

## CHAPTER III

# GYNECOLOGIC TREATMENT MEASURES

In planning treatment for a patient with a pelvic disorder it must be kept in mind that in many instances the pelvic disturbance is only the local manifestation of some general functional derangement, and that even in the case of a strictly local lesion adequate general functioning is necessary to full local restoration. This fact, so important in planning effective treatment, is becoming more and more evident as modern research reveals the details of the interlocking system of endocrine, vitamin, and other nutritional controls.

Treatment of the gynecologic patient therefore must begin, like the examination, with attention to general conditions. This is to avoid wasting time and expense on prolonged treatment for some local disorder the clearing up of which can be attained only by a combination treatment correcting also other serious derangements. The hasty dosing with ovarian hormones for all pelvic ills is a case in point, and the same may be said of the easy yielding to the indiscriminate and prolonged use of many other remedies which the obliging salesman highly recommends for disorders about which he is blissfully ignorant.

Having ascertained that the patient is in good general condition or arranged for adequate care of any obvious deficiency in that direction, we are ready to consider what additional measures may aid in removing the pelvic disturbance. These special therapeutic aids may be grouped under the following headings:

- Endocrines
- Vitamins
- Bactericides
- Hemostatics
- Plasma Balance
- Allergy Treatment
- Thermotherapy (fever therapy and refrigeration)
- Neurotherapy and Psychotherapy
- Local Measures

How do these various remedies bring about desired changes in pelvic functioning? The determination of the details of changes brought about in tissues and functioning by different medicines belongs to the large subject of pharmacology. While there is not space here for consideration of this general feature of therapy, it is well to call attention to its importance in the understanding and rational application of the various remedial agents. Functioning of the internal organs is conditioned largely by the autonomic nervous system, which has a set of accelerator (motor) fibers and inhibitory fibers extending to all organs. This involuntary nerve-control apparatus governing function is acted upon by different remedies in different ways, the details of which have

been worked out by pharmacologic investigation. Fig. 324 shows the intimate connection between the autonomic nerve terminals and the effects of certain medicines. Somewhat similar connections between minute anatomy and physiology and remedial action extend to many remedies employed. Not all medicines act through the nerves; some produce their effects directly on the functioning cells.

Incidentally, such studies, extending throughout the great field of experimentation, bring us ever nearer to that most interesting contact-point where minute structural change becomes functional manifestation. Ordinarily we think of structure as something fixed, visible, palpable, with function as the evanescent, formless, nonmaterial result. The great problem of modern medical research is the determination of exactly what takes place in the cell to produce

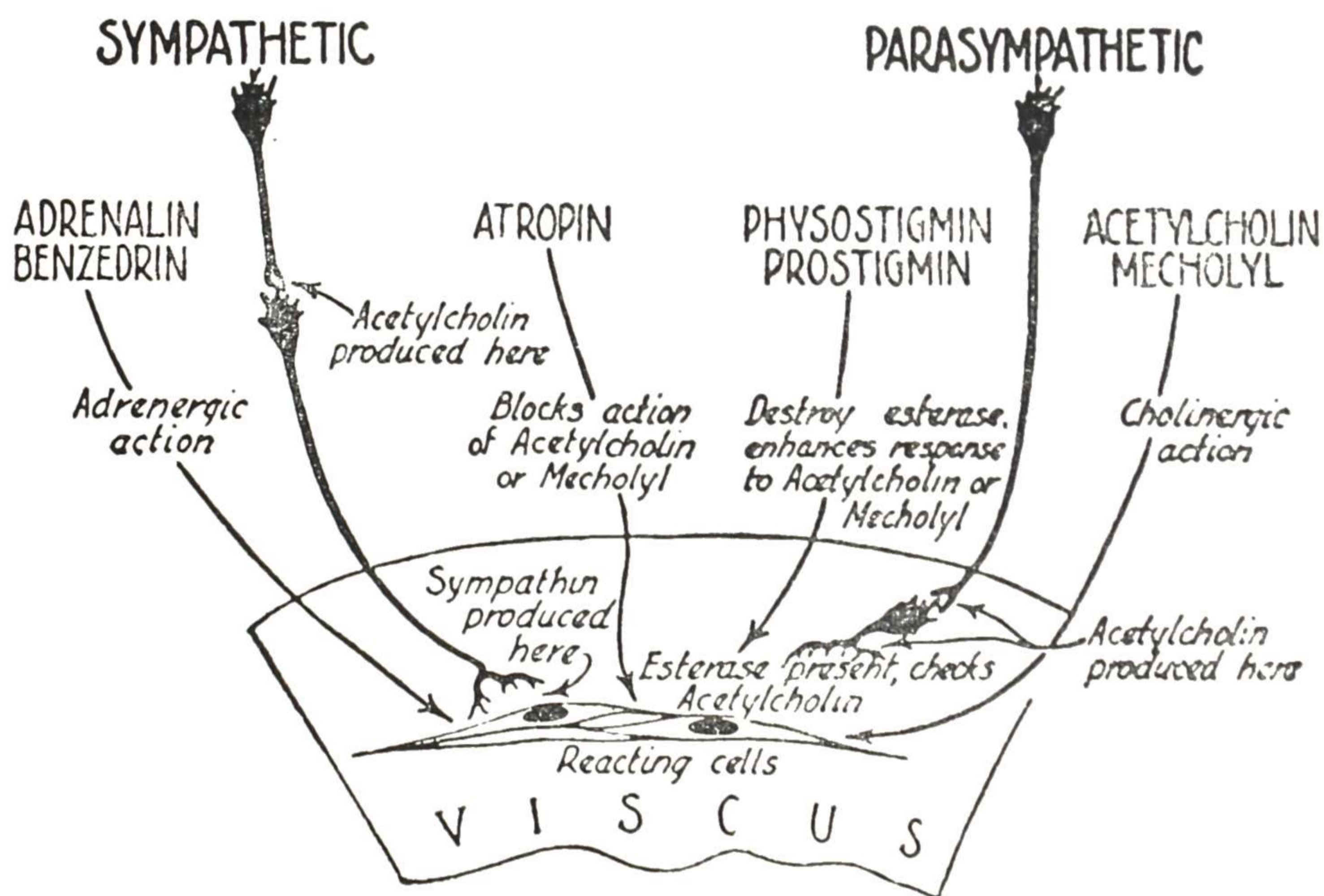


Fig. 324.—Presentation by Myerson of the working hypothesis of human autonomic pharmacology. (Myerson—J. A. M. A.)

each of the multitude of normal functions (physiology) and of abnormal results (pathology) and of remedial effects (pharmacology). Hence the shift in emphasis, in study and teaching, from the gross structure to that minute and still strictly-censored manufacturing plant, the cell.

Though not all connections between remedial agents and their results have been worked out, the study of those that are known is important for the most effective treatment in any field.

The purpose of this chapter is to give a general view of the remedial resources available for the correction of disturbances in this field and also some indication as to the types of disturbance amenable to certain classes of remedies. The application of therapeutic measures to the treatment of particular diseases will be discussed in the chapters on those diseases.

## ENDOCRINES

Endocrine therapy is useful in many functional disturbances of the genital tract and in some organic diseases. The hormones particularly concerned in gynecologic disturbances are considered in the following order: thyroid, parathyroid, pituitary and placental, ovarian, testicular, adrenal, pancreatic (insulin). Standardized preparations of the hormones having gonadal effects are given later in the table.

### Thyroid Hormones

The interrelationship between the thyroid and the gonads has long been recognized, and thyroid has been used in sterility, amenorrhea, dysmenorrhea, and menorrhagia. The mechanism of this relationship, however, is not so well understood. Numerous methods have been used to study the relations, and many facts have been determined, including the following: (a) estrin increases the basal metabolism in ovariectomized women; (b) estrin decreases the basal metabolism in ovariectomized rats, in hyperthyroid rats, and in normal guinea pigs and rabbits.

The effect of the estrogens on the thyroid is probably indirect, through the inhibitory action on the pituitary.

### Parathyroid Hormones

A relationship between the female sex hormones and the parathyroids is known to exist, though the mechanism is still obscure. Postthyroidectomy tetany rarely occurs in men. Attacks of tetany are frequently associated with the menstrual cycle, and in cases of chronic tetany the acute attacks occur regularly at menstruation. A study of the calcium and phosphorus blood levels reveals very little deviation from the normal. The sex hormones evidently affect the neuromuscular excitability in human parathyroid tetany through a separate mechanism. The diminution of ovarian activity by radiation helps to control the aggravating symptoms in selected cases.

### Pituitary Hormones

The pituitary hormones have been discussed at length in Chapter I. The chief ones used in treatment are the gonadotropins—those derived from the pituitary itself and those derived from the placenta. The latter are called chorionic gonadotropins and they come from two sources, the urine of pregnant women and the serum of pregnant mares. Their uses in menstrual disturbances and in sterility are discussed in the appropriate chapters.

### Ovarian Hormones

The *follicular* or estrogenic hormones used in therapy, given in approximately their ascending order of effectiveness in clinical use, are: estriol, estrone, estradiol, estradiol benzoate, estradiol dipropionate.

Since the isolation of estradiol from follicular fluid it is generally conceded to be the true follicular hormone found in the ovary. Estrone, or theelin, and estriol, or theelol, are excretion products of dihydroxytheelin, or estradiol. A benzoic acid ester of estradiol that has been prepared synthetically is more effective than estradiol because it facilitates the use of a larger dosage and the effect is prolonged. Because of the confusion in dosage designation caused by the introduction of these two synthetic substances, each with a different criterion for standardization, an explanation of the present status of dosage is given.

One international unit of estrone has a specific estrus-producing activity of  $\frac{1}{10,000}$  mg. of the crystalline estrone standard, hence 1 mg. of estrone equals 10,000 international units. The dosage of crystalline estradiol is expressed in Allen-Doisy rat units, or by weight, 1 mg. equals 12,000 rat units. No international unit has been established for estradiol. Estradiol benzoate is standardized in Allen-Doisy rat units and also in international benzoate units. One international benzoate unit has an estrus-producing activity of  $\frac{1}{10,000}$  mg. of a standard preparation of estradiol benzoate. One rat unit of estradiol benzoate is approximately equal in activity to two international benzoate units.

The hormones mentioned are used chiefly for the treatment of menstrual disturbances and sterility and troublesome climacteric symptoms.

In addition to the follicular ovarian hormones (natural estrogens) there are certain other preparations having estrogenic effects—for example, stilbestrol, octofollin, and hexestrol. Stilbestrol (diethylstilbestrol) is a synthetic substance related to the stilbenes. It has an estrogenic potency three or four times that of estrone, and also is relatively inexpensive. It has certain disagreeable toxic effects with some patients (nausea, dizziness, etc.). However, these may usually be avoided by (a) limiting the dosage to the minimum required to control the symptoms (ordinarily  $\frac{1}{2}$  mg. or less daily), (b) giving the dose at bedtime, and (c) interrupting the treatment at regular intervals as mentioned under Methods of Administration (page 256). The advantages and disadvantages of stilbestrol are now well established by a mass of experimental and clinical reports (1943 review by Abarbanel et al.) and it is put on the market in convenient forms by various drug firms.

Hexestrol (dihydrostilbestrol) is a less potent and less toxic preparation of the stilbene group, with clinical effects accordingly. The detailed results obtained by its use in several series of cases have been reported, a 1943 report being that of McElroy, Snyder and Clark.

Octofollin (2-4-di(parahydroxyphenyl)-3-ethyl hexane) is a synthetic estrogenic substance different from the stilbene group. Several series of results have been reported, a recent one being by Roberts, Loeffel, and MacBryde, who conclude (1) that octofollin is effective in the treatment of hypogonadal symptoms in women, (2) that it is relatively nontoxic, and (3) that the effective oral dose is from 5 to 10 mg. daily when continuous treatment is used or from 10 to 15 mg. daily for interrupted treatment.

The *corpus luteum* hormone (progesterone) is used intramuscularly as progesterone and orally as a hydroxyprogesterone. The chief clinical uses of progesterone are for menstrual disturbances and sterility and threatened abortion.

The employment of these various hormones in particular disorders is taken up under those disorders. A helpful article on the clinical use of the ovarian hormones was recently given by Willard M. Allen (see Reference List).

### Testicular Hormones

The action of the male hormone has been discussed in Chapter I. Testosterone is the most potent of the androgens. It can be given intramuscularly as testosterone propionate, by injection as free testosterone, orally as methyl testosterone, or by implantation as testosterone.

### Adrenal Hormones

The important relationship of the adrenal cortex hormones (corticosterone, desoxycorticosterone) to the sex hormones is being gradually elucidated. The

TABLE OF STANDARDIZED HORMONE PREPARATIONS  
HAVING GONADAL EFFECTS

(Shows types of preparations, not complete list.)

ESTROGENS	Intra- muscu- larly	Estrone (Theelin)	Theelin in oil (Parke, Davis)	0.1, 0.2, 0.5, 1.0 mg. (0.1 mg. equals 1,000 International Units)
			Estrone (Lilly)	0.1, 0.2, 1.0 mg.
			Estrone (Abbott)	0.1, 0.2, 0.5, 1.0 mg.
		Estrogens from preg- nancy urine (Estrone, Estradiol, Equilin, Equilenin, Hippulin)	Amniotin (Squibb)	0.2, 0.5, 1.0, 2.0 mg.
			Estrogenic hormones (Upjohn)	0.2, 1.0 mg.
			Folestrin (Armour)	0.2, 0.5, 1.0, 2.0 mg.
			Menformon (Roche- Organon)	1,000 I.U. 5,000 I.U. 10,000 I.U.
			Plestrin (Harrower)	0.2, 0.5, 1.0 mg.
			Thelestrin (Carnrick)	0.2, 1.0 mg.
		Estradiol benzoate	Progynon-B (Schering)	500 R.U. about 1,000 I.U. or 0.083 mg. 1,000 R.U. or 0.166 mg. 2,000 R.U. or 0.333 mg. 6,000 R.U. or 1.000 mg. 10,000 R.U. or 1.666 mg.
			Ben-Ovocycin (Ciba)	0.1, 0.2, 1.0 mg.
			Dimenformon (Roche- Organon)	1,000, 2,000, 10,000 R.U.
		Estradiol dipropionate	Di-Ovocycin (Ciba)	0.1, 0.2, 1.0, 2.5, 5.0 mg.
			Progynon DP (Schering)	0.1, 0.2, 1.0, 2.5, 5.0 mg.
			Follarco (Schieffelin)	0.1, 0.2, 0.5, 1.0 mg.

ESTROGENS  
Continued

Orally	Estriol (Theelol)	Theelol kapseals (Parke, Davis)	0.06, 0.12, 0.24 mg.
		Estriol capsules (Abbott)	0.06, 0.12, 0.24 mg.
		Emmenin liquid	120 Day Oral Units in 4 c.c.
		Emmenin tablets (Ayerst-McKenna)	120 Day Oral Units per tablet
		Estrogenic hormone capsules (Upjohn)	1,000, 2,000, I.U.
		Estriol pulvules (Lilly)	0.06, 0.12 mg.
		Folestrin granules (Armour)	1,000 2,000, 4,000 I.U.
		Plestrin capsules (Harrower)	1,000, 2,000, I.U.
		Amniotin capsules (Squibb)	1,000, 2,000, I.U.
	Follareo (Schieffelin)	1,000, 5,000, 10,000 I.U.	
	Estradiol	Progynon DH tablets	0.1, 0.5 mg.
		Progynon DH solution (Schering)	60 R.U. per c.c.
		Dimenformon tablets (Roche-Organon)	1/24 mg., 1/6 mg.
		Ovocylin tablets (Ciba)	0.1, 0.2, 0.5 mg.
	Nasal Spray	Amniotin in oil (Ayerst-McKenna)	20,000 I.U. in 30°c.c.
Progynon DH nasal spray (Schering)		0.4 mg. (about 4,800 R.U.) per 30 c.c.	
Vaginal Suppositories	Theelin suppositories (Parke, Davis)	0.2 mg., 2,000 I.U.	
	Amniotin pessaries (Squibb)	0.1, 0.2 mg.	
	Kolpon inserts (Roche-Organon)	juvenile 0.05 mg. adult 0.10 mg.	
	Folestrin suppositories (Armour)	0.1, 0.2 mg.	
	Progynon DH suppositories (Schering)	juvenile 480 R.U. adult 480 R.U. 4,800 R.U. (Estradiol)	
	Ovocylin suppositories (Ciba)	juvenile 0.04 mg. adult 0.04 mg.	
Ointment	Progynon DH ointment (Schering)	360 R.U. per Gm. 1,800 R.U. per Gm. (Estradiol)	
	Ovocylin ointment (Ciba)	0.03, 0.15 mg. per Gm. (Estradiol)	
Synthetic Chemicals with Estrogenic Action			
	Stilbestrol tablets (various firms)	0.1, 0.25, 0.5, 1, 5 mg.	
	Hexestrol tablets (various firms)	0.1, 0.25, 0.5, 1, 3 mg.	
	Octofollin tablets (Schieffelin)	0.5, 1, 2, 5 mg.	

PROGESTERONE	Intramuscularly	Lipo-Lutein (Parke, Davis)	
		Proluton (Schering)	½ mg., 1, 2, 5, 10 mg.
		Nalutron (Winthrop)	1, 2, 5 mg.
		Progestin (Lilly)	1 mg.
		Progestin (Upjohn)	1, 2 mg.
		Progestin (Roche-Organon)	1, 5 mg.
		Progesterone (Carnrick)	½, 1, 5 mg.
	Orally	Lutocilin (Ciba)	1, 5, 10 mg.
		Pranone (Schering)	5, 10 mg.
ANTERIOR PITUITARY GONADO- TROPINS	Intramuscularly	Preloban (Winthrop)	150 gonadotropic R.U.
		Ambinon (Roche-Organon)	50 gonadotropic R.U.
		Prephysin (Chappel)	25 gonadotropic R.U. 100 gonadotropic R.U.
		Gonadotropic Factor (Armour)	300 Collip U.
		Gynatrin (Searle)	100 R.U.
		Gonadotropic Factor (Ayerst- McKenna)	
WHOLE ANTERIOR PITUITARY	Intramuscularly	Ant. Pituitary Extract (Squibb)	
		Ant. Pituitary (Sharp & Dohme)	
		Polyansyn (Armour)	
PREGNANT MARE'S SERUM	Intramuscularly and Intravenously	Gonadogen (Upjohn)	10 Cortland-Nelson Units = 200 I.U. 20 Cortland-Nelson Units = 400 I.U.
		Anteron (Schering)	250 I.U. 400 I.U.
		Gonadin (Cutter)	200 I.U.

