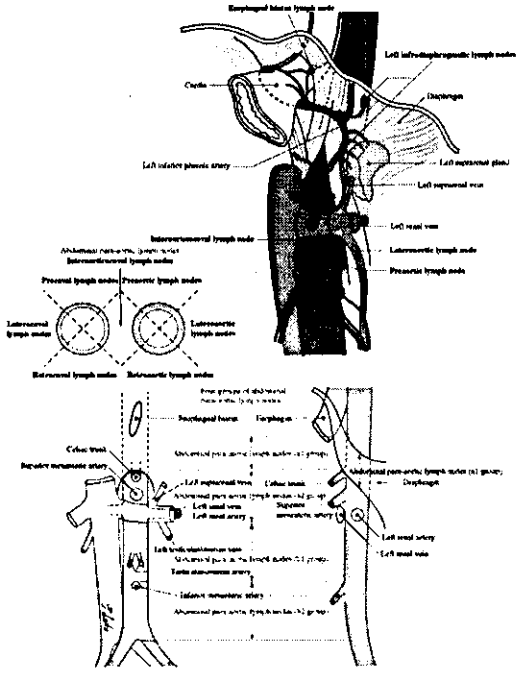

Fig. 13. Lymph nodes around the abdominal aorta

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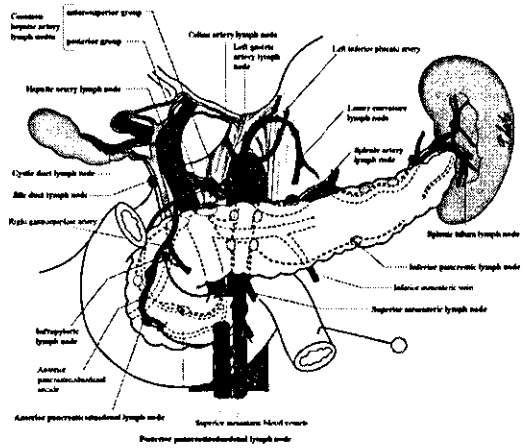

Fig. 14. Lymph nodes around the pancreas and along the biliary tract (anterior view)

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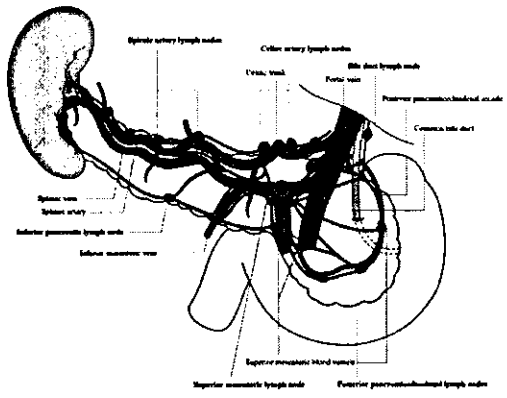

Fig. 15. Lymph nodes around the pancreas and along the biliary tract (posterior view)

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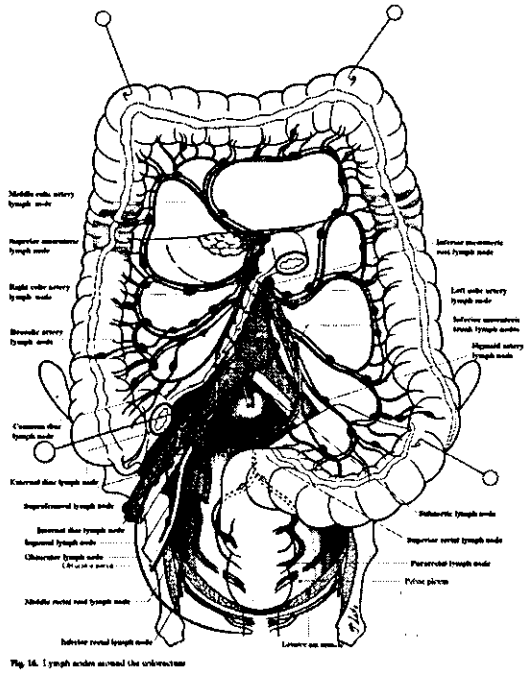