<p><b>ANTERIOR PITUITARY-LIKE HORMONES</b> from pregnancy urine or chorionic gonadotropin</p>	<p>Intramuscularly</p>	<p>{</p>	Antuitrin-S (Parke, Davis)	120 I.U. 600 I.U.	
			Follutein (Squibb)	100 R.U. 500 R.U.	Stable a year
			Korotrin (powder) (Winthrop)	100 I.U. 500 I.U.	Stable indefinitely
			Pregnyl (powder) (Roche-Organon)	100 I.U. 500 I.U.	
			A.P.L. (Ayerst-McKenna)	100 I.U. 500 I.U. 1,000 I.U.	
			Pranturon (powder) (Schering)	150 I.U. 750 I.U.	
			Apestrin (Harrower)	100 I.U.	
<p><b>MALE HORMONES</b></p>	<p>Intra-muscularly</p>	<p>{ Testosterone propionate</p>	Oreton (Schering)	5, 10, 25 mg.	
			Pernandren (Ciba)	5, 10, 25 mg.	
			Neo-Hombreol (Roche-Organon)	5, 10, 25 mg.	
	<p>Ointment</p>	<p>{ Testosterone propionate</p>	Oreton F toplicator (Schering)	2 mg. each	
			Pernandren ointlets (Ciba)	4 mg. each	
			Neo-Hombreol dosules (Roche-Organon)	4 mg. each	
	<p>Orally</p>	<p>{ Methyl-testosterone</p>	Oreton M (Schering)	10 mg.	
			Metrandren (Ciba)	10 mg.	
			Neo-Hombreol (Roche-Organon)	10 mg.	
<p><b>ADRENAL CORTEX</b></p>	<p>{ Intramuscularly Intravenously Orally</p>	<p>{</p>	Cortate (Schering)	5 mg. (desoxycorticosterone)	
			Cortalex (Upjohn)	Extract of 5 Gm. of adrenal tissue	
			Adrenal Cortex Extract (Wilson)		
			Precorten (Ciba)	5 mg. (desoxycorticosterone)	



chemical formula of desoxycorticosterone is the same as that of progesterone with the addition of a hydroxyl group on the 21-carbon atom. Progesterone has been isolated from the adrenal cortex, and the life of adrenalectomized rats can be maintained by the administration of progesterone.

An androgenic substance (andrenosterone) having one-fifth the potency of androsterone has been isolated from the adrenal cortex.

Though as yet there are no criteria for the use of adrenal cortex in pelvic endocrine disorders in women, its use will probably be extended in that direction as our knowledge of its various actions is enlarged.

### **Insulin**

Insulin, the hormone from Langerhans cells of the pancreas, has been found to give relief in certain cases of dysmenorrhea. Its mode of action has not been worked out, but it has been successfully employed in patients with low, normal, and high blood sugar levels.

## **VITAMINS**

The rapidly developing knowledge of vitamins has brought considerable aid in the handling of pelvic disorders. Fig. 325 shows the principal vitamins and their connections and time of discovery. Those of particular importance in genital tract disturbances are A, B, C, E, and K. The vitamin deficiencies produce nutritional defects which lower ovarian function and, if continued, produce degenerative changes in ovarian structure.

How are these serious local nutritional effects brought about? Is it a direct or an indirect effect? The intimate relationship existing between general nutrition and vitamins and endocrines was demonstrated in this connection by Stephens and Willard Allen. They found that in guinea pigs with undernourishment sufficient to reduce body weight 20 to 30 per cent in two weeks, there were retrogressive and atrophic changes in the ovary. These were similar to those found after hypophysectomy. Vitamin supplements did not affect the result, but the administration of gonadotropic hormones did—indicating that the degenerative changes in the ovary were due in part to the inability of the undernourished pituitary to produce gonadotropic hormones in sufficient quantity to maintain ovarian structure and function. Similar results of the effects of inanition on the thyroid had been demonstrated by Stephens.

### **Vitamin A**

Vitamin A is a factor in maintaining epithelium in normal condition, and epithelial cells represent to a large extent the functioning part of each organ. The higher specialized the epithelium becomes, the earlier slight nutritional defects are lightly to be noticed. One of the first noticeable effects of vitamin A deficiency is on a specialized tissue of the eye, causing difficulty in seeing in dim light. This "night blindness" is likely to be accompanied with general lack of vigor, easy fatigue, sleeplessness, dry hair, and rough skin.

The maintenance of normal squamous epithelium depends on the normal nutrition of the basal layer, which supplies new cells as the surface cells become keratinized and cast off. Keratinization represents a normal degenerative change, but under vitamin deficiency

it becomes exaggerated to a pathological condition, which in the cornea may lead to impaired vision and even to ulceration. In the skin, the hyperkeratinization affects especially the hair follicles, causing masses of cells which plug the follicles and produce minute bumps on the skin surface resembling exaggerated "goose skin." This condition, designated keratosis pilaris, lichen pilaris, ichthyosis follicularis, etc., which with its uncomfortable, harsh, dry, itchy condition may affect the vulvar surfaces, has been shown to be due to vitamin deficiency. Lehman and Rappaport state, "Every case in the series investigated by us that might have been designated keratosis pilaris, ichthyosis follicularis or the like proved by photometric test to be deficient in vitamin A and responded to vitamin A therapy."

It was found that vitamin A deficiency produced permanent cornification of the vaginal epithelium in rats.

In castrated rats with diets deficient in vitamin A, estrus could be produced only by the administration of both vitamin A and estrogens, not by either alone. The influence of vitamin A deficiency is evidenced not only in the vaginal mucous membrane but through the gonad glands also. Sutton and Brief found a significant increase in the basophiles or "castration cells" in vitamin-A deficient rats of both sexes, indicating a partial castration effect.

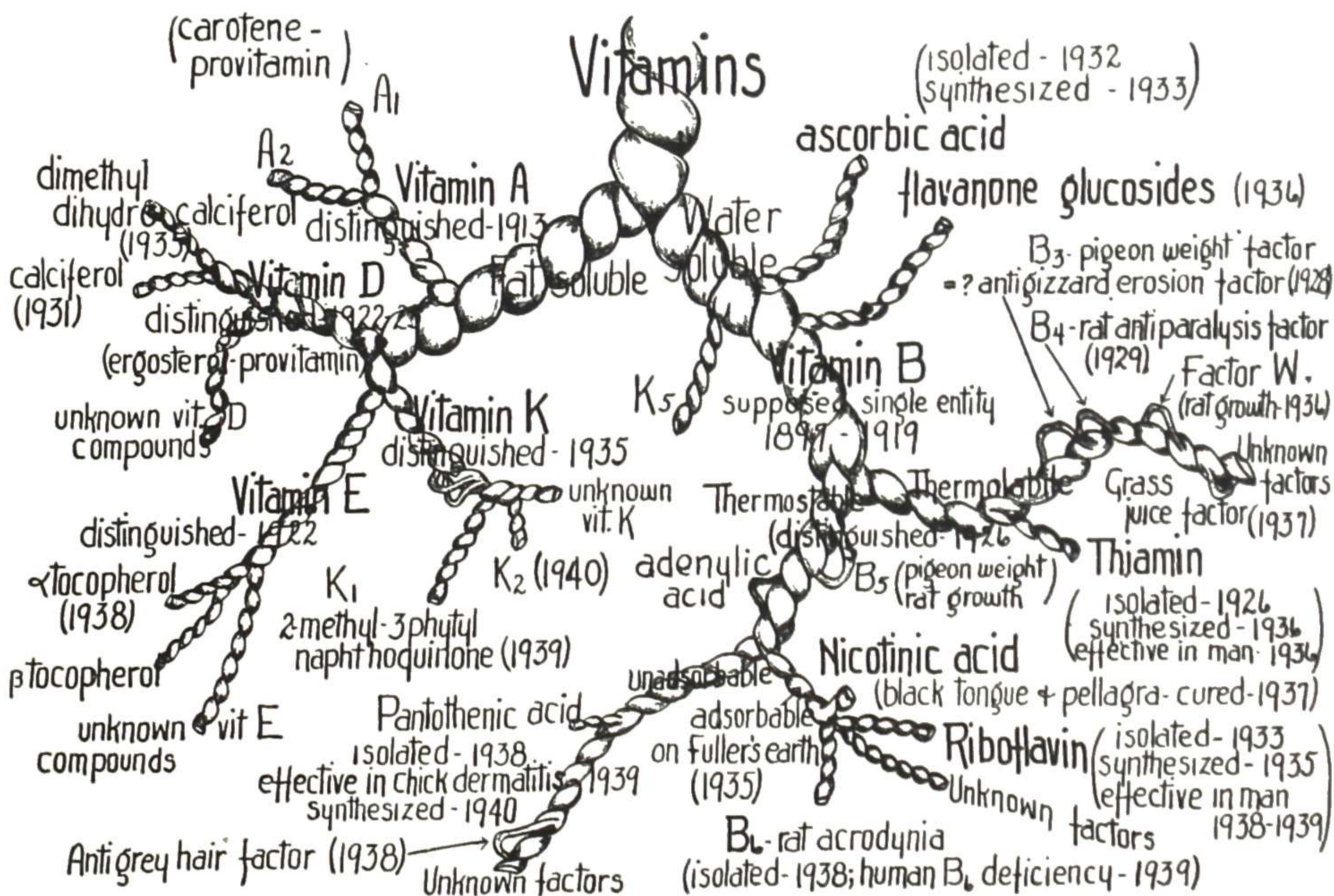


Fig. 325.—Diagrammatic representation of the interrelationship of the vitamins. They are schematically differentiated into the water-soluble and the fat-soluble fractions; the latter group is further separated into its thermolabile and its thermostable components. Certain of these substances have been shown to be essential to human nutrition and effective in the treatment of specific deficiency diseases. The physiologic properties of many are as yet undetermined. (Spies, Hightower and Hubbard—J. A. M. A.)

In the human, relief of senile vaginitis in thirty cases by vitamin A therapy has been reported by Simpson and Mason. In vulvitis due to vitamin A deficiency, the skin becomes dry and rough and later a papillary eruption appears. These papules are formed by hyperkeratosis of the hair follicles. A keratinizing metaplasia of their ducts is responsible for the absence of sweat glands. The sebaceous glands atrophy and undergo the same process. Similar lesions are present also over most of the body in advanced cases, as illustrated in the article by Lehman and Rappaport and also in dermatological textbooks.

Therapy in vitamin A deficiency consists in giving 25,000 unit capsules, ten to twelve per day. Dependable preparations are put out by reliable drug firms under different trade names. A capsule of the above potency is on the

market under the name of afoxin (Winthrop). The treatment is continued until the skin returns to normal or, with vaginitis, until the symptoms clear.

### Vitamin B Complex

Vitamin B Complex is helpful in treating certain cases of neuritis, also in radiation sickness and in loss of appetite and undernourishment. These conditions are found in many gynecological patients, particularly in those having irremovable carcinoma.

Imler and Wammock gave their results in the treatment of twenty-one patients for severe radiation sickness with synthetic vitamin B<sub>1</sub> (thiamin chloride). Quoting from the abstract:

They find that daily injections of 3,000 international units will, in the majority of cases, give rapid and complete relief. Infrequently a recurrence of symptoms requires increase in the dosage. One patient receiving roentgen therapy to the left side of the neck required a temporary increase to 4,500 international units daily by hypodermic injection to control the recurrent nausea and another required 10,000 to eliminate nausea and vomiting. The results obtained with the hypodermic administration are definitely superior to those following the peroral use.

The treatment of outpatients presents a problem in that radiation sickness cannot be satisfactorily relieved by the oral administration of large doses of vitamin B<sub>1</sub>. It is difficult for these patients to retain their confidence and cooperation, with the result that they fail to continue the medication as prescribed and occasionally refuse to follow the course of radiation therapy. This undesirable factor can be overcome by requiring the patient to return for daily injections of vitamin B<sub>1</sub>. Smaller daily doses are more effective than are massive doses given on alternate days.

The dose of B<sub>1</sub> or thiamin hydrochloride for neuritis or malnutrition due to vomiting varies from 5 to 25 mg. daily. Nicotinic acid is helpful in the vaginitis of pellagra patients. In persistent anorexia and in vomiting the effect is often striking and most helpful.

### Vitamin C

Vitamin C (ascorbic acid, cevitamic acid) is the vitamin which prevents scurvy. It is supposed to be important in wound healing. It has been reported helpful in certain cases of internal bleeding.

Wolbach states: "Vitamin C is necessary for the formation of all intercellular substances having collagen as their basis; and its absence prevents the formation of the matrices of white fibrous tissue, cartilage, bone, and dentine." In the excellent "Vitamin Reference Book" by Squibb it is pointed out that the various manifestations of vitamin A deficiency are due in part to failure of endothelial cells to form cement substance. Capillary fragility is common, and consequently minor hemorrhages are relatively common. The reduced immunologic response seen at times may be the result of the lessened ability to form collagen, a substance which aids in segregating infectious organisms. Hence in persistent infection with undernourishment in a gynecological patient, particularly if associated with a hemorrhagic tendency, the possibility of vitamin C deficiency should be considered and standard testing carried out, that vitamin C therapy may be instituted if needed.

Vogt reported that gynecologic hemorrhages in the young may be effectively treated by oral or intravenous administration of cevitamic acid, the

hemorrhage usually stopping after the first injection. Stephens and Hawley reported that large amounts of orange juice given to four patients with hemophilia and two with chronic thrombocytopenic purpura had no effect on the hemorrhagic manifestations, blood picture, or capillary resistance. Boeger and Schroeder found oral administration of vitamin C ineffective, while intravenous use stopped the bleeding and increased thrombocytes.

### Vitamin E

Vitamin E has been called the antisterility vitamin. It is supposed to be an aid to fertility, particularly in the prevention of habitual abortion. There is much variance of opinion on the efficacy of vitamin E in sterility and in threatened abortion, but there are enough reliable reports to indicate that it is definitely helpful in these cases. Shute has made extensive reports on the use of wheat germ oil in threatened abortion and also in senile vaginitis of certain types, and from his extensive experience he concludes that it is exceedingly helpful. Saturation of the patient stopped the bleeding and uterine tenderness promptly in many cases of threatened abortion, and when the germ oil therapy was stopped the bleeding and uterine tenderness returned.

Since the synthesis of vitamin E its potency has been increased about 170 times. Most of the commercial products contain a mixture of alpha and beta tocopherols. Some of the newer products are tocopherex (Squibb), tofoxin (Winthrop), ephynal acetate (Hoffman-LaRoche).

### Vitamin K

Vitamin K is the coagulation vitamin, which regulates the clotting of blood and the control of bleeding. It is designated the "coagulation factor" because it appears necessary to the formation of prothrombin. It was named "K" by its Danish discoverer (Dam) after "Koagulation," as they spell it. Vitamin K deficiency occurs mostly in patients with obstructive jaundice; persons able to handle ordinary balanced diets usually get a sufficient amount apparently. Experiments indicate that the exclusion of bile from the intestine prevents the absorption of vitamin K in the food taken. Hence when administering vitamin K orally, bile salts also must be given.

Its administration preoperatively is indicated in gynecological patients when the clotting time is prolonged, and especially if there is any tendency to jaundice. More recently it has been found to increase the prothrombin in newborn babies suffering from hemorrhagic disease, and its use is advised as a prepartal procedure during the last several weeks of pregnancy. Whether it will be helpful in other types of bleeding has not yet been definitely determined. Some of the commercial preparations are Synkamin (Parke, Davis), Thyloquinone (Squibb), and Quino-thrombin (Lederle).

### General Remarks on Vitamins

Before passing from the subject of vitamins it may be well to call attention to certain general points. These are mentioned in Squibb's vitamin book previously referred to. Clinically recognizable single vitamin deficiencies are rare, but there are many cases of mixed deficiencies involving two or more

vitamins. Also, it is not the clear-cut advanced avitaminosis that is encountered, but mild grades that may be classed as subclinical.

The high incidence of subclinical vitamin deficiency disorders indicate the necessity of adjusting diets where possible, and of providing vitamin supplements where modification of the patient's dietaries is impracticable. The vitamins may be ranked as follows in order of their probable deficiency:

1. Vitamin D: Because it has the most limited distribution.
2. Vitamin B<sub>1</sub>: Because it is stored only to a limited extent, and effects and symptoms of subclinical B<sub>1</sub> avitaminosis are fairly common.
3. Vitamin A: Because it occurs for the most part in the relatively more expensive foodstuffs, and hence is apt to be lacking in many diets.
4. Vitamin C: Because the changing food habits of recent years suggest that, except in the case of infants, there is not likely to be a deficiency of this vitamin.
5. Vitamin E: Last, because the general opinion seems to be that average diets supply a sufficient quantity of this factor.

### **BACTERICIDES**

There are classes of remedial agents directed particularly against invading bacteria. Such invasion may be checked by direct lethal effect on the bacteria or by strengthening the defensive forces of the body so that they accomplish the task. These remedies may be grouped under three headings: bactericidal drugs (chemotherapy), antitoxin and serobacterin treatment, and foreign protein treatment.

#### **Chemotherapy**

In recent years there have been developed certain drugs of the sulfonamide group which by direct or indirect action assist in overcoming infectious processes. These new remedial agents have revolutionized the therapy of infections. They have special indications and contraindications, mentioned in the literature of each, which must be carefully considered when using the drug. Under proper supervision and precautions large doses have been given without harm and with great benefit in various kinds of serious infection, including peritonitis and blood-stream infections. The danger signals are: dizziness, cyanosis, nausea and vomiting, anemia, leucopenia, and fever which appears between the seventh and tenth days of therapy after a preliminary drop in temperature.

Sulfathiazole is specially effective in gonorrhoea. Sulfadiazine is less toxic in large dosage, and the troublesome precipitation of crystals in the urinary tract may be prevented by alkalinizing the urine and giving plenty of water (Gilligan, Garb, and Wheeler). Sulfamerazine has the same advantages and disadvantages as sulfadiazine with somewhat smaller dosage requirements (Hall and Spink).

Penicillin, the remarkable antibacterial agent from common mold, has proved effective in cases resistant to the sulfonamides. However, nearly all is still required by our armed forces, though every effort is being made to increase production so that civilian requirements also may be supplied.

#### **Antitoxin and Bacterin Treatment**

The most striking and certain effects of antitoxin therapy are seen in the cure of diphtheria by diphtheria antitoxin and the prevention of tetanus by antitetanic serum. Antistreptococcal serum has occasionally proved beneficial in puerperal infection and in other forms of acute streptococcal invasion.

Bacterin treatment, or vaccine treatment as it is frequently designated, is based upon the idea of creating active immunization by stimulating the formation of antibodies by injecting killed bacteria or their products in increasing doses. Stock bacterins were used and also autogenous bacterins made from cultures from the patient.

In an endeavor to lessen the marked reaction (fever, etc.) associated with bacterin treatment, bacterin preparations have been treated with corresponding immune serum. Such a treated preparation is designated "serobacterin" or "sensitized" vaccine. There is much less reaction, and the diminution of the troublesome reaction is supposed not to interfere with the stimulation of antibody formation. On account of less reaction, the serobacterins may be used freely, even in very ill patients in whom the bacterin reaction was sometimes dangerous. Another advantage of the serobacterin or immunized vaccine is that the immunity begins at once, while with the plain vaccine eight to ten days are required for the development of immunity, and time is an important factor in effective aid when the body defenses are being overwhelmed by acute infection.

These immunized vaccines are put out under various trade names, such as serobacterins (Mulford) and immunogens (Parke, Davis). The results of treatment with bacterial vaccines have been variable. Some serious cases have been greatly benefited while in others there seemed to be no effect. The fact that this treatment seemed to turn the scales favorably in some desperate cases of blood stream infection, indicates its employment in those cases not yielding to the newer bactericidal drugs and other measures.

In addition to specific bacterins (made from the kind of organism or organisms supposedly responsible for the infection), nonspecific bacterins may be employed, for example typhoid vaccine or colon bacillus vaccine. This method of producing the "nonspecific shock" which arouses the defensive mechanism of the body has been used as a substitute for the foreign protein treatment (described next) to avoid the allergic or anaphylactic reaction of milk or other protein in large quantity.

Krieg reports his experience with 172 patients so treated, using colon bacillus vaccine. The sterilized suspension of colon bacilli was given by intradermal injection. A "series" consisted of six injections, given two injections per week, starting with  $\frac{1}{4}$  c.c. and increasing  $\frac{1}{4}$  c.c. with each injection up to 1 c.c. He found the intradermal method of administration easier to execute, less uncomfortable and safer than either the intravenous use of typhoid vaccine or the intramuscular injection of boiled milk. His conclusions were that the results were about the same as from the more severe type of "nonspecific shock," and the disturbing reactions less severe. Details are given in this article.

### Foreign Protein Treatment

The injection of any foreign protein into the body tends to stimulate the reticulo-endothelial system as an aid to the defence forces. This use of protein is spoken of as "nonspecific" because no particular protein is required. For many years this was used to some extent by the employment of antitoxic serums and bacterin treatment, and it is possible that the foreign protein in the injections was a factor in the results secured. However, the amount in these long-used injections was comparatively small.

Later much larger amounts of foreign protein were injected in the form of milk, with marked beneficial results in many forms of acute inflammation, including pelvic inflammation. The treatment consisted of the intramuscular injection of from 5 to 10 c.c. of sterilized milk. Now there are available special milk preparations put up by manufacturing firms in convenient sterile packages for this purpose, with dosage and directions for that particular preparation in the package.

In addition to the beneficial effects of these "foreign protein" injections, there are certain disadvantages. An important one is hypersensitization, resulting in anaphylactic reaction on second dose with some individuals or allergic reaction on even primary dose with certain allergic persons.

Foreign protein treatment for infections has been largely superseded by chemotherapy with the sulfonamides, which is preferable when it is successful. When, however, it is unsuccessful or contraindicated by developments, foreign protein treatment may be indicated. In an allergic individual or one who has received a previous serum injection recently, it would be preferable to use the plain bacterial vaccine treatment (not serobacterin, which contains serum) of the specific or nonspecific type.

### HEMOSTATICS

Hemostatics act principally in two ways—by constricting the uterine wall and blood vessels and by increasing the general coagulability of the blood. There is also a third way in which bleeding may be lessened, namely, by the action of a hormone or other substance in the uterus affecting the local coagulability of the blood or the permeability of the vessel walls. The presence of such a substance may be a factor in the endocrine regulation of the starting and stopping of the normal menstrual flow.

In the first class belong the various ergot preparations and the pituitrin preparations. In the second class come the calcium preparations. Calcium gluconate is one very largely used. Vitamin K has been described. Other general agents for controlling bleeding in gynecologic cases are fibrinogen or thrombogen preparations, put out under various trade names by different firms, pectin, and snake venom.

Pectin preparations have been shown to act together with calcium in reducing clotting time 40 to 50 per cent. Arhemapectin is one such preparation. It may be given orally or intramuscularly or intravenously. Moccasin venom has been used with success in the treatment of functional bleeding. The undesirable sensitization was a drawback, but Peck and Marx have succeeded in separating the antihemorrhagic factor from that causing the sensitization reactions. In hemophilia, Timperley found that egg white incubated at 37° C. for several days in the presence of potassium bromide gave an extract which controlled the bleeding. Styptysate, a preparation from a medicinal plant, has been found helpful in controlling a persistent bleeding tendency in uterine conditions, for which it is administered orally. It may be used also locally for local bleeding.

## PLASMA BALANCE

Plasma is a convenient term by which to designate the body fluid which circulates in the blood vessels and fills the intercellular spaces in the tissues. The functioning cells of the various organs work in and live on this vital fluid, which brings necessary supplies and carries away the waste products. The plasma is literally the river of life for the body, which depends on its constant flow and fairly constant quantity and quality. The cellular elements of the blood and tissues largely monopolized attention for a long time, but studies in recent years have shown that variations in the quantity and quality of the plasma have a serious bearing.

Disturbances in the quantity or quality of this fluid are reflected in disturbances of cell activity appreciable by physical examination or laboratory methods. Edema, dehydration, acidosis, alkalosis, and hypoproteinemia are conditions of the plasma of sinister significance to functioning, especially in surgical patients requiring still further drain on the reserve of vitality. The salient facts in regard to the first four have long been known and generally used in the preoperative and postoperative handling of surgical patients, but the facts concerning the fourth need emphasis and wider understanding and use. Elman gives an instructive résumé from which are the following quotations:

**Hypoproteinemia.**—Under normal conditions the concentration of protein in the plasma is about 7 grams per cent; of this, but a few tenths of a gram are due to fibrinogen. If this is subtracted, as it is when blood is allowed to clot so that serum is obtained instead of plasma, there is little significant change in the total figure. What remains is a combination of the two remaining proteins, namely, albumin and globulin. Under normal conditions the albumin concentration is roughly twice that of the globulin concentration. The relationship between the two is often spoken of as the A/G ratio, a figure which may or may not be of significance. Of much greater importance is the actual concentration of the albumin fraction inasmuch as it is the fall in the albumin fraction which is usually observed in hypoproteinemic states. From the practical point of view, then, we should really speak of hypoalbuminemia rather than hypoproteinemia. Moreover, it is the albumin fraction which is concerned mostly with maintaining osmotic pressure of the blood, and it is the osmotic function of the plasma protein which is mostly involved in the deficiency states just discussed. It is probable that the globulin fraction has more to do with the carrying of immune bodies than with maintaining the osmotic pressure of the blood.

The chemical method used in determining the concentration of serum or plasma protein is extremely important. Variations which are obtained by inaccurate methods may be quite valueless. Errors may occur either in the determination of the protein or in the fractionation of albumin and globulin or in both. Of the two methods for the determination of protein we use and emphatically advise the Kjeldahl procedure in preference to nesslerization in measuring nitrogen. We also use and advise that separation of albumin and globulin be effected with the centrifuge rather than with filter paper. Details can be found in most biochemical texts. The actual fall in serum protein, particularly in the albumin fraction, is often 50 to 75 per cent of the normal. In general a serum protein of below 5 grams per cent or a serum albumin of below 2 grams per cent is considered abnormally low and is often accompanied by nutritional edema.

While there is a definite relationship between the clinical occurrence of nutritional edema and the level of serum albumin, there is a considerable lag in this relationship. There may be rare occasions when the serum albumin is near normal, yet edema exists. On the other hand, the albumin may fall even below 2 grams per cent without demonstrable clinical edema which will, however, inevitably develop if the low serum albumin persists for a sufficiently long period of time. It is, therefore, often misleading to speak of a critical



level of serum albumin. It is important to realize that edema of the interstitial tissue may occur for a long time before it is evident clinically as a swelling which pits on pressure.

A second source of confusion is the relationship of the plasma volume to plasma protein concentration. This is important in evaluating the significance of hypoproteinemia. Actually the plasma volume may vary so much, especially when intravenous fluids are being given, that the concentration of plasma protein must always be considered in relationship to changes in the concentration of the red blood cells which is a rough measure of the variations in relative plasma volume. It is, therefore, of importance to measure the hematocrit or red cell concentration whenever a serum protein or serum protein concentration may be observed in patients receiving fluids due entirely to the dilution of the plasma, which can be very readily followed by frequent determinations of the red blood count or the hematocrit.

**Toxic Destruction of Protein.**—A second type of protein deficiency which can be measured occurs in many patients in whom there is an abnormal destruction of tissue protein. This is revealed by finding an excessive excretion of nitrogen in the urine. This phenomenon has long been observed in a good many serious illnesses, notably in the infections. It also occurs following extensive trauma and is frequent in seriously ill patients after a serious operation. The important point about this type of protein deficiency is that replacement therapy should take such a loss of nitrogen into account, i.e., administration of protein nourishment is extremely important in any individual who is losing a great amount of nitrogen due to the actual effects of the disease process itself. There are actually very little data in regard to this type of protein derangement in surgical patients. It is probable that further study will reveal that not only does this type of toxic destruction of protein occur rather frequently but that many of the clinical manifestations are due actually to such a phenomenon. Regardless, however, of such further observations it seems apparent that this type of derangement has definite therapeutic implications which must be recognized if we are to use protein replacement therapy.

**Surgical Shock.**—During the past few years it has become increasingly apparent that plasma loss, i.e., fluid containing 7 per cent protein, is an important feature of the circulatory failure in shock. This is particularly true in severe burns, in the therapy of which plasma in large amounts is decisive, in contrast to the ineffectiveness and even danger of injecting large quantities of saline and glucose alone. It is not too much to say that an acute hypoproteinemia occurs in severe burns, in severe hemorrhage, and probably in other examples of surgical shock. The fall in blood volume in all of these conditions is due to loss of fluid containing protein which must be taken into account if we are to practice true replacement therapy. In other words, the acute protein loss cannot be remedied by the injection of saline and glucose alone; fluids possessing colloids capable of exerting long-lasting osmotic pressure must be used and for this plasma is ideal. While the value of whole blood in surgical shock is generally recognized it is not often realized that the plasma portion is the most significant; in burns in fact the red cells are not even needed. The amount of plasma required may be tremendous; in a severe burn as much as 10 to 20 c.c. per kilogram (700 to 1400 c.c. for an adult) may be necessary to meet the loss and return fluid balance to normal.

#### Methods of Protein Administration

**Oral Administration.**—Needless to say the oral method of administering fluids and food should always be used when possible. This seems to be an unnecessary statement. However, there has been so much parenteral injection of fluids in recent years that it seems important to emphasize the fact that the oral method should be used whenever the patient can ingest and assimilate food or fluid in this manner. The oral method is, of course, convenient but there are certain factors which must be observed. In the first place, proteins vary in their biological activity. This is due to the fact that the efficacy of the proteins depends upon their constituent amino-acids, of which 11 are essential or indispensable, i.e., these 11 cannot be synthesized by the body and must be supplied. The biological value of the protein, therefore, depends upon the relative proportions of these 11 amino-acids. It has long been known that certain proteins are very rich in these essential amino-acids and, indeed, contain all of them. These biologically active proteins are

present in eggs, milk and meat with soy beans perhaps to be added. Obviously, if the patient is suffering from an acute or chronic protein deficiency and is having difficulty in ingesting a large amount of food, it should be the duty of the physician to see that the kind of protein given is of a biologically active sort. In this way the protein deficiencies can be met with a relatively small amount of protein. The dose of such proteins is ordinarily given as 1 gram per kilogram per day. This dose may be increased in patients who need protein urgently.

A second factor in the administration of protein by mouth is the possibility that in sick patients digestion is not normal and that even though an adequate protein diet is ingested, digestion and absorption are so impaired that the efficiency of the protein diet is not wholly achieved. Such a situation may develop in hypoproteinemia because nutritional edema of the intestinal mucosa occurs interfering with normal function. Deficient absorption occurs also in various types of pancreatic insufficiency, in diarrhea and in intestinal fistula. When oral alimentation is insufficient for such reasons or is impossible or inadequate for other reasons, protein must be given parenterally.

**Transfusion.**—One of the earliest methods for the correction of hypoproteinemia was the use of whole blood transfusions. This indeed is true replacement therapy although a more accurate method is the use of plasma alone, particularly if there is no deficiency in the red blood cells. In recent years the use of plasma has become more and more extensive, particularly because it can usually be given without the necessity of typing. Plasma is ideal in acute hypoproteinemia, i.e., in surgical shock and after severe burns, although it should be remembered that large amounts may be required.

In chronic hypoproteinemia, unfortunately, transfusions often correct protein deficiency inadequately, particularly when the deficiency is pronounced and much protein is needed to restore conditions to normal. In such patients it has been found that the administration of one or two or even many transfusions is apt to produce but a transient and very slight increase in the concentration of serum protein. Indeed, in Barnes Hospital recently as much as 1000 c.c. of plasma was injected into a 40 kilogram patient on three successive days with pronounced though transient clinical improvement but without increasing the level of hypoproteinemia, which was about 4 grams per cent. Obviously, in such a case the serum protein or plasma is being utilized for other purposes of the body than in replacing the serum protein. This, indeed, is what one would expect in any patient who is suffering from a severe protein depletion. There are other requirements for protein besides plasma. When these requirements are unsatisfied by the normal channels the blood plasma is drawn upon. Obviously, therefore, the injection of plasma protein serves to supply not only the missing protein in the blood stream but also missing protein throughout the entire body. For example, to supply an average adult with 70 grams of protein per day would require the plasma from about 2500 c.c. of whole blood each day. This is probably the explanation of why transfusions either of whole blood or of plasma are very apt to be disappointing when large amounts of protein are required.

**Parenteral Injection of Amino-Acids.**—Because of the practical difficulties in giving a sufficient amount of protein in the form of plasma and whole blood in patients in whom the oral method is impossible or ineffective, it occurred to us several years ago that it might be possible to supply the protein needs of the body by means of a mixture of amino-acids injected intravenously. Absorption of amino-acids from the intestinal tract is, indeed, the normal method by which digested protein is assimilated. Internal protein metabolism also occurs by continuous hydrolysis and synthesis, the connecting link being the constituent amino-acids. During the course of the study many problems developed which proved difficult to solve; a short preliminary note was published previously in this Quarterly. The complete solution of these difficulties seems close to realization at the present time. It is now possible to prepare a crystal clear solution containing all of the amino-acids of hydrolyzed casein. This preparation has proved innocuous on intravenous injection; nearly 400 such injections have been given with no untoward reactions. The clinical improvements as well as evidences of protein synthesis and positive nitrogen balance have been definite; details are described elsewhere. It is probable that this particular intravenous preparation will soon become available for general use in patients requiring protein nourishment and unable to take anything by mouth.

### ALLERGY TREATMENT

The widespread tendency to allergic reaction must be taken into consideration in seeking the cause for unexpected persistence of a disorder in the genital tract. This applies especially to disturbances of the external genitals and vagina, where contact allergy may be a factor, but it must be considered also in unduly-persisting uterine, tubal, and ovarian disorders. It may be the primary cause, the allergic manifestation localizing in the pelvis because of menstrual congestion or other favoring condition, or it may be simply an associated factor, possibly induced by the products of the primary disease.

Allergy is a term much used with a hazy idea as to meaning and limitations. In fact, the limitations themselves are rather hazy, for a large class of allergic disturbances carries the designation atopy (strange disease), and there are many strange diseases. Custom and classification, however, have brought order into the matter. The term allergy was originally used by Von Pirquet to designate altered capacity of the tissues to react to bacteria and to nonbacterial substances, giving the two divisions of allergy.

From the first division come the various reaction tests to determine the presence in the body of a particular bacterium, and incidentally the probability of its responsibility for a deep lesion present. The second division, reaction to nonbacterial substances, includes the great mass of disorders commonly called allergic. These nonbacterial allergies are divided into classes as shown in the table (which is from the helpful exposition of Allergy by H. L. Alexander in Barr's three-volume work *Modern Medical Therapy in General Practice*, Williams & Wilkins Company). "Atopy" is used to designate the heredity class of allergic disturbances, of which the principal representatives are bronchial asthma, hay fever, and infantile eczema. "Physical" allergy is that due to heat, cold, light or mechanical irritation.