Fig. 16. Lymph nodes around the colon/rectum

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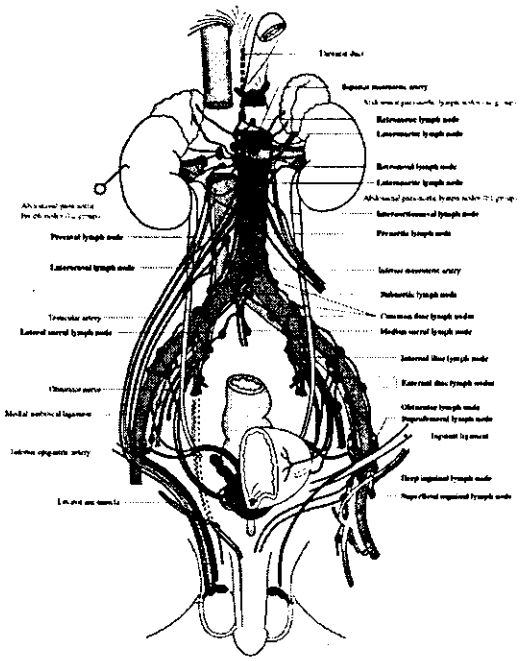

Fig. 17. Lymph nodes in the urogenital system (male)

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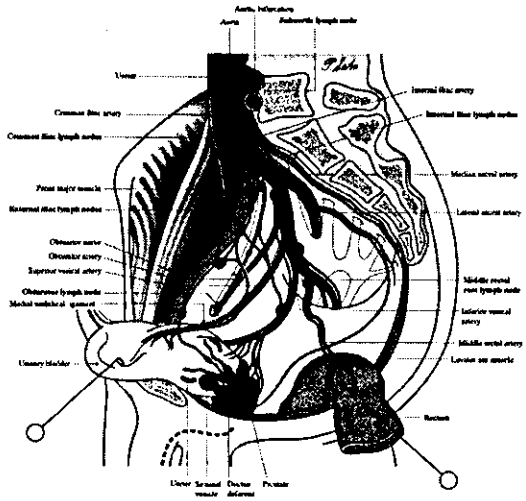

Fig. 18. Lymph nodes in the pelvis (male)

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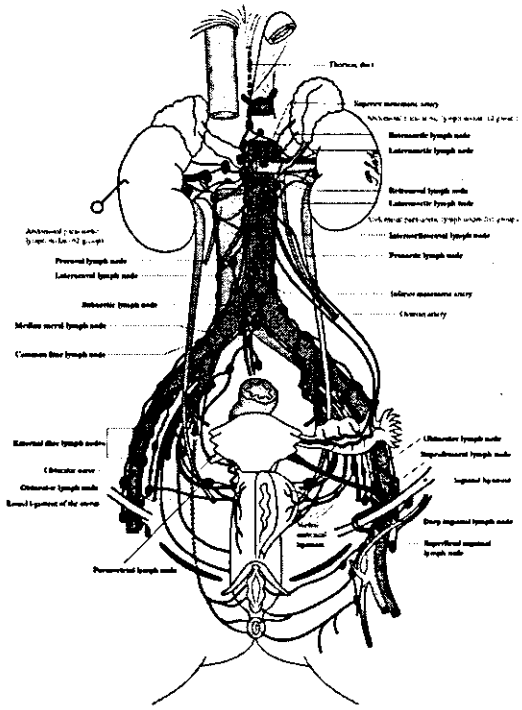

Fig. 19. Lymph nodes in the urogenital system (female)

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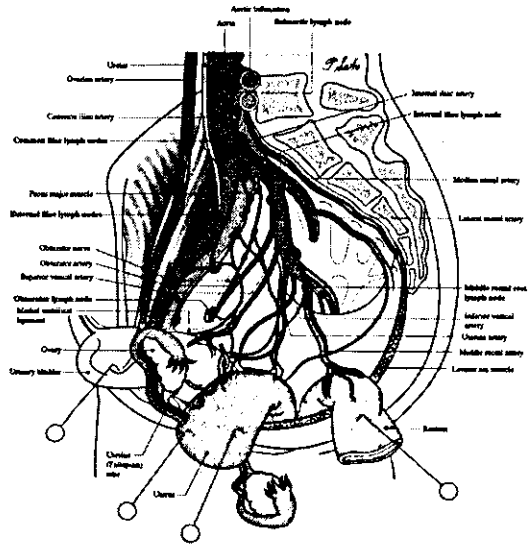