COMPARATIVE DIFFERENCES BETWEEN MEMBERS OF THE NONBACTERIAL ALLERGY GROUP  
(H. L. ALEXANDER)

ALLERGIC DISORDER	OCCURRENCE	HEREDITY	AGE OF ONSET	SKIN TESTS	ANTI-BODIES	PRINCIPAL CLINICAL EXPRESSIONS
Atopy	Undetermined percentage affected	Determining factor	Mostly earlier decades	Cutaneous intracutaneous passive transfer	Reagins	Bronchial asthma, hay fever, vasomotor rhinitis, infantile eczema, gastrointestinal disturbances
Contact dermatitis	All humans probably susceptible	No influence	Any age. More frequently in adults	Patch test	None	Eczematoid lesions limited initially to sites of contact
Physical allergy	Small number affected	No influence	Mostly earlier decades	None	None	Urticaria, low blood pressure, syncope, increased gastric acidity
Drug allergy	Small number affected	None in most cases. Some are atopic	Any time of life	Rare	None	Cutaneous and visceral symptoms of atopy. Also fever, lymphadenitis
Serum allergy	Large number affected	None excepting in special instances	Any time of life	Positive to serum after 1st injection in most cases	Precipitins	Urticaria, fever, arthralgia, lymphadenitis, asthma, collapse, death

In a series of 32,000 tests (the number for a particular substance varied from about 300 to 5,000), the following percentages of positive reactions were obtained. Contact substances (contact by inhalation or otherwise): feathers, 20 per cent; orris root, 16 per cent; pyrethrum, 9 per cent; horse dander, 16

per cent; cat, 9 per cent; cattle, 8 per cent; dog, 8 per cent; wool, 11 per cent. Foods: wheat, 22 per cent; barley, 10 per cent; rye, 8 per cent; oats, 6 per cent; corn, 5 per cent; rice, 5 per cent; spinach, 13 per cent; beans, 12 per cent; potato, 12 per cent; tomato, 11 per cent; carrot, 11 per cent; peas, 11 per cent; egg, 18 per cent; milk, 14 per cent; chocolate, 13 per cent; pork, 8 per cent; beef, 7 per cent. This is only a partial list of the many substances to be considered, but it shows the percentage of definite reactions to many common contact and food articles. In persistent irritation about the external genitals, clothing materials must be considered and rayon, now used so much, must be added to the wool and silk.

This hasty glance at allergy should call attention to it in connection with gynecologic disorders and lead to investigation in that direction in troublesome conditions which persist without evident cause. The present knowledge of the various ramifications of the subject is most helpfully summarized in the exposition previously referred to.

There have been cases reported in which the patient had cyclic asthmatic attacks because she was sensitive to her own menstrual blood. Desensitization with blood drawn during the menses resulted in cure.

## THERMOTHERAPY

Thermotherapy includes fever therapy and refrigeration therapy. Fever is one of the defensive mechanisms of the body. Raising the body temperature has been found to lessen the vitality of invading organisms and to increase the body resistance to their poisons.

Refrigeration lowers the activity and vitality of cells. Cancer cells will succumb to injury that the surrounding normal tissue cells may recover from. Based on this principle of greater vulnerability is the selective killing of cancer cells by radium, x-ray, and other forms of destructive energy, and it was hoped that refrigeration also might prove valuable in this direction.

### Fever Therapy

Formerly induced inefficiently by hot water or steam or dangerously by inoculation with some fever-producing organism, it is now brought about and regulated by special apparatus which, though complicated, is well controlled and safe under trained management.

Fever therapy is being used in many types of infection with varying results. In gynecology its chief use is in gonococcal inflammations which do not respond to treatment with the sulfonamides. In certain cases of brucellosis, in pelvis and elsewhere, the results have been outstanding. Alone or in combination with other measures it promises help in many resistant disorders. Combination of fever therapy with sulfonamide therapy or with Elliott local heat treatment has proved helpful in refractory cases. This type of treatment requires particular management, with specially trained attendants and careful selection of cases by a physician familiar with the indications and contraindications.

Bromberg gave an excellent review of the subject in reporting the results in 290 cases with 1,300 treatments in the fever therapy department of Barnes Hospital, and the following items and quotations are from his article.

In 24 cases of gonococcal inflammation (other than arthritis) in women (salpingitis, metritis, cervicitis), 83 per cent were cured, 12.4 per cent improved, and one (4.6 per cent) not improved. "In the average case in this gonococcal series a total of twenty-one hours of fever was necessary to effect a cure. Of this amount sixteen hours were at 106° F. plus, and five hours at from 104° to 106° F. As a rule the chronic cases required less fever than the acute cases. Our criteria of cure were the same as those outlined by Owens and Desjardins et al."

In 40 cases of gonococcal arthritis, 80 per cent were cured, 17.5 per cent improved, and one case (2.5 per cent) not improved. "The one patient who was unimproved after fever therapy was considered by some consultants to be suffering from a type of nongonococcal arthritis. 'Improved' means eradication of the focus of infection and complete freedom from symptoms but some residual limitation of joint motion from the disease. In four of the seven patients in this category, ankylosis of the affected joint was present before fever therapy."

"Conclusions: 1. Artificial fever therapy is of established benefit in gonococcal infections. It is particularly useful in complicated gonococcal infections or in those patients who have failed to improve under a more conservative regimen such as sulfanilamide and local treatment.

"2. Artificial fever is a useful adjunct to chemotherapy in the treatment of neurosyphilis and has the advantage of controllability and safety when compared to malaria and other infectious thermogenic agents.

"3. Fever therapy is probably the best available treatment for Sydenham's chorea.

"4. This therapeutic procedure gives promise of real benefit in the treatment of brucellosis, rheumatic fever, certain inflammatory eye conditions and in other disease states which have been known to respond favorably to nonspecific protein therapy in the past.

"5. Artificial fever therapy has inherent dangers and should be strictly an institutional procedure in the hands of expert personnel.

"6. The results achieved in the treatment of 290 patients at Barnes Hospital are reported and analyzed under separate disease headings. There have been no fatalities."

### Refrigeration

General refrigeration or cryotherapy or "hibernation" with cold has been experimented with extensively, particularly in patients with cancer which is advancing in spite of other measures. It was used with the hope of checking the cancer or of relieving the pain and distress more satisfactorily than with other methods of treatment. Though there has been much enthusiastic writing about it, perusal of the literature and personal reports from competent observers, who visited the headquarters of the work and hopefully watched patients under treatment, are not encouraging as to any substantial results and raise apprehensions of definite injury.

It was thought that local refrigeration might bring about benefits without the dangers of general refrigeration. Gordon and Cresci gave local refrigeration a careful trial in ten cases of advanced genital cancer, with the idea of going on to general refrigeration if the results justified it. Their summary follows:

Ten patients with advanced genital cancer, nine cases of carcinoma of the cervix, and one case of carcinoma of the vulva received local refrigeration therapy. In six cases the duration of therapy was 96 to 900 hours. Temperature was maintained between 40° F. and 50° F. in one case, at 50° F. in three cases, at 50° F. to 55° F. in two cases, and 60° F. in one case. Control of temperature was satisfactory.

Notable diminution in size of the tumor mass was observed in three cases, and pain was relieved in two cases.

Serial biopsies showed cellular degenerative changes in only one case. Marked necrosis of the cancerous refrigerated area was found at necropsy in three cases, in two of which fistulas were present with complete destruction of the ureter. Death occurred in coma in four cases, and it is our opinion that death was hastened by local refrigeration therapy.

## NEUROTHERAPY AND PSYCHOTHERAPY

Treatment for pain occupies a large place in the various fields of practice including gynecology. It involves the study of nerve and cerebral sedatives of the different types. In terminal cancer cases especially, the resources of the neurologist and the neuro-surgeon may be needed to assist in giving relief.

The nerves convey the impulses from the various parts of the body and the mind interprets those impulses. These interpretations determine the patient's actions and outlook. They also form the symptoms which she relates to the physician. There may be trouble in the lines of communication or in the central office of interpretation, which exaggerates or modifies or interprets as terminal something that is remote from the genital tract nerve terminals.

Many nervous patients with gynecologic symptoms need the careful neurologic and psychiatric investigation and treatment which the competent neurologist can give. Psychotherapy has been critically investigated and sympathetically studied in recent years by reliable physiologists and clinicians, and methods of treatment have been worked out which, in conjunction with necessary medication or operative measures, will greatly hasten the cure in many cases, and will restore to health some patients otherwise incurable.

In these cases there are, of course, symptoms not accounted for by the gynecologic lesion, nor by lesions found elsewhere. Pain or paresthesia persisting or recurring without apparent reason should arouse suspicion that it may be of mental or psychic origin and requires treatment accordingly. Neurologic investigation and advice may be helpful also in many nervous, depressed individuals, with trying domestic problems that overtax their nervous stability.

## LOCAL MEASURES

For a glance over our resources, it is well to divide the large array of local measures into groups according to effects, as follows: cleansing (douches, applications), pH regulating, antiseptic, hemostatic, hygroscopic, anesthetic and antipruritic, growth promoting, supporting (pessaries, tampons, packings), cauterization and coagulation and excision, dilating, stretching (pressure treatment, massage), postural exercises, local heat (hot douches, circulating hot water, circulating hot air, diathermy), local cold (ice bag, circulating cold water), radiation (radium, x-ray), operations.

### Cleansing

The simplest form of local treatment is the removing of irritating material. This is accomplished at home with the vaginal douche, and at the office by cleansing with cotton balls either dry or moistened with some solution, usually a mild antiseptic solution. In the trichomonas vaginitis cases, some prefer a solution of soap (*sapo viridis*).

The vaginal douche apparatus is preferably of the gravity type, consisting of a two-quart container (rubber bag or metal can) with rubber tubing and a hard rubber douche nozzle. The bulb type of apparatus is not so effective, even though accompanied with attractive spray drawings. The principle of the gravity douche and also the general arrangements for it are indicated in Fig. 326. The douche bag is hung three or four feet above the level of the surface on which the patient lies, and the hips are elevated slightly so that the solution will flow to the top of the vagina. Usually the most convenient arrangement is for the

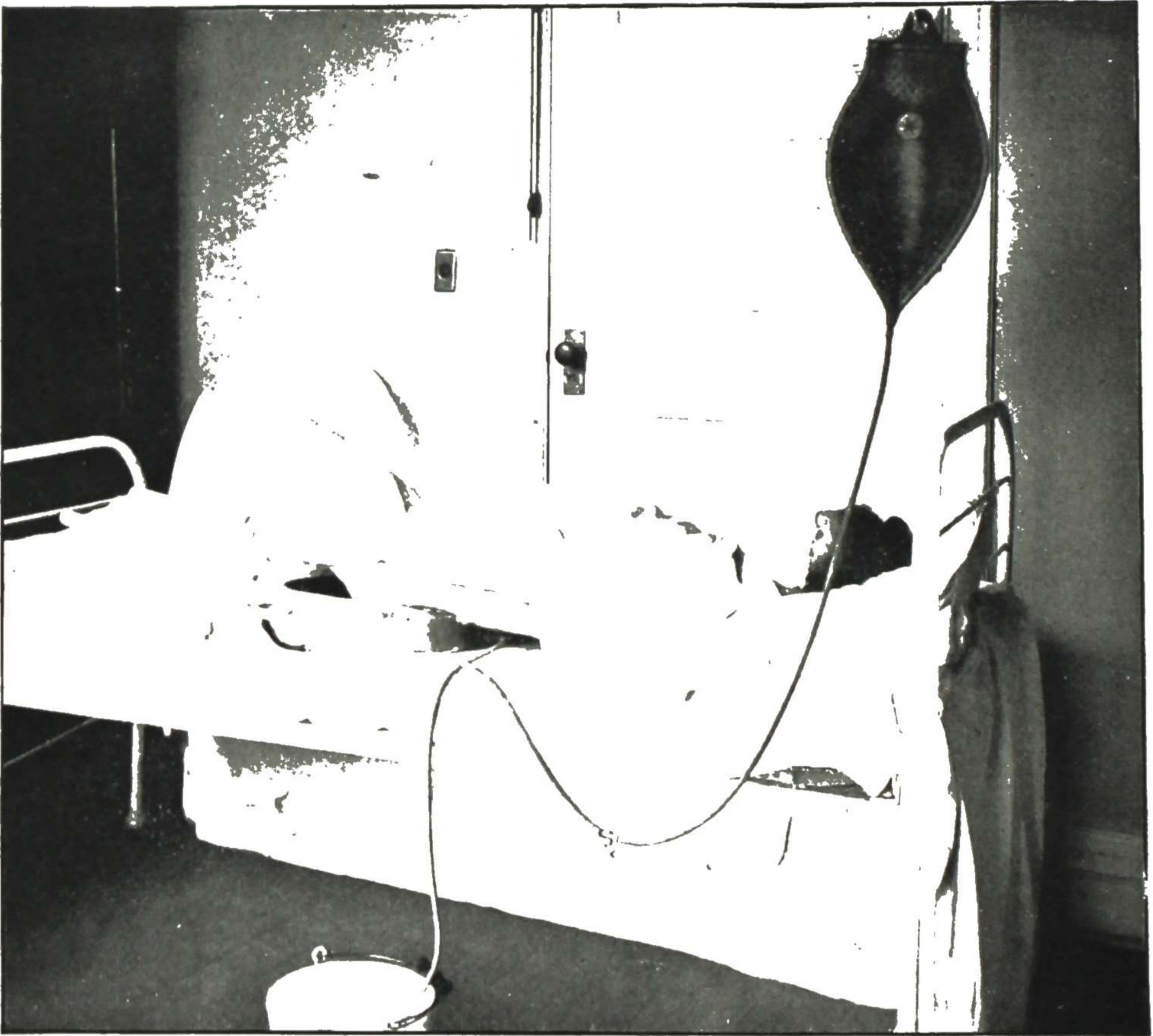


Fig. 326.—Patient arranged for the long hot vaginal douche. Notice that the patient's hips are elevated and that the douche pan has an outlet tube leading into a bucket beside the bed. The douche nozzle has a thick end and the openings are at the side, so that there is no possibility of the water being forced into the uterine cavity. The douche bag may be hung at any height required to give the desired rate of flow.

patient to lie in the bathtub with a folded towel under the hips. If the patient is too ill or otherwise incapacitated for getting in and out of the bathtub, a douche-pan may be used on the bed as shown in Fig. 326, with rubber sheeting or oilcloth for protection, tubing to conduct the solution from the douche-pan to a bucket beside the bed if a large douche is to be used, and a wide board to be slipped under the mattress to prevent undue sagging.

The douche bag and tubing and nozzle are scalded out by running hot water through them, and then wrapped to protect from dust. Ordinarily the

douche consists of hot water from the faucet, cooled to comfort with cold water and then the special solution or powder added and mixed well.

Vaginal douches should be used only when there is some definite indication for them. They are not required for mere cleanliness; in fact, they may interfere somewhat with normal physiology and the germicidal vaginal contents which tend to keep the vagina in healthy condition.

The simple cleansing douche may be used when there is a troublesome increase in the normal muco-epithelial secretion or when there is some mucopurulent discharge not requiring a special douche. The water should be just comfortably warm, and the addition of salt (sodium chloride), teaspoonful to the quart, is preferable to the use of plain water. A mild douche of pleasant odor may be made by adding a teaspoonful of compound zinc sulphate powder (Pulv. Zinc. Sulf. Co., N.F.) to two quarts of warm water. This contains the principal ingredients used generally in the numerous advertised proprietary douche preparations with attractive names and fancy prices.

### pH Regulating

The acidity of the normal vaginal contents is around pH 4, and any marked tendency toward alkalinity favors the growth of pathogenic organisms and the consequent development of vaginitis. As explained and illustrated in the previous chapter under pH determinations, this has been so well worked out that it is known which organisms flourish at different stages of pH increase (Fig. 250) and, vice versa, one can judge about what the pH is by the type of discharge and organisms found.

An important factor in the cure of vaginitis is the restoration of normal pH of the vaginal contents. This is accomplished by acid douches and the use between douches of powders or tablets containing a carbohydrate to be converted into acid, to encourage the growth of the Döderlein bacillus which normally makes the conversion. For acid douche use one-half to one teaspoonful of lactic acid (U.S.P.) in two quarts of warm water or three tablespoonfuls of a good grade of white vinegar to two quarts of water. The following is the prescription with directions for the lactic acid douche.

℞ Lactic Acid, U.S.P. 1 lb.

Sig.: For local use only. One-half to one teaspoonful to two quarts of warm water. Use as directed.

Acidifying powders consist of glucose or B-lactose with starch and boric acid in various proportions. The powder is blown into the vagina or packed in at the office treatments, and for home use it is put in capsules for introduction into the vagina by the patient. Acidifying tablets are supplied by drug manufacturers, usually with the addition of a mild antiseptic agent to assist in the elimination of the pathogenic organisms. These powders and tablets are used in the treatment of the various forms of vaginitis, the details of which are given in the next chapter.

### Antiseptic

The antiseptic douche is used in those cases of purulent discharge or mucopurulent discharge in which the admixture of pus is so prominent that an active



germicidal effect is important. A very satisfactory antiseptic douche is made by adding a teaspoonful of lysol to two quarts of warm water. In some cases a potassium permanganate douche (1:5,000 solution) is more satisfactory.

Mercury bichloride was formerly often prescribed for an antiseptic douche. But the concentrated solution for making the douche is dangerous when remaining in the medicine cupboard of the home. So many fatal cases of accidental poisoning from bichloride solution or tablets have occurred that it is not advisable to prescribe the drug for home use.

As to antiseptic solutions for office application, the following have some antiseptic effect: silver nitrate (1 to 10 per cent), protargol (2 to 10 per cent), argyrol (10 to 20 per cent), mercurochrome (1 to 10 per cent), tincture of iodine diluted to half strength for disinfecting surfaces. The silver preparations, particularly argyrol, tend to lessen the hypersensitiveness of inflamed surfaces and diminish the discomfort. The tincture of iodine (diluted) may be used for sterilizing the cervical canal and the sound-ends for dilating.

As a drying and mildly antiseptic powder boric acid and kaolin, equal parts, may be used. Another such powder is xeroform (bismuth tribromphenate) and boric acid (1 to 4). Xeroform has proved a very satisfactory substitute for iodoform. Its action in stimulating healthy granulation is similar to that of iodoform, and it has practically no odor. It is about as effective as other iodoform substitutes and less expensive.

### Hemostatic

The following have local hemostatic effects: copper sulphate (10 per cent solution), adrenalin (1:1,000 solution), and styptysate liquid. The copper sulphate solution is used as an astringent on eroded areas. Adrenalin is used to check bleeding at some spot, for example, where a polyp or specimen has been removed. The end of a tampon is moistened with a few drops of the adrenalin solution and placed against the bleeding spot, and left until the next day. Styptysate liquid may be used in the same way. It comes in 10 c.c. bottles for local use. Tannic acid added to the xeroform and boric acid powder (1-1-4) makes a convenient astringent powder. An astringent powder is likely to be uncomfortable on an inflamed or irritated surface.

### Hygroscopic

Glycerin, either plain glycerin or boroglycerin (boric acid 50 per cent) is used for its hydroscopic (water-extracting) effect. Special drugs may be incorporated in the glycerin for special effect. The application is made by soaking one end of a tampon in the desired glycerin preparation and then introducing it through the speculum into the upper part of the vagina, the medicated end being placed against the cervix. These glycerin tampons are used particularly in acute and chronic inflammatory conditions in the pelvis. They seem to assist materially in diminishing the pain and soreness and they certainly exercise a decided effect on the adjacent tissue fluids, for the patients often remark on the large amount of water which comes from the vagina when using these glycerin tampons.

Formerly ichthyol-glycerin was used on tampons a great deal and for long periods, but there is now doubt as to the advisability of this use, for it has been shown that in susceptible animals prolonged application of coal tar preparations favors cancer development.

### **Anesthetic and Antipruritic**

For surface anesthetization, cocaine solution (10 to 20 per cent) may be used, applied on cotton and left for five minutes. Novocain solution ( $\frac{1}{4}$  to  $\frac{1}{2}$  per cent) sterilized is used for subcutaneous or submucous injection for removing small growths or pieces of tissue for microscopic examination. A powder may be made somewhat anesthetic by adding orthoform, for example, orthoform added to the xeroform and boric acid powder (1-1-4), or chloretone (chlorbutanol) may be added instead of orthoform in the same proportion. Various special anesthetic preparations are put out by manufacturers, such as nupercaine ointment and diothane ointment.

Antipruritic agents are used principally in pruritus vulvae and are taken up in detail under that disorder.

### **Growth Promoting**

Estrogens applied locally in the vagina stimulate the epithelium to full growth. Hence such application is indicated in vaginitis in individuals where the protective epithelium is thinned, as in children before puberty and in the atrophic conditions after the menopause. Thinness of epithelial covering opens the way to infection, which is likely to persist until a good protective epithelial covering is restored. For this purpose vaginal suppositories are principally used, the manufacturers putting up estrogenic suppositories convenient for home use. Some of the desired local epithelial rebuilding may be secured by estrogens hypodermically, but the suppository treatment has been found to be better.

### **Supporting**

Pessaries, packings, and tampons come in this category.

Pessaries are appliances introduced into the vagina for the purpose of holding the uterus or vaginal wall in proper position. They are made of hard rubber or soft rubber, usually the former. Those made of soft rubber are generally hollow and contain air or flexible wire. Occasionally a pessary is made of glass or block tin or some other material. With the development of plastics, pessaries may be secured in translucent plastic material.

Supporting pessaries are used principally for retrodisplacement of the uterus and for prolapse of the uterus, and hence will be considered in detail under those subjects. The uterine stem, frequently referred to also as stem pessary, is simply a cervical plug for keeping the canal well open over a considerable period of time. It is used principally in the treatment of obstructive dysmenorrhea, and is considered in detail under that subject. It may be used, also, after amputation of the cervix or excision of the cystic area, to insure preservation of a good wide canal.

Gauze packings are used principally after vaginal operations, to check oozing by pressure and to give support for a short time. Cotton tampons may be

employed in the same way, but they are used most in office treatment, to hold medicine in position at the vaginal vault or to keep inflamed surfaces separated. A vaginal tampon is simply a piece of absorbent cotton or common cotton or wool or gauze, of the desired size and shape, with a short loop of string by which it may be removed from the vagina by the patient after a specified time. Details are shown in Fig. 327.

Ordinarily, all tampons are introduced by the physician. When, however, it is advisable that tampons be applied at home by the patient, between the office visits or in conditions in which the patient cannot well come to the office,

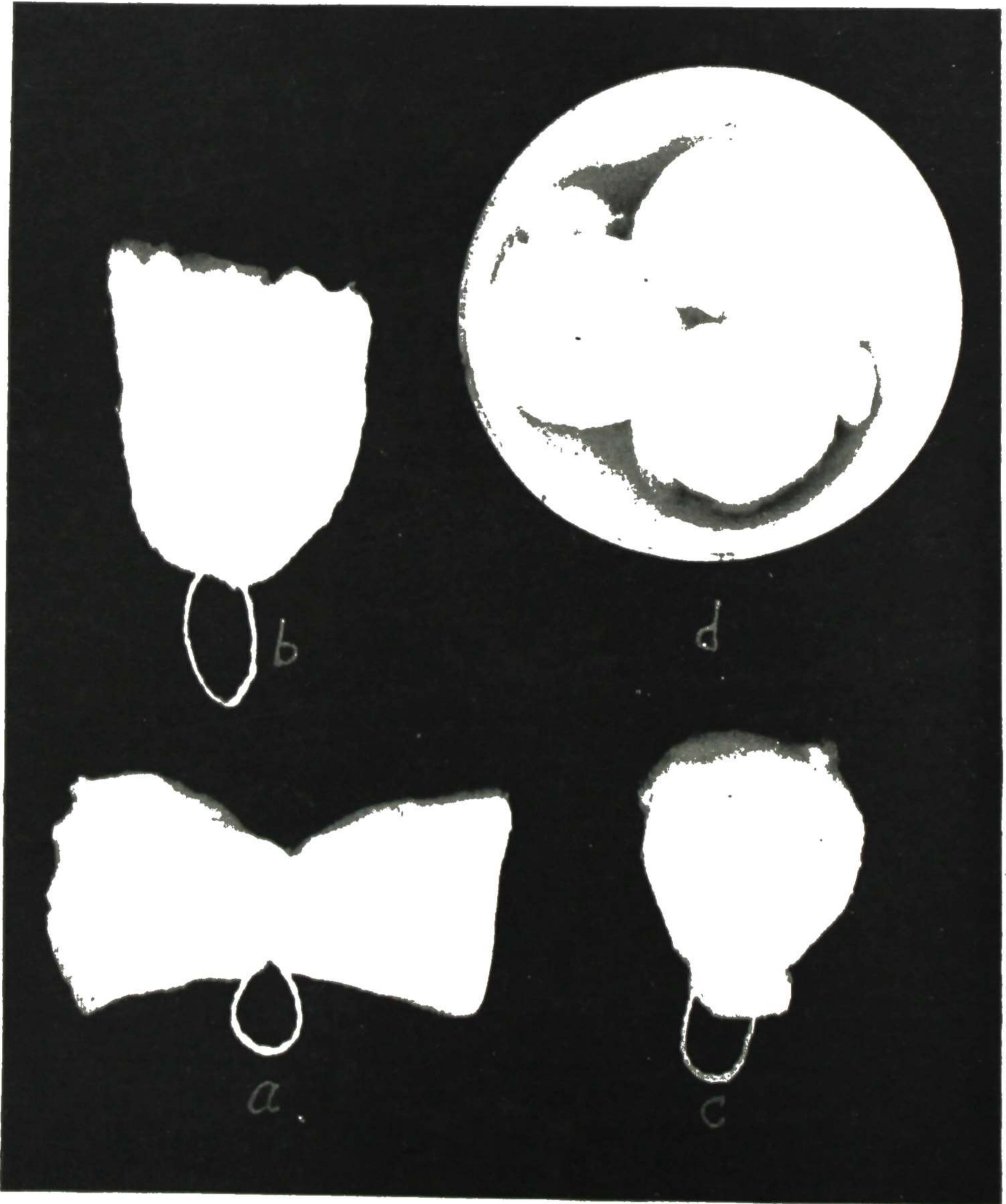


Fig. 327.—Preparation of tampons. *a*. A piece of cotton of the required size with a strong string tied about the middle and also a loop tied. *b*. The same, with the ends folded up preparatory to receiving powder in the hollow formed there or to being dipped into an application-solution. *c*. Another satisfactory way of making a tampon. The piece of cotton is folded and the ends are tied together and the string looped. *d*. A small bowl containing tampons ready for use.

the tampon-capsule may be employed. It is introduced after the warm douche for hygroscopic effect in acute or subacute pelvic inflammation. Boroglyceride or 5 per cent ichthyol in glycerin is commonly used, and the patient puts the medicine in the capsule, as indicated in Fig. 328, just before introducing the capsule into the vagina.

Specially prepared tampons for absorbing the menstrual flow are sold and are used by many, with or without the usual outside pad as desired. They are particularly useful when the flow is very free or the individual has special activities (acrobat, dancer) or circumstances make frequent changes of pad inconvenient. Thorton presents an instructive study of 110 individuals using menstrual tampons and examined at regular intervals, and concludes that no harm results.

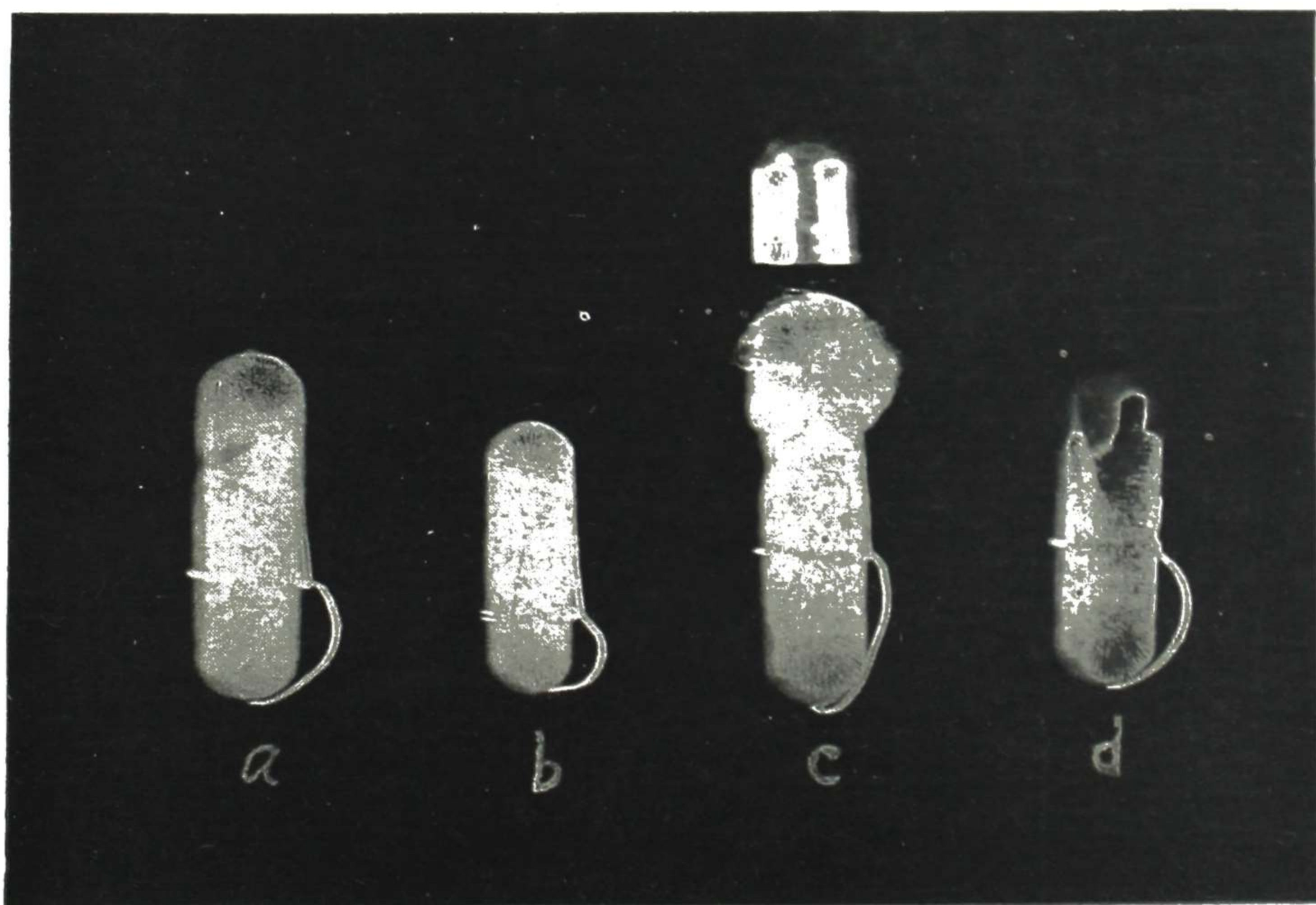


Fig. 328.—Tampon capsules. *a*. Large size. *b*. Small size. *c*. The cap removed, showing the tampon. *d*. A tampon capsule prepared, ready for introduction. The cap was removed and the medicine poured into the cap, which was then replaced.

### Cauterization, Coagulation, Electric Excision

In gynecologic work, the ordinary small electric cautery, with thin points similar to those used in nose work, is used principally for linear cauterization of the cervix. The large short wave or high frequency machine is used with the cutting current for conization of the cervix with the cutting wire or radio knife, or with the coagulating current for coagulation or for hemostasis by touching bleeding points. These methods are considered in detail under Cervicitis in Chapter VII.

### Dilating

Dilating is required in cases of stenosis of the vagina and of the cervical canal. In either location the stenosis may be congenital or may be acquired from severe inflammation in childhood or later. In the vagina, stenosis inter-

feres with coitus and may interfere with vaginal drainage to an extent to prolong vaginitis. In some cases the narrowing may be overcome gradually by dilating treatments, with fingers or speculum or large vaginal dilators of hard rubber or plastic or metal. Glass dilators have been used, but there is danger of breakage and injury. Where the condition is marked or unyielding operative division of the obstructing tissue is required, with special suturing to preserve the space gained.

In stenosis of the cervical canal, dilation in the office may overcome the trouble in the milder cases. But if the stenosis is marked or attempts at dilation painful, operative dilation in the hospital under anesthesia is advisable.

### Stretching

Stretching of tissue is required principally in adherent retrodisplacement which has become a factor in sterility or is causing trouble otherwise. There are two measures which may be employed in attempting to bring forward a corpus uteri held back by thin adhesions, namely, pressure treatment and massage.

Pressure treatment is applied by means of mercury distending a colpeurynter which has been introduced into the vagina, the hips having been elevated properly to direct the pressure. It is used principally in adherent retrodisplacement of the uterus, and the details concerning it are given under that subject.

Pelvic massage had wider application before the development of the more effective means of influencing pelvic circulation and exudates. Now the application is principally to stretch adhesions for mobilization of the uterus to permit lifting it from a troublesome malposition. The movements are largely those of deep bimanual examination and attempts to lift the retrodisplaced fundus uteri and stretch the tissue holding it. Sometimes a kneading of the shortened infiltrated tissue, between the vaginal and abdominal finger tips, will aid in the softening and stretching process.

### Postural Methods and Exercise

#### KNEE-CHEST POSTURE

The patient supports herself on the knees and chest (Fig. 329). The head rests on a pillow, with the face turned to one side, and the breasts are brought as closely as possible against the table or bed. To take the correct posture and thus secure the desired effects, particular attention must be given to three details as follows:

a. The clothing must be well loosened about the abdomen—hence the best times to take this postural exercise at home are in the evening just after going to bed, and in the morning just before rising.

b. The thighs should be perpendicular, as shown in Fig. 329, so as to raise the hips as high as possible. Unless particular attention is paid to this point the thighs are likely to slant backward (Fig. 330) or forward, and part of the desired elevation is missed.

c. The back should be curved downward and elbows gotten out of the way so that the breasts come against the bed (Fig. 329). This is to bring the chest as low as possible and give a steep inclination to the peritoneal cavity, so that

the pelvic contents will gravitate toward the abdomen. Fig. 331 shows a common error in this respect, the chest being still too high.

The effect of the knee-chest posture is to take temporarily all downward pressure off the pelvic organs and permit them to gravitate toward the abdominal cavity (Fig. 329). The downward pressure on the pelvic organs is for the time being relieved, the local circulation is improved and a movable retrodisplaced fundus uteri tends to gravitate forward toward the normal position. The effect is much increased if the vagina be opened with the fingers so that air may enter. The position may be maintained from one to ten minutes; ordinarily the patient is directed to take the posture for one or two minutes

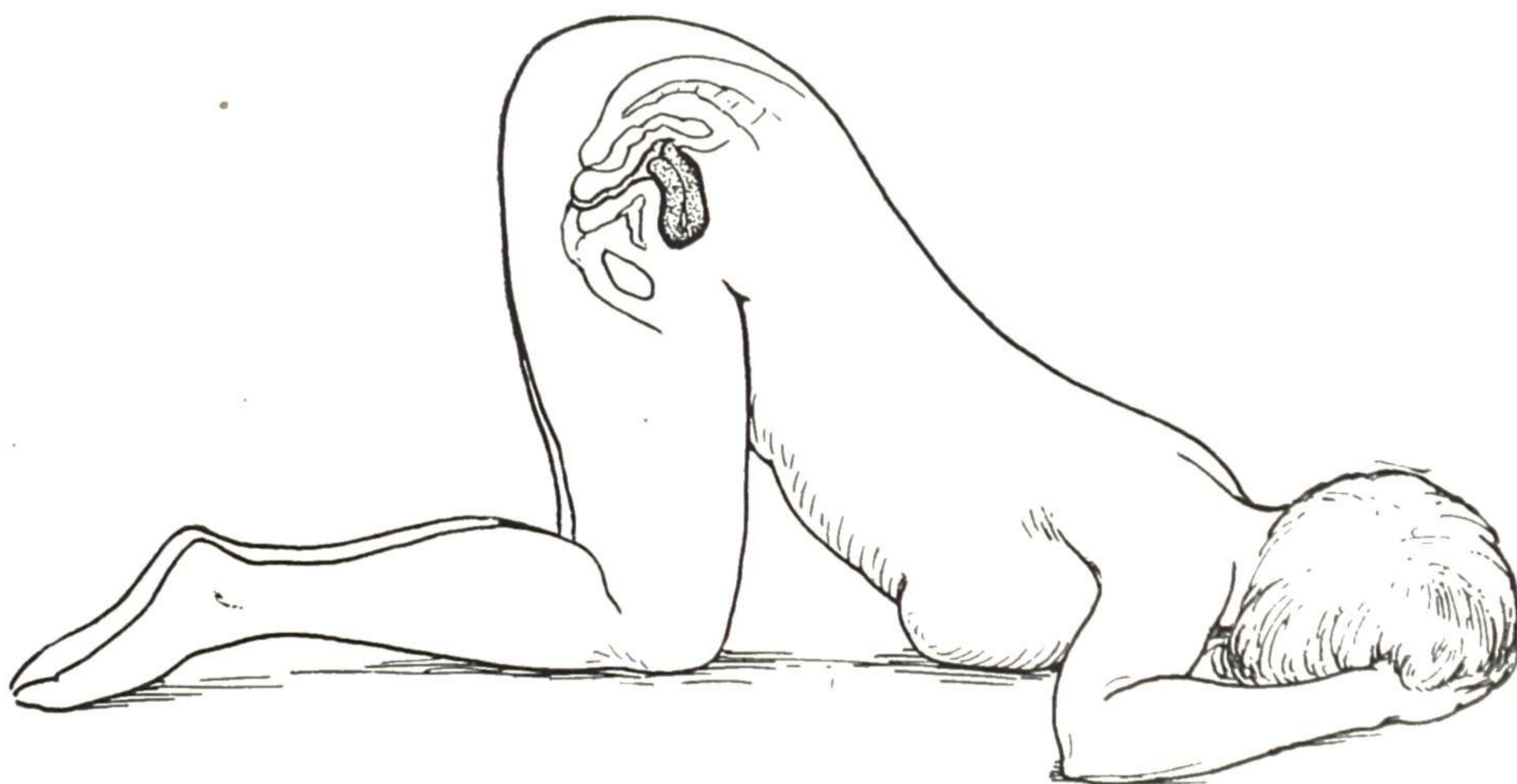


Fig. 329.—The knee-chest posture, showing the pelvic structures in outline and the tendency of the uterus to gravitate forward.