Fig. 20. Lymph nodes in the pelvis (female)

●2003増刊特集●女性診療科医のための薬物療法マニュアル

薬　剤

5．婦人科で用いられる抗癌剤

5. Chemotherapeutic agents in gynecologic cancer

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Key Words プラチナ製剤，タキサン，トポイソメラーゼⅠ/Ⅱ阻害剤

summary

婦人科で用いられる抗癌剤にはプラチナ製剤，アルキル化剤，タキサン，植物アルカロイド，トポイソメラーゼⅠ/Ⅱ阻害剤，代謝拮抗剤，抗癌性抗生物質などがあげられる．それらの効果，禁忌，用量，作用機序，副作用，臨床成績などを簡単に述べる．

はじめに

婦人科癌化学療法の歴史は卵巣癌における歴史そのものである．アルキル化剤のナイトロジェンマスタード単独使用が1950年代に始まり，その後シクロフォスファミド（CPA）やフルオロウラシル（5-FU），塩酸ドキソルビシン（ADR）などが卵巣癌に対する抗癌剤として単剤で用いられるようになった．しかし，当時の化学療法の効果は満足のいく成績ではなかった．

1960年代に開発されたシスプラチン（CDDP）は卵巣癌に対して極めて高い奏効率を示し，その治療法を大きく変化させた[1]．その後CDDPとADR・CPAとの多剤併用療法（CAP療法）が上皮性卵巣癌の標準治療法となり，卵巣癌の短期予後は飛躍的に改善した[1]．

さらにADRの心毒性を軽減するための誘導体の開発やCDDPの腎毒性をおさえたカルボプラチン（CBDCA）の開発によりCAP療法も少しずつ変遷をとげた．

しかし，1980年代後半になりプラチナに対する薬剤耐性が卵巣癌における最大の予後因子となり，プラチナ耐性癌に対する新たな抗癌剤の登場が待たれた．この時期に開発された新規抗癌剤として，エトポシド（VP-16），塩酸イリノテカン（CPT-11），パクリタキセル（PTX）がある．これらの抗癌剤はプラチナ製剤との交差耐性を示さないことから，卵巣癌に対する化学療法の選択の幅がさらに広がり，本邦ではPTXが1997年末より臨床応用され，ようやく欧米と足並みがそろった状況である．

さらに1990年代には癌化学療法において画期的な出来事としてCDDPの主な副作用である骨髄抑制の対策としての薬剤，いわゆるG-CSF製剤が開発され比較的用量の多い治療法の試みも可能となった．また癌化学療法の主な自覚症状である悪心・嘔吐も多数の$5HT_3$レセプター拮抗薬の開発により急性期では80%以上制御され，治療のコンプライアンスは格段に向上した．

ほかの婦人科癌においても化学療法の進歩は目覚ましいものがある．とくに胚細胞腫瘍でのBEP療法，絨毛性疾患におけるEMA-CO療法などの

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臨床応用で大幅な予後改善効果を認めている．子宮頸癌においては従来の放射線療法単独のみならず，化学療法との同時併用（Concurrent Chemoradiation：CCR）や術前化学療法（Neoadjuvant Chemotherapy：NAC）なども施行されるようになった．また子宮体癌においてはCAP療法のみならずPTXを併用した治療が検討されている．