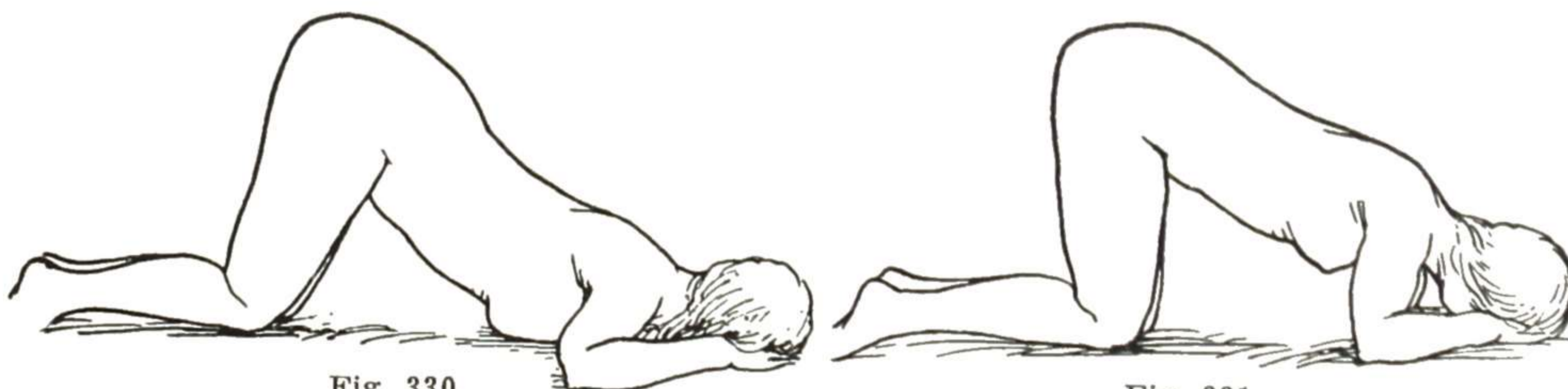


Fig. 330.

Fig. 331.

Fig. 330.—Incorrect knee-chest posture. The knees are too far back.

Fig. 331.—Incorrect knee-chest posture. The chest is not brought down to the bed.

twice daily. The knee-chest posture is used by the patient at home in certain cases to supplement other measures when they are not effective alone. Used for two or three months after labor, this is exceedingly useful in preventing retrodisplacement of the uterus.

#### MONKEY TROT

With the feet flat on the floor and about three feet apart the patient bends over, keeping the knees straight, and places her hands on the floor with the palms flat. The patient now walks about on her hands and feet, keeping the knees stiff, for three minutes. The jarring which attends this exercise helps to

make the uterus gravitate forward. The monkey trot exercise gives an exaggerated knee-chest posture effect, and may be used in the same types of cases.

#### CONTRACTION OF ABDOMINAL MUSCLES

Voluntary systematic exercise of the abdominal muscles is a useful and simple procedure which is very helpful to certain gynecologic patients. It is one of the most effective measures that can be employed in the treatment of that affection which is so distressing to many women, namely, prominence of the abdomen from relaxation of the wall. This is seen principally following confinement, the abdominal muscles, overstretched from the pregnancy, having never regained their tone. The strengthening of the abdominal wall gives

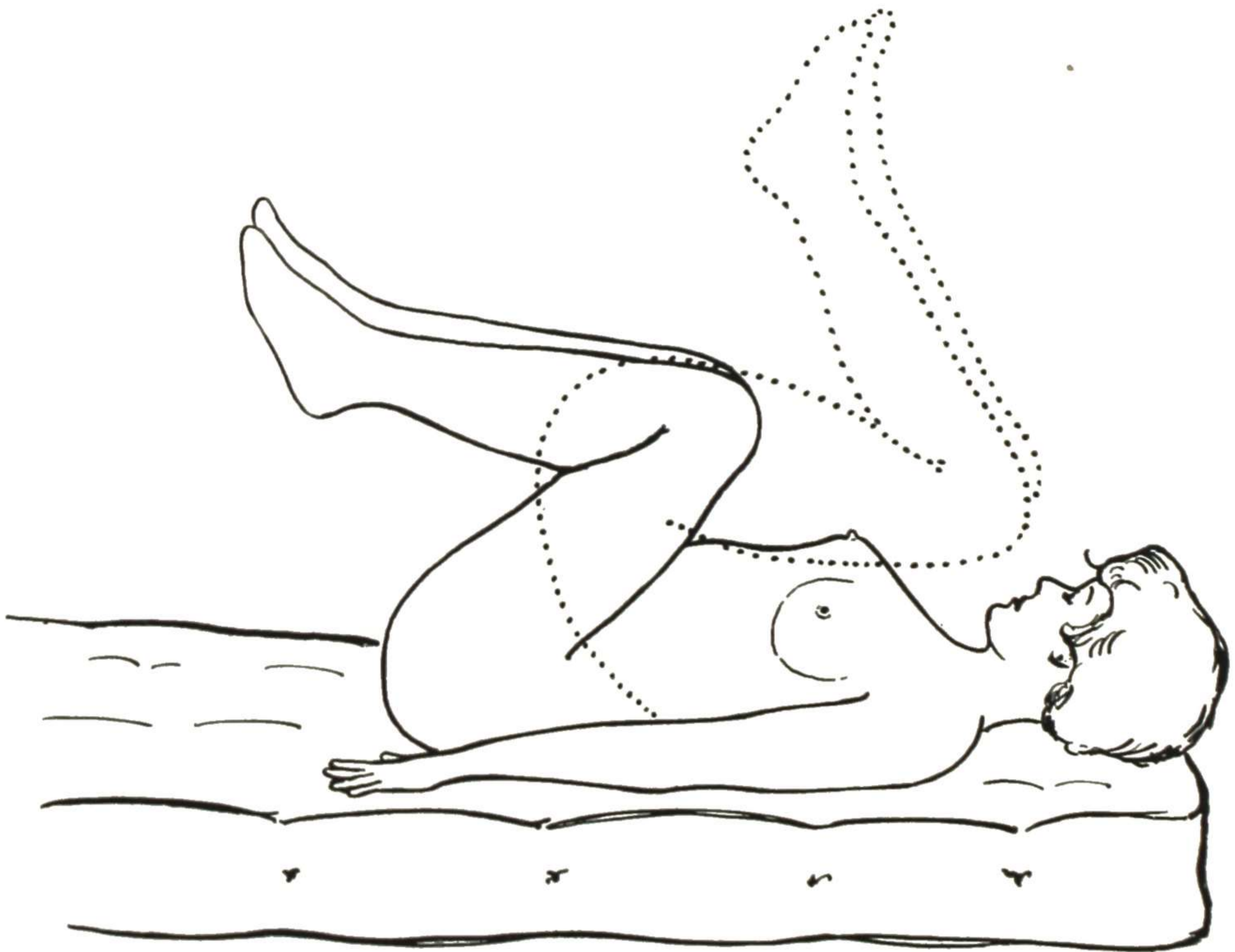


Fig. 332.—Knee to chin exercise to strengthen and shorten the abdominal muscles.

better support to all the abdominal organs and is beneficial in enteroptosis, chronic constipation, and other conditions influenced by loss of abdominal wall support.

The weakness of the abdominal wall is due to weak, stretched muscles, and the purpose of the exercise is to shorten and strengthen these muscles. The patient lies flat on her back in bed with the thighs flexed on the abdomen and the knees bent (Fig. 332). This is the starting position. The exercise consists in pushing forward and downward with the chin and upward with the knees, attempting to touch the knees with the chin. This exercise contracts the recti and at the same time, by tilting the pelvis upward, decreases the distance between the origin and insertion of the muscles. In this way the muscles are shortened

and strengthened. This exercise should be done five or six times to start with, and gradually increased to twenty times with each exercise period.

There is another exercise which helps to strengthen the abdominal muscles. This consists in having the patient raise her head and shoulders from the recumbent position to the half sitting position (Fig. 333). The arms should be folded over the chest. The object is not to raise to the full sitting position, but simply to exercise the abdominal muscles by raising the head and shoulders a moderate distance and holding them there. The movements are most effective when made *slowly*, so as to get long contraction of the muscles.

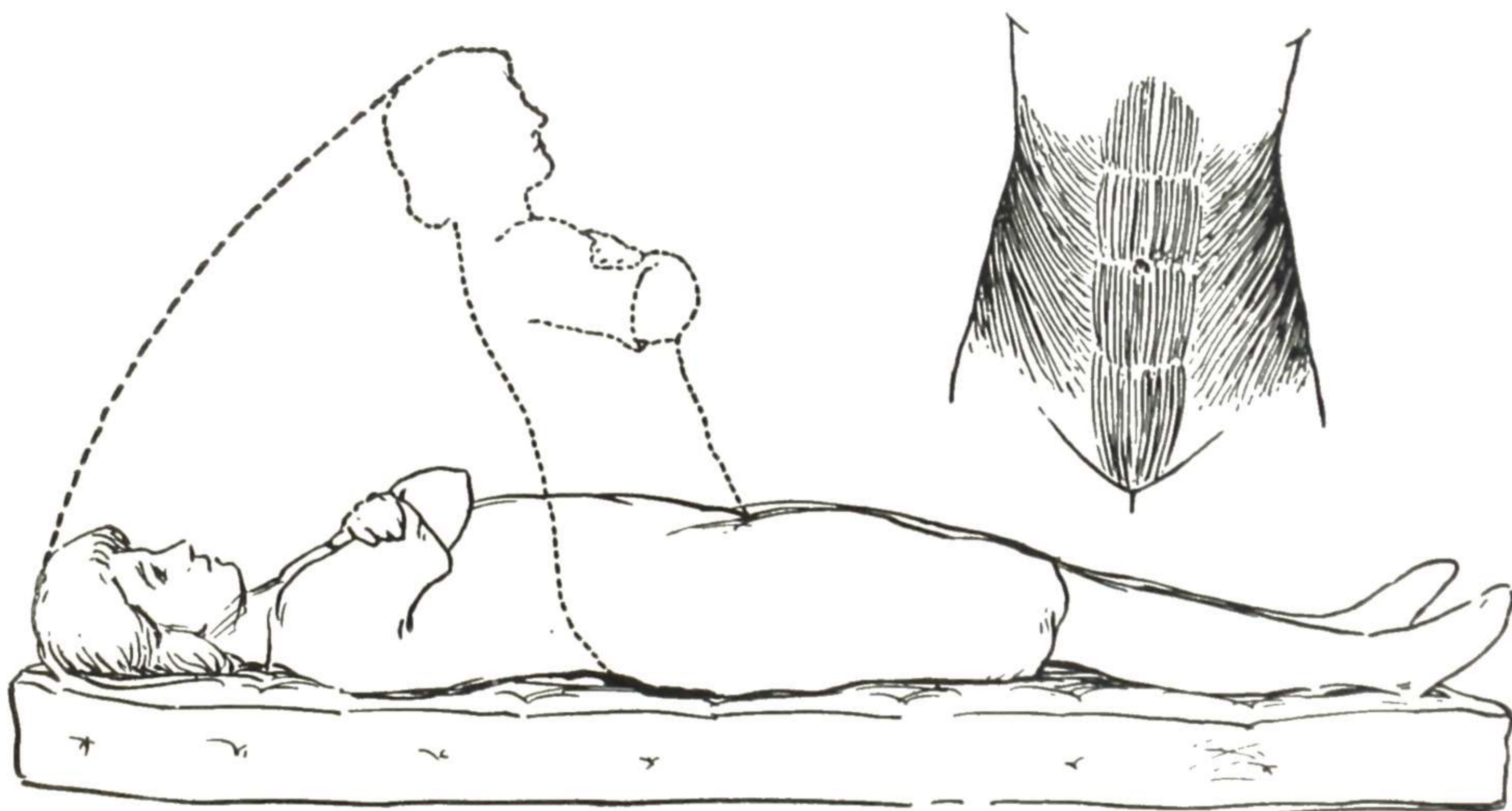


Fig. 333.—The "raising exercise" to strengthen the abdominal muscles. The central abdominal muscles are exercised by raising straight up and the lateral muscles by raising laterally.

### Local Heat

Heat to the pelvic organs may be applied in several different ways, the indications varying with the location of the trouble and its nature and severity. Moist heat may be applied by means of hot douches or sitz baths, or by the time-honored hot stupes or the less troublesome hot pastes. Dry heat may be supplied by the hot-water bag or by the more convenient electric heating pad or by the infrared lamp. Higher degrees of heat, with the required regulation, may be administered with the hot-air chamber or by the circulation of hot water or air through a vaginal bag, or by the use of diathermy.

### LONG HOT DOUCHE

When it is desired to obtain heat effects from the vaginal douche, attention must be given to certain special points, as follows:

a. The patient should be lying down, with hips elevated so that the water will run well up about the cervix and vaginal vault.

b. The water should be as hot as the patient can take comfortably. Starting with warm water, hotter water is added as the tissues become accustomed to the heat, but it should not be so hot as to cause discomfort.



c. The douche should be of long duration (twenty to thirty minutes). This prolongation of the douche is secured by using a large amount of water (two to four gallons) and giving it slowly, just fast enough to prevent cooling of the water; or the bag can be hung on the hot-water faucet or connections made with both faucets for mixing as desired.

d. The patient should rest in bed for at least an hour afterward, a very good plan being to take the douche at bedtime.

#### ELECTRIC HEATING PAD

This is sometimes designated as an "electrotherm." It is heated by a current through a cord, which is attached in the ordinary light socket. This is very useful in applying heat for long periods, which may do much toward relieving the patient's discomfort. Care should be taken to keep the electric pad dry, or a short circuit may occur. Also, the patient should be watched until it is seen that she stands the heat well and that the pad is working satisfactorily.

#### INFRARED LAMP

In recent years the infrared lamp has been used as a source of heat in the treatment of pelvic inflammations. The lamp should be adjusted so that it is about three feet above the abdomen and focused so that most of the rays are concentrated on the lower abdomen. It is doubtful whether the infrared rays themselves have any special beneficial effect, but the advantage from the heat created is evident.

The lamp should not be used for long periods; fifteen minutes, two or three times a day, should give the desired clinical results, and longer periods are enervating to the patient.

The infrared light is localized in its effect and has the advantage that it can be directed on a small painful area. It is useful especially in neuritis or arthritis (sacroiliac, lumbar), in which conditions it often gives much relief. It may also be used over a moist application on the abdomen in order to keep the application warm.

#### HOT-AIR CHAMBER (ELECTRIC OR LAMP-HEATED)

The most effective application to the lower abdomen for the systematic application of dry heat is the *hot-air* chamber. This method, long used in other parts of the body in the treatment of chronic inflammation, has proved helpful also in like lesions in the pelvis. Various forms of apparatus are available for the purpose. Gellhorn devised a convenient one for use where electricity is available and gave a résumé of the subject. This convenient "abdominal baker" (Fig. 334) is used a great deal about the hospital in the care of gynecologic patients, for pelvic and other painful abdominal conditions.