この稿では作用機序別に個別の薬剤を表1～3にまとめ，さらにそれらの併用療法を疾患別に整理して，代表的な化学療法について概説する．

表1　婦人科癌で現在本邦で使用される抗癌剤（プラチナ・タキサン）

分類	一般名（略語）	商品名	作用機序	用量規制毒性（DLT）	使用上の注意
プラチナ製剤	Cisplatin（CDDP）	ブリプラチン ランダ	DNAの架橋形成による細胞障害	腎不全 末梢神経障害 聴覚障害	投与前の十分な補液
	Carboplati(CBDCA)	パラプラチン	CDDPと同じ	骨髄抑制（とくに血小板減少）	悪心・嘔吐CDDPより軽度
	Nedaplatin（254-S）	ネダプラチン	CDDPアナログ	骨髄抑制	
タキサン	Paclitaxel（PTX）	タキソール	微小管の安定化と過剰形成により細胞分裂を阻害	骨髄抑制　過敏症 末梢神経障害 脱毛	過敏反応予防に前投薬必要　非吸収性の輸液セットの使用
	Docetaxel（DTX）	タキソテール	PTXと同じ	骨髄抑制　一過性の浮腫　末梢神経障害はPTXより少ない	前投薬原則不要

表2　婦人科癌で現在本邦で使用される抗癌剤（抗癌性抗生物質・植物アルカロイド）

分類	一般名（略語）	商品名	作用機序	用量規制毒性（DLT）	使用上の注意
抗癌性抗生物質	Doxorubicin（ADR）	アドリアシン	DNA/RNAの合成阻害と細胞膜の障害		心毒性がある
	Epirubicin(Epi-ADR)	エピルビシン	ADRと同じ	骨髄抑制	ADRに比べ心毒性や消化器毒性が少ない
	Mitomycin C(MMC)	マイトマイシン	ADRと同じ	骨髄抑制	
	Bleomycin（BLM）	ブレオ	DNA切断　チミン・チミジンの取り込み	肺毒性 （肺線維症）	
トポイソメラーゼ阻害剤	Irinotecan（CPT-11）	トポテシン カンプト	トポイソメラーゼI阻害によるDNA合成阻害 （S期特異性）	骨髄抑制 下痢	重篤な下痢で致命的になることがある
	Etoposide（VP-16）	ベプシド ラステット	トポイソメラーゼII阻害によるDNA合成阻害 （G2/S期特異性）	骨髄抑制	大量使用で続発性白血病を誘発することがある
植物アルカロイド	ビンクリスチン(VCR) ビンブラスチン(VLB)	オンコビン エクザール	微小管と結合して分裂阻害		

表3　婦人科癌で現在本邦で使用される抗癌剤（アルキル化剤・代謝拮抗剤）

分類	一般名（略語）	商品名	作用機序	用量規制毒性（DLT）	使用上の注意
アルキル化剤	Cyclophosphamide（CPA）	エンドキサン	DNA/RNAをアルキル化することで転写を阻害	骨髄抑制	大量投与で出血性膀胱炎
	Ifosphamide（IFM）	イホマイド	CPAの誘導体だが交差耐性はない	神経毒性 出血性膀胱炎	中枢神経系の毒性がある
代謝拮抗剤	Methotrexate（MTX）	MTX	葉酸代謝拮抗剤		
	5-Fluorouracil（5-FU）	5FU	ピリミジン拮抗薬		

表4　上皮性卵巣癌の抗癌剤の組み合わせ

併用療法	薬剤（略語）	投与量	投与日	休薬期間
CAP	CPA	500mg/m²	day 1	3～4 weeks
	ADR	50mg/m²	day 1	
	CDDP（CBDCA）	75mg/m²（AUC= 5～9）	day 1	
CP/CJ	CPA	900（or750）mg/m²	day 1	3～4 weeks
	CDDP（CBDCA）	75mg/m²（AUC= 5～9）	day 1	
TP	PTX	175mg/m²	day 1（24hrs. Inj.）	3～4 weeks
	CDDP	75mg/m² day1	day 1	
TJ	PTX	175mg/m²	day 1（3hrs. Inj.）	3～4 weeks
	CBDCA	AUC= 6-7.5	day 1	
CPT-11+CDDP	CPT-11	50～60mg/m²	day 1/ 8 /15	4 weeks
	CDDP	60mg/m²	day 1	
CPT-11+MMC	CPT-11	120～140mg/m²	day 1/15	3 weeks
	MMC	7mg/m²	day 1/15	
EP	VP-16	100mg/body	day 1-5	3～4 weeks
	CDDP	50mg/m²	day 1	
DP	DTX	75mg/m²	day 1	3～4 weeks
	CDDP	75mg/m²	day 1	