#### CIRCULATING HOT WATER IN VAGINAL BAG

The supplying of heat to the pelvic tissues by the circulation of hot water through a vaginal bag, with apparatus for maintaining high temperature and automatically regulating it, was developed by C. R. Elliott, and later experiences reported on by Holden and Gurnee, and also by Counseller. An impor-

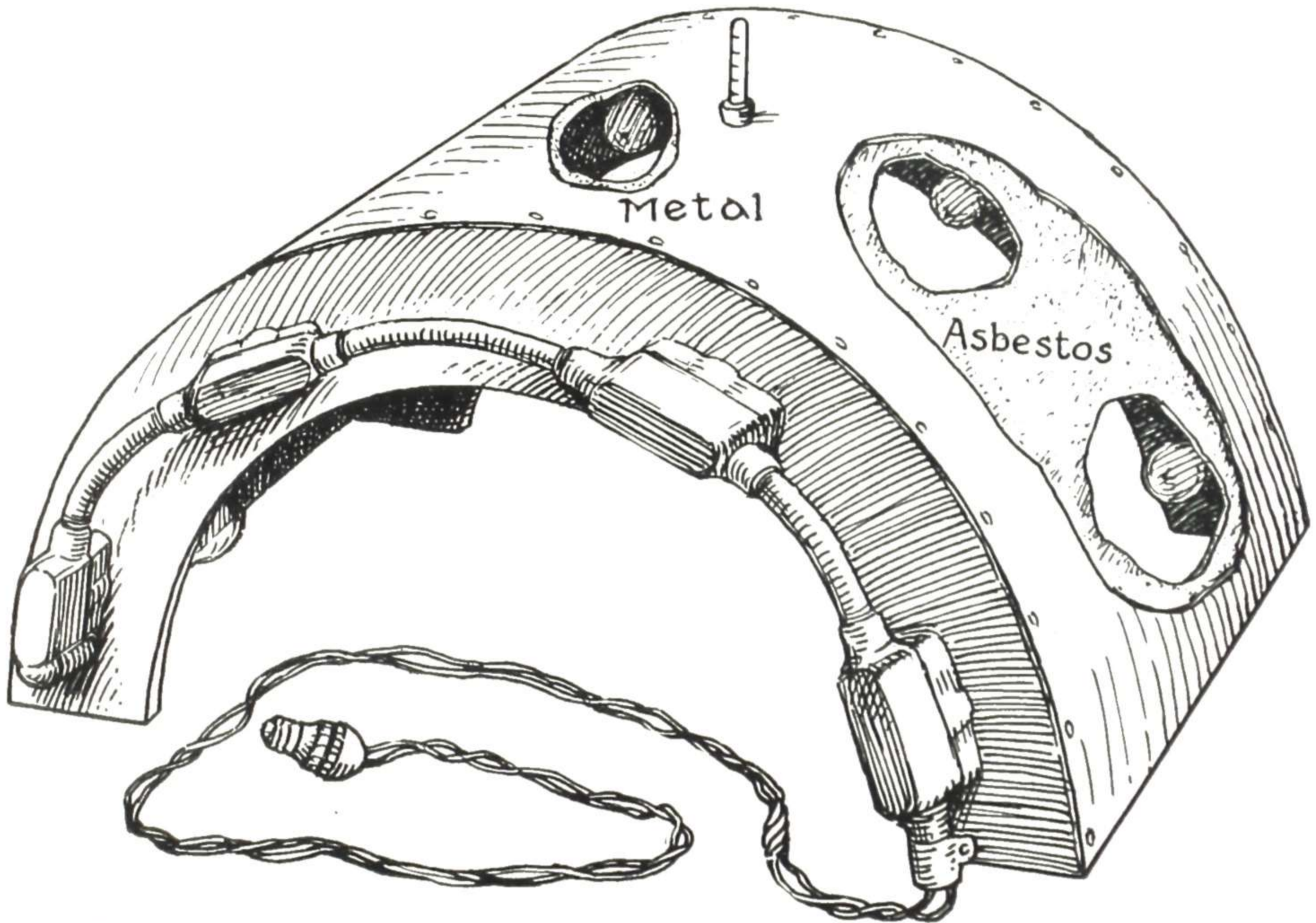


Fig. 334.—Apparatus for dry heat treatment. It may be connected to the ordinary socket on any light circuit. There are eight electric lights. The lights used may be varied in size and number as desired. The metal case, with heavy asbestos lining and the careful covering of all wires, permits the bed clothing to be laid over this apparatus without danger. (Gellhorn—*Am. J. Obst. and Gynec.*)

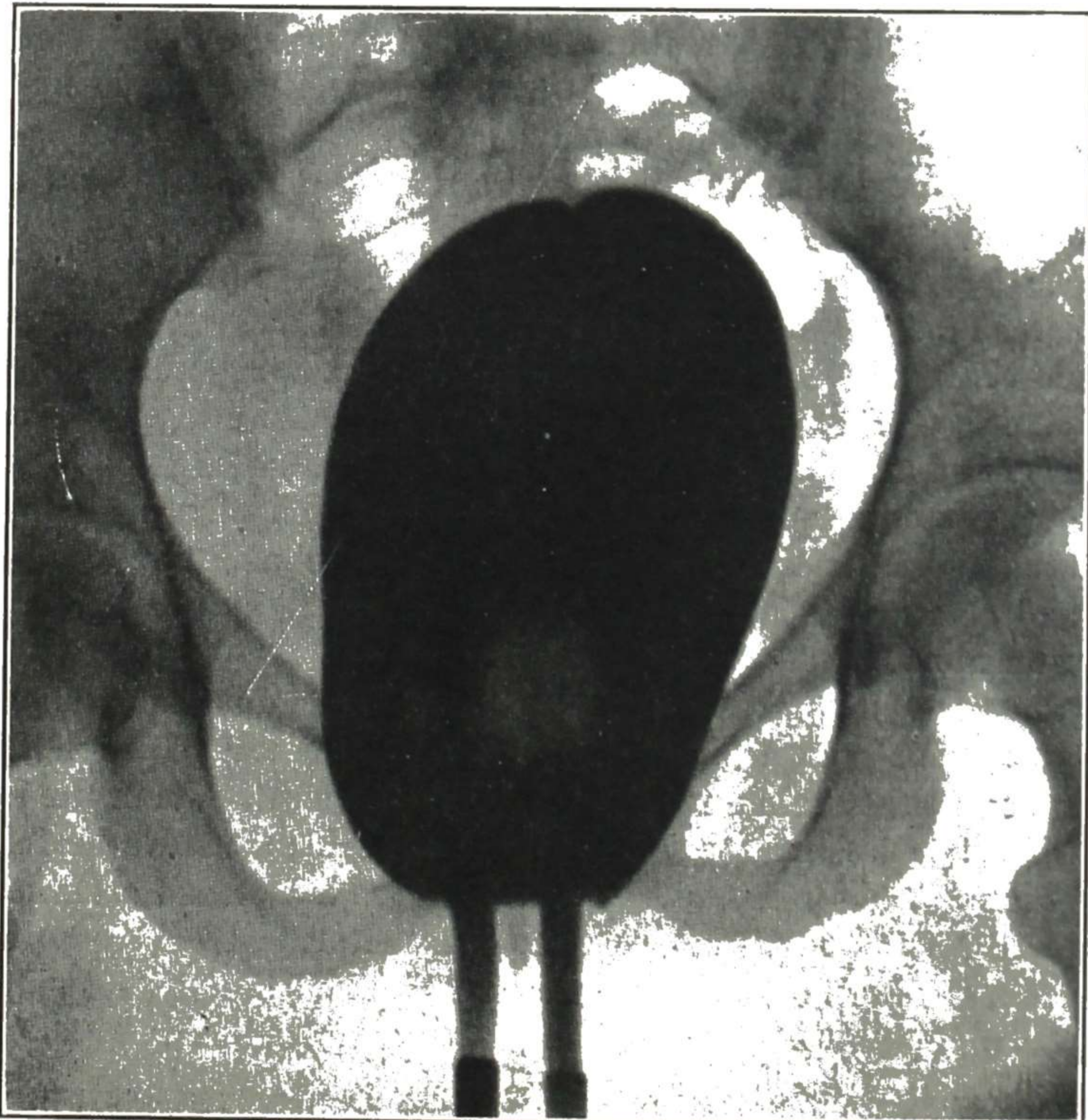


Fig. 335.—Showing distended bag in position in vagina, with the inlet and outlet tubes for the circulating hot water. (Holden and Gurnee—*Am. J. Obst. and Gynec.*)

tant feature is the distention of the vagina, bringing the heat close to the deeper tissues. This marked distention of the rubber bag in the vagina is shown in Fig. 335. This method of treatment, like other forms of heat application, is used principally in pelvic inflammatory conditions and in neuralgia and neuritis.

The Elliott treatment requires expensive apparatus and specially trained assistants for its safe and effective use. All this is fully justified if it gives the patient benefits which cannot be secured by simpler and safer measures. Whether or not it accomplishes this is doubtful. Reports are conflicting, and Cosgrove and Waters have reported severe burns and sloughing from its use.

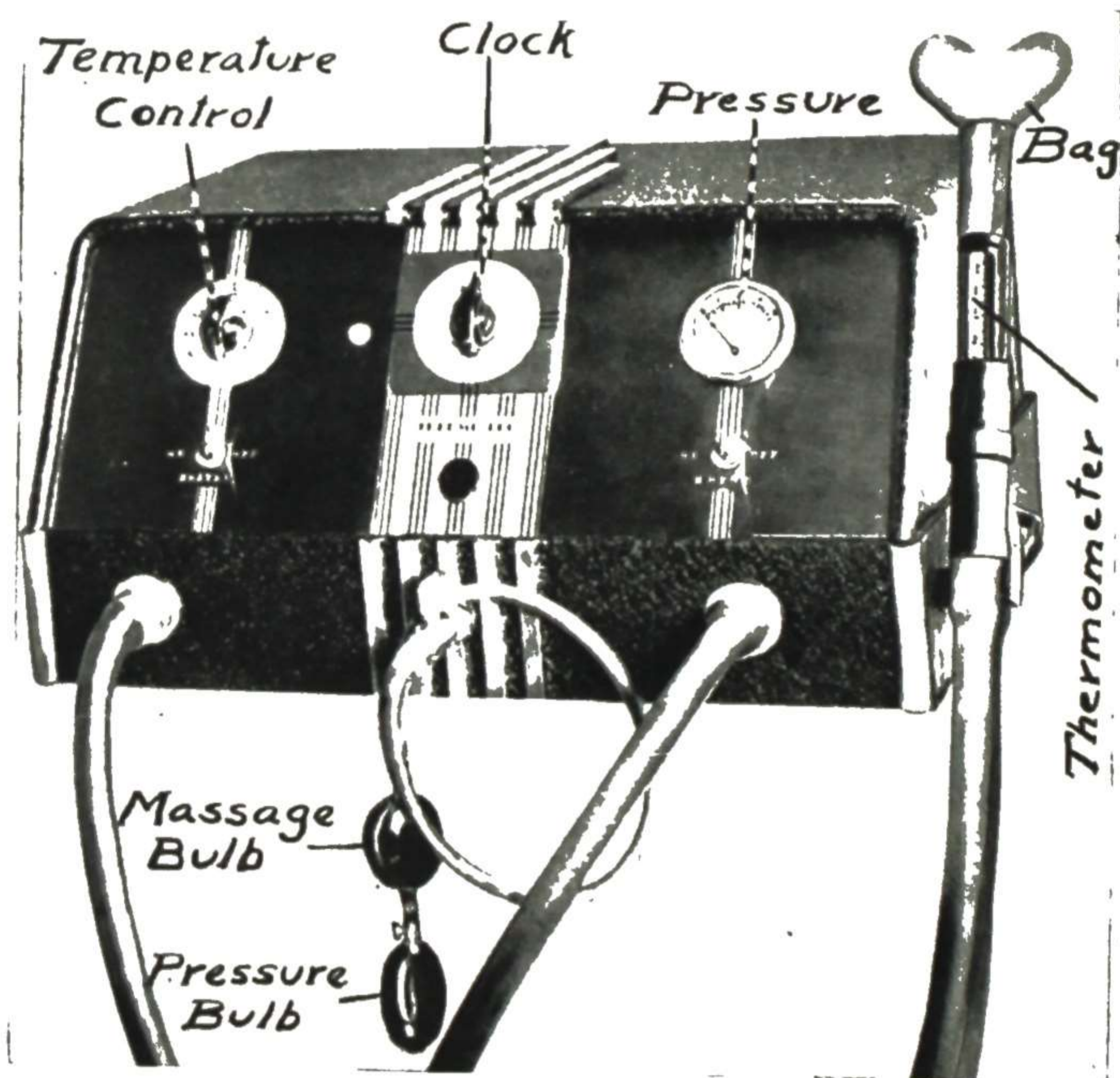


Fig. 336.—Apparatus for pelvic heat treatment by circulating superheated air in a rubber bag in the vagina. Provision is made for even distention of the vagina and for a large measure of automatic control of the treatment. (Falls, Newman and Kobak—*Arch. Phys. Therapy.*)

#### CIRCULATING HOT AIR IN VAGINAL BAG

Falls, Newman and Kobak report experience with the pelvic application of heat by means of an apparatus for circulation of hot air inside a bag in the vagina. The apparatus, shown in Fig. 336, is arranged for thermostatic control, and it is claimed that the danger of overheating and vaginal-wall damage is eliminated. Full details are given in the article (see Reference List).

#### DIATHERMY

There are three methods used in giving diathermy treatment with high frequency current. The first is the so-called ordinary diathermy in which the vibration rate is only six hundred thousand (600,000) to one million per second. With this type of diathermy two metal electrodes are used in contact with the skin. The second type is the high frequency alternating electric field. With

this type as well as with the third type the vibratory rate is twelve and one-half to thirty million per second. With short wave therapy, metallic applicator pads insulated with rubber are used on the patient's skin instead of placing the metal plate directly against the skin. The heat is created in the intervening tissue structures through the molecular activities created the same as with the ordinary diathermy type. The other type of short wave therapy is given with the high frequency electromagnetic field. With this method the current is sent through a so-called induction cable applicator. With the cable, heating is effected not by the current passing through the body, but rather by the flow of secondary current induced in the body as the current flows in the coiled-up cable near or on the mass of tissue being treated. Any of these methods can be used in gynecology.

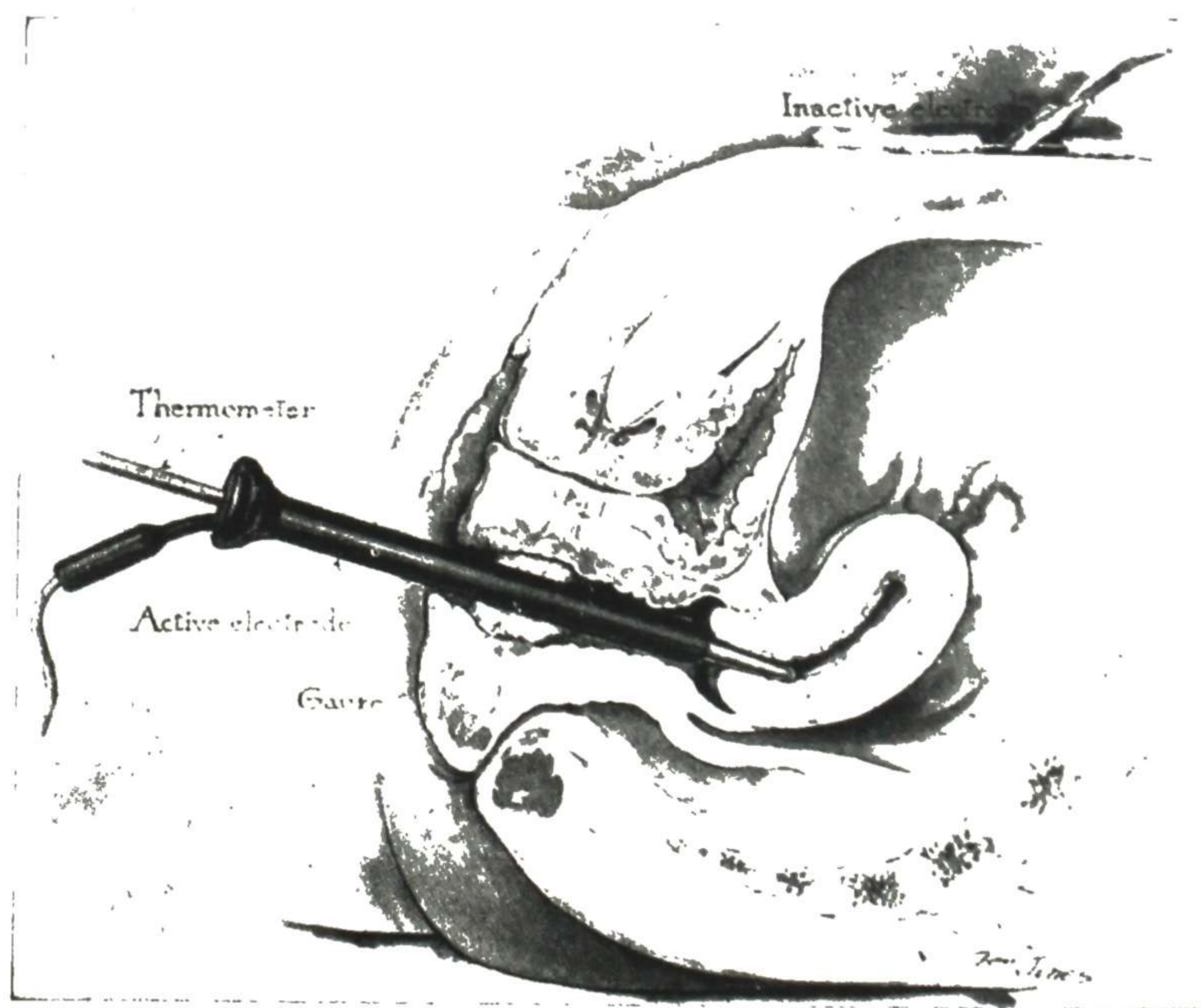


Fig. 337.—The Corbus active electrode or thermophore for use in the cervix uteri. It may be used also in the urethra. The inactive electrode is seen just back of the symphysis pubis, separated from the skin by a wet pad. By means of the diathermy current the heat is passed between the two electrodes; the active electrode being the smaller, becomes the hottest. The thermometer that passes into the core of the instrument registers the temperature of the electrode. (Corbus—*Surg., Gynec. and Obst.*)

**INDICATIONS.**—The indication for pelvic diathermy is any condition in the pelvis requiring heat, which includes acute and subacute infections, whether gonorrheal or otherwise. Before the days of chemotherapy and estrogenic therapy for gonococcus infections diathermy was a very important method of treating vulvovaginitis in children and gonorrheal infections of the urethra, Skene's glands, and the cervix. For these conditions the corpus electrode was very satisfactory and diathermy is still valuable in those cases that do not respond to chemotherapy and those cases which are sensitive to the sulfonamides. For general pelvic diathermy the belt electrode and the large vaginal electrode are used. Since these treatments should be controlled by some one

familiar with diathermy treatment in general no extensive description of technique is given here. In Fig. 337 the Corbus electrode is shown. Further technical information may be obtained from articles in the Reference List, particularly the article by Waters and that by Krusen.

### Cold

In some cases local cold gives more relief than local heat. In most cases, however, pelvic pain, inflammatory or otherwise, is relieved more by heat than by cold, consequently the rule is to use heat first, and if that fails then try cold.

There are several ways of applying cold. The ordinary ice bag is a convenient and satisfactory method. If no regular ice bag is at hand, the ice may be put in a hot-water bag, which does very well as a substitute. The circulating cold water coil may be used for more extensive cold treatment, which extends into the refrigeration treatment already mentioned.

### Radiation Treatment

Radiation therapy is useful in a great many pelvic diseases, both malignant and nonmalignant. It may be given with radium or with x-rays or with a combination of the two.