プラチナ製剤（白金錯体）

Cisplatinum（CDDP），Carboplatin（CBDCA），Nedaplatin（254-S）

プラチナ製剤は婦人科癌化学治療の中心の一つであるが，その作用機序はDNAの架橋形成により細胞分裂を阻害し，増殖を抑制する．プラチナ製剤は現在CDDP，CBDCA，254-Sの3剤である．この3剤は現在臨床の場で多く使用されており，単剤でも多剤併用療法でもその有効性に差は認められない．これまではCAP療法が標準化学療法として卵巣癌に対し行われてきたが，近年はPTXにプラチナ製剤を併用する治療を卵巣癌の標準治療[2]とした考えから，CDDPとCBDCAのどちらが併用薬として有用かの比較試験がGOG[3]，AGO[4]などで行われ，臨床的効果は同等で副作用が軽度なCBDCAが標準となっている（表4）．

副作用であるが，CDDPは腎毒性が強いため投与の前日から十分量の水分投与を必要とする．CBDCAではその必要がないが，その投与量の決定には通常カルバートの計算式「投与量（mg）＝AUC値（GFR＋25）」が用いられ，腎機能に応じた投与量の設定が行われている．その他にCDDP

はCBDCAに比べ嘔気・嘔吐が強く，CBDCAは血小板減少が用量制限因子（DLF）となることがある．

子宮体癌ではCAP（CDDP＋ADR＋CPA）療法が広く行われている（表5）．

進行癌および再発癌に対して45%前後の奏効率と報告[5]されており，CAP療法の有効性が認められた．

子宮頸癌ではCDDPの開発にともないその化学療法の成績は向上している．主な多剤併用化学療法としてPVB（CDDP＋ビンブラスチン（VLB）＋ブレオマイシン（BLM），BOMP（BLM＋ビンクリスチン（VCR）＋マイトマイシンC（MMC）＋CDDP），MEP（MMC＋エトポシド（VP-16）＋CDDP）などの報告がある（表6）．これらの治療は進行，再発症例に行った場合は20～50%の奏効率との報告がなされている．

これに対し後治療を前提としたNACとして局所進行例を対象とした場合その奏効率は70%以上と高く，その有効性が示唆され，現在臨床研究（RCT）が行われている．

また最近放射線療法にFP（CDDP＋5-FU）を併用したCCR療法も極めて注目され[6]，世界中で多くのRCTが行われ，標準治療の検討がなされている．

ネダプラチン（254-S）はCDDPの誘導体であるが，骨髄抑制がDLFとなる．CDDPの代わりに254-Sを用いたBOMP療法（modified-BOMP）が当科においても行われており一定の治療効果を認めている．

表5　子宮体癌の抗癌剤の組み合わせ

併用療法	薬剤	投与量	投与日	休薬期間
CAP	CPA	500mg/m²	day 1	3～4 weeks
	ADR	30-50mg/m²	day 1	
	CDDP	50-75mg/m²	day 1	
CA	CPA	500mg/m²	day 1	3～4 weeks
	ADR	60mg/m²	day 1	
AP	ADR	50mg/m²	day 1	4 weeks
	CDDP	50mg/m²	day 1	
TAP	PTX	135mg/m²	day 1	3～4 weeks
	ADR	30mg/m²	day 1	
	CDDP	50mg/m²	day 1	

表6　子宮頸癌の抗癌剤の組み合わせ

併用療法	薬剤	投与量	投与日	休薬期間
BOMP	BLM	7mg/m²	day 1	4 weeks
	VCR	0.7mg/m²	day 1	
	MMC	7mg/m²	day 1	
	CDDP	50mg/m²	day 1	
PVB	CDDP	60mg/m²	day 1	4 weeks
	VBL	4mg/m²	day 1	
	BLM	15mg/m²	day 1	
FP	5-FU	500mg/m²	day 2～5	3 weeks
	CDDP	50mg/m²	day 1	(放射線併用)
PAM	CDDP	70mg/m²	day 1	4 weeks
	ADR	40mg/m²	day 1	(頸部腺癌に効果)
	MMC	5mg/m²	day 2～3	