#### RADIUM

CANCER.—Radium is one of our most effective remedies against cancer. It has a selective action on cancer cells, in so far that cancer cells may be destroyed without destruction of adjacent tissue cells. This selective action depends on the fact that cancer cells are younger, less stable, and consequently less resistant to destructive influences than the surrounding mature tissue cells. This difference in resistance is apparent also in regard to heat. That is, in a cautery incision through a malignant growth the cancer cells are killed over a certain area in which the tissue cells still maintain vitality. This fact has long been noted and used in the handling of malignant growths. If the application of heat be prolonged and carefully graduated, the zone of selective action may be somewhat widened, but at best it is a very narrow zone. With radium, however, the zone of selective action is wonderfully wide. With proper screening, to limit the softer ("burning") rays, the selective devitalizing action on cancer cells may be extended to six centimeters or more. The effective destructive action varies much in different cases, however, and we cannot yet be certain in a particular individual just how far the cancer cells will be completely devitalized. In addition to the direct devitalizing effect on the cancer cells, there is a stimulation of the connective tissue, causing proliferation. This connective tissue proliferation isolates the remaining nests of cancer cells, and the subsequent contraction diminishes their nutrition. In a certain zone this process eventually starves to death the already damaged cancer cells, while farther out the cancer-cell nests lie dormant for a longer or shorter period. It is hoped in time, by proper screening, dosage, and technique of application, to extend the effective selective action so that we can depend uniformly on killing the cancer cells out to the limit of the pelvic cavity. The selection of cases for radium treatment, the combination with x-ray or operation, and other items, are taken up under cancer of the uterus and other forms of cancer.

In the application of radium for pelvic cancer, precautions must be taken against two serious harmful effects. First, there is danger of sloughing, extending into the rectum or bladder or ureters. There is a certain area immediately about the radium in which all tissue is destroyed. The limitation of this area, without interfering with the therapeutic effect of the radium, requires judgment in the use of metallic screening, of tissue screening, and of distance screening by gauze packing. Second, in some cases after heavy radium treatment there has occurred an exaggerated connective tissue contraction, or fibrosis, eventuating in painful nerve constriction and even in occlusion of the rectum, necessitating colostomy. Another late devitalization effect is seen in the bladder ulcers and mild rectal strictures coming on in from one to three years, but yielding very well to local treatment. Further details in regard to these complications will be found under Cancer of the Uterus (Chapter IX).

**MYOMA.**—Radium is an effective remedy also in selected cases of uterine myoma and in certain cases of persistent uterine bleeding from other causes. It is particularly useful in hemorrhagic conditions near the menopause. The metrorrhagia is diminished or eliminated, and in many cases there is shrinking in the size of the tumor. It is especially indicated in certain patients not in good condition for operation, where malignancy and infection and submucous myoma can be excluded. It is beneficial in selected cases of uterine bleeding from other causes, such as subinvolution, myometrial hyperplasia, and chronic metritis. However, the sterilizing ovarian effect must be kept in mind, and contraindicates this treatment in most patients in the child-bearing period. The details concerning the use of radium in uterine myoma and in other forms of uterine hemorrhage are considered in the chapters dealing with those diseases.

*Special Knowledge Required.*—The safe and effective use of radium in gynecologic conditions requires special radium knowledge and special gynecologic knowledge. In this situation its use is a form of surgery in which the knife is replaced by the more deeply penetrating radium, and carries all the responsibility of other types of pelvic surgery.

### X-RAY

**CANCER.**—In the treatment of cancer, the x-ray has much the same effect as radium. While it lacks the advantage of concentrated application directly to the interior of the cancer, such as radium application within the uterus for uterine carcinoma, it has the advantage of wider distribution of influence. Consequently in extensive uterine cancer, deep x-ray treatment is indicated to devitalize the metastatic cells and the portions of the main growth that lie beyond the effective reach of radium applied within. In certain superficial malignant growths it effects a cure, and in deep-seated growths it usually exercises a marked retarding influence. Improvement in technique and effectiveness is going on rapidly, and there is substantial reason to hope for the later development of uniform curative effects in deep-seated cancers. Sarcoma is especially amenable to its influence. For the present, x-ray and radium treatment should supplement each other—radium for concentrated local application to or within the growth, and x-ray for its widespread influence on

metastases and outlying portions of the growth. The definite selection of cases for x-ray treatment is considered under Cancer of the Uterus and other forms of malignant disease.

**OVARIES.**—Under the influence of the x-ray, the ovaries gradually atrophy and lose their function. This makes it useful in cases of excessive ovarian activity, as in sexual hyperesthesia (nymphomania). In addition to lessening the ovarian activity in these cases, the x-ray may be applied to the external genitals to diminish the congestion and hypersensitiveness there, though heavy dosage or repeated application to the external genitals must be avoided, as it is likely to lead to troublesome x-ray dermatitis.

In certain conditions in which it is advisable to diminish ovarian activity, x-ray is useful. By continuing the treatment long enough the patient may be rendered permanently sterile. Thus it constitutes a two-edged weapon—one that is exceedingly effective in various directions but requires much care and judgment in handling. There are cases in which sterilization, with the coincident diminution in the pelvic blood supply, would be of great benefit; while in other cases, any effect in this direction must, for various reasons, be carefully avoided.

**UTERUS.**—The ovarian effect just mentioned tends to diminish the blood supply of the uterus and thus influences favorably nonmalignant pathologic conditions in that region. Properly selected cases of myoma are generally greatly benefited by this treatment. Its use, however, should always be accompanied or preceded by diagnostic curettage, to determine whether or not malignancy is present. As its antihemorrhagic effect is dependable to a considerable extent on its influence in checking ovarian function, its use should be avoided in younger women. The selection of the particular cases suitable for x-ray treatment is taken up under the various topics (Uterine Myoma, Menorrhagia, Metrorrhagia, etc.).

**EXTERNAL GENITALS.**—X-ray treatment is beneficial in tuberculosis of the vulva. It is used also in pus infections of the skin, subcutaneous tissues, and lymph nodes (acne, boils, carbuncle, cellulitis, and adenitis). However, x-ray treatment for pruritus vulvae and conditions which cause it, carries certain dangers which make such treatment inadvisable, except occasionally to give temporary relief while the condition is being investigated as to type of curative treatment required. This point is considered under Pruritus Vulvae (Chapter IV).

**X-RAY A SPECIALTY.**—The development of x-ray work generally has become so extensive that it constitutes a specialty in itself. The results depend on the accurate selection and coordination of numerous technical details, which vary greatly in different classes of cases. The best results can be secured only by one thoroughly familiar with the therapeutic use of x-ray in the various affections. The treatment is not given a fair chance when applied in a haphazard way by one familiar only with its diagnostic use. This fact should be kept in mind in every estimation of x-ray results. Again, the wise choice of treatment, x-ray or otherwise, in the various gynecologic affections mentioned, depends, of course, on a careful consideration by the gynecologist of all the methods of treatment, and the selection of the one that will best meet the con-

ditions present in the individual case. The definite selection of cases for x-ray treatment is further considered under the various diseases.

#### RADIATION IN THE CHILD-BEARING PERIOD

Radium and x-ray are in most cases definitely contraindicated during the child-bearing period, but there are certain exceptions to this general rule. In these cases they should, however, always be used very cautiously and only after less drastic and safer methods have proved of no avail.

In some cases of intractable menorrhagia and metrorrhagia during puberty which have not responded to endocrine medication plus other measures, small doses of radium (never over 300 mg. hr.) may be used, and have in some cases regulated the flow and apparently helped to establish normal menstruation.

In cases of ovarian hypofunction and in certain cases of sterility, small doses of x-ray (20 per cent of erythema dose) or radium (150-200 mg. hr.) have been used to stimulate the ovaries. A few patients with amenorrhea have been caused to menstruate after light x-ray exposure. In this type of case the ovarian function is already below par, and the margin of safety between the stimulating dose and the dose which may cause permanent damage to the impaired organ is so narrow that extreme caution is necessary.

In cases where uterine bleeding is so severe that temporary sterilization is necessary, Wintz has been able to regulate the x-ray dosage so as to destroy follicles of a certain maturity and cause cessation of menses for varying periods, depending on the size of the dose. When the menses become reestablished, they are normal in a large percentage of cases. This is not without danger, however, for occasional patients have had permanent cessation of menses. Another danger which must always be remembered is the effect on the fetus in future pregnancies. Although there have been many cases reported in which normal healthy children have been born after comparatively large doses of x-ray given for castration, there have also been enough cases of malformed fetuses born after doses of x-ray or radium to show that this is a definite factor to consider when giving radiation during the child-bearing period.

#### Operations

Careful anatomic and pathologic investigations have demonstrated that many pelvic lesions are of such nature and so situated that a cure can be effected by nothing short of operative treatment, with its direct handling of the diseased tissues and extirpation of the hopelessly damaged. In some cases this is evident from the very nature of the lesion. On the other hand, in many cases the question as to whether or not operative treatment will be necessary can be answered decisively only after nonoperative measures have been given a thorough trial.

In pelvic operative work, benefit is secured to the patient ordinarily through one or more of four ways: (a) removal of a diseased structure, (b) correction of a malposition, (c) release of adhesions fixing structures, or (d) restoring lost support. Before recommending operation, the surgeon should have determined that in the conditions present there is a strong probability of being able to do one of these things to the benefit of the patient. For example, when



abdominal operation is being considered for an inflammatory infiltration in the pelvis, it is important to determine, among other things, whether the mass of infiltration is in the broad ligament or in the peritoneal cavity. If it is an adnexal or other mass within the peritoneal cavity, it can probably be extirpated. If it is an infiltration of the connective tissue of the pelvis, the extirpation of any considerable part of it is not a practical proposition, unless complete hysterectomy is carried out at the same time. Preoperative determination of this point (that the trouble is an infiltration of the connective tissue) may save the patient from a futile operation and also point the way to beneficial nonoperative treatment.

The operative measures suitable for the various diseases will be mentioned in the appropriate chapters.

### METHODS OF ADMINISTRATION

Various types of administration are employed in gynecologic medication, particularly for the endocrines. Of the common methods (oral, subcutaneous, intramuscular), the oral is ordinarily the most convenient for the patient and the least disturbing and expensive. With the extended use of enteric-coated tablets and the advances in hormone preparations, more and more are being made effective by oral administration. When such are available, the patient may be spared the troublesome "shots" and the frequent office trips which they necessitate. Sevringhaus emphasized the advantages of oral administration in his instructive article "Treatment of the Menopause."

Vaginal suppositories supply local estrogenic effect for building up protective epithelium in atrophic (senile) vaginitis and in the vaginal inflammations of childhood. Estrogenic ointment may be used for local effect on the skin or for absorption through inunction.

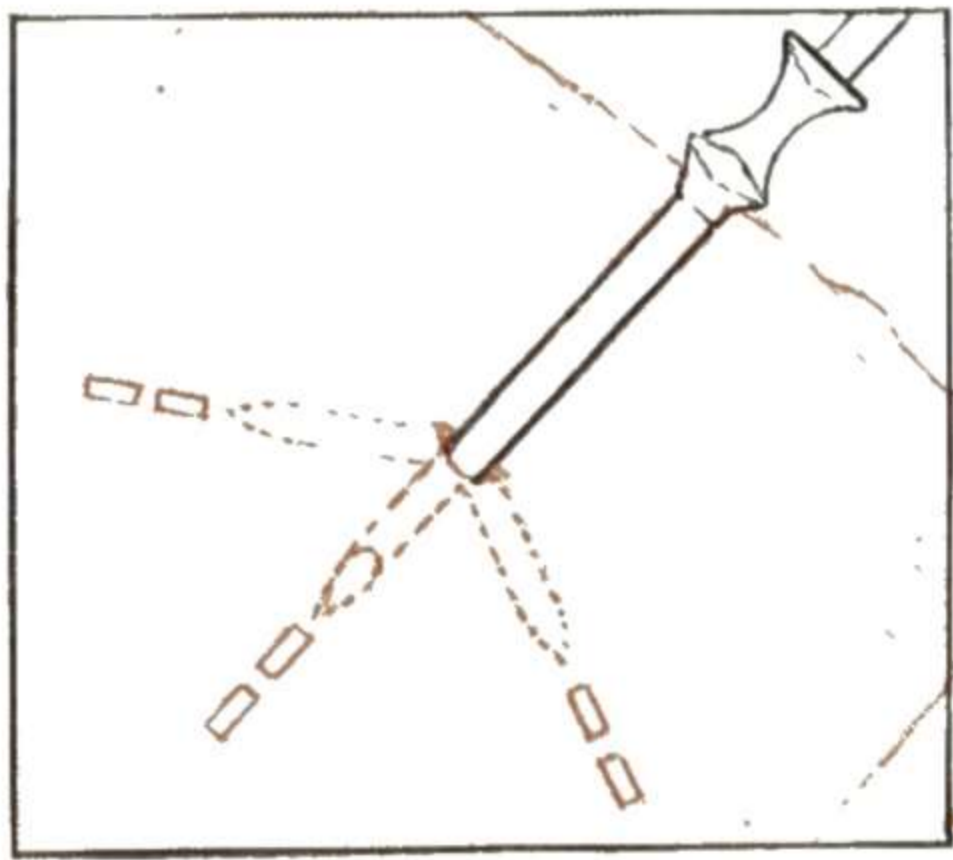
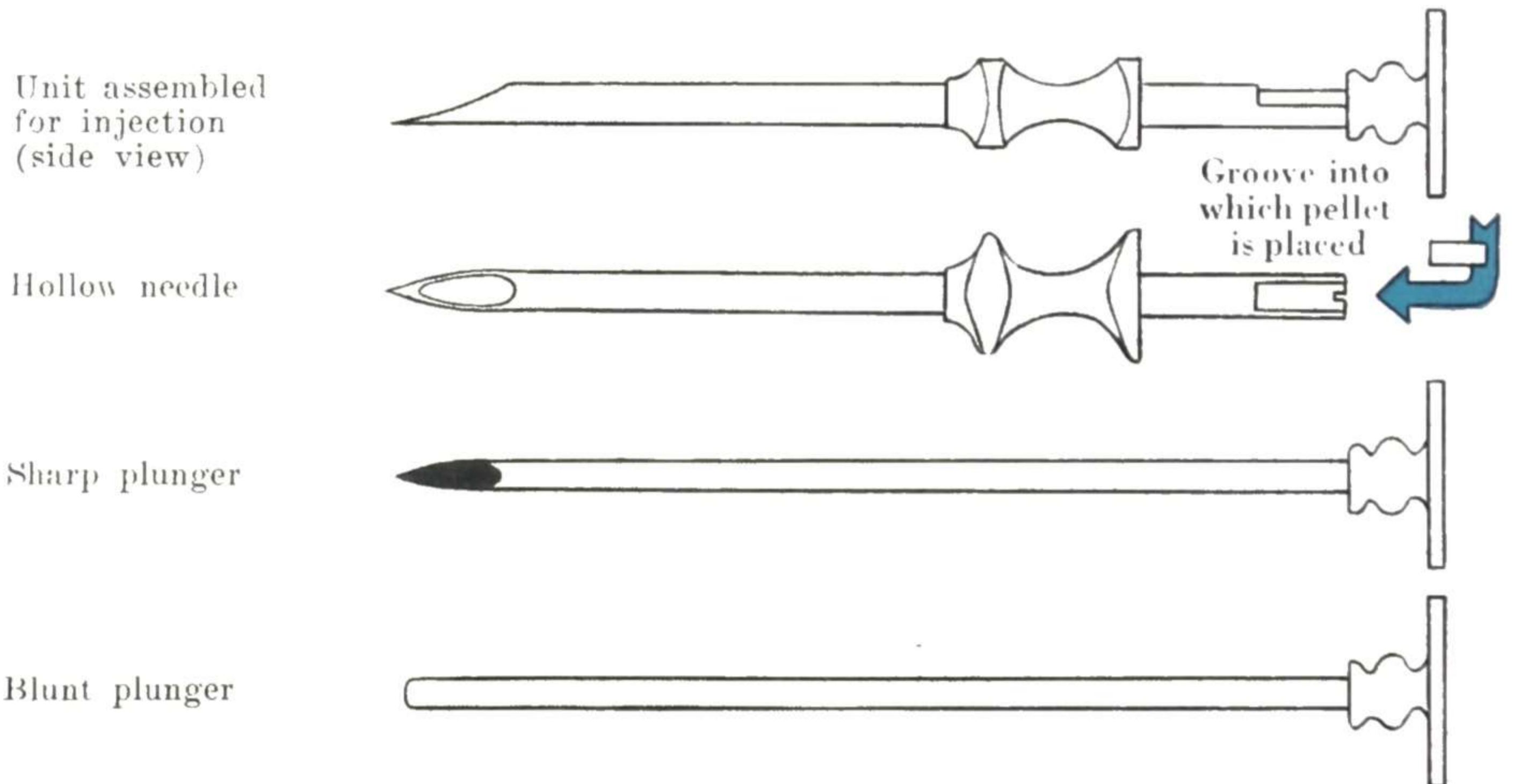
Pellet implantation subcutaneously may be employed with benefit in cases requiring gradual absorption over a long period. The methods of implantation are by hollow needle (injector) or by incision, the technique being shown in Figs. 337A and 337B. TeLinde and Bennett give a helpful consideration of clinical results and of the injector technique.

Sublingual administration (absorption from tablet under tongue or between lip and gums) has the advantage of putting the medicine in the general circulation before passing through the liver, where considerable absorption may take place. Walton reports on the sublingual absorbability of various drugs. Some drug firms are making special sublingual tablets—for example, linguets of metandren (Ciba).

Cyclical estrogen therapy (medication interrupted at regular intervals) diminishes disagreeable cumulative effects and is distinctly advantageous. Palmer presents an instructive consideration of this method, and for stilbestrol advises for climacteric symptoms "between 0.1 and 0.5 mg. daily by mouth for twenty-one days, followed by a five- to ten-day interval without therapy. The estrogen withdrawal interval should fall at the time of expected menstruation, and cycles of therapy should be started twenty-four to forty-eight hours after the onset of a new phase of uterine bleeding if it comes."

# PELLET IMPLANTATION BY INJECTOR METHOD

The Kearns Pellet Injector (two-thirds natural size)



Radial implantation of pellets in 3 different positions. The needle is not removed until all pellets are in place.

Lateral view of pellet in situ. Pellets have been placed in the subcutaneous tissue.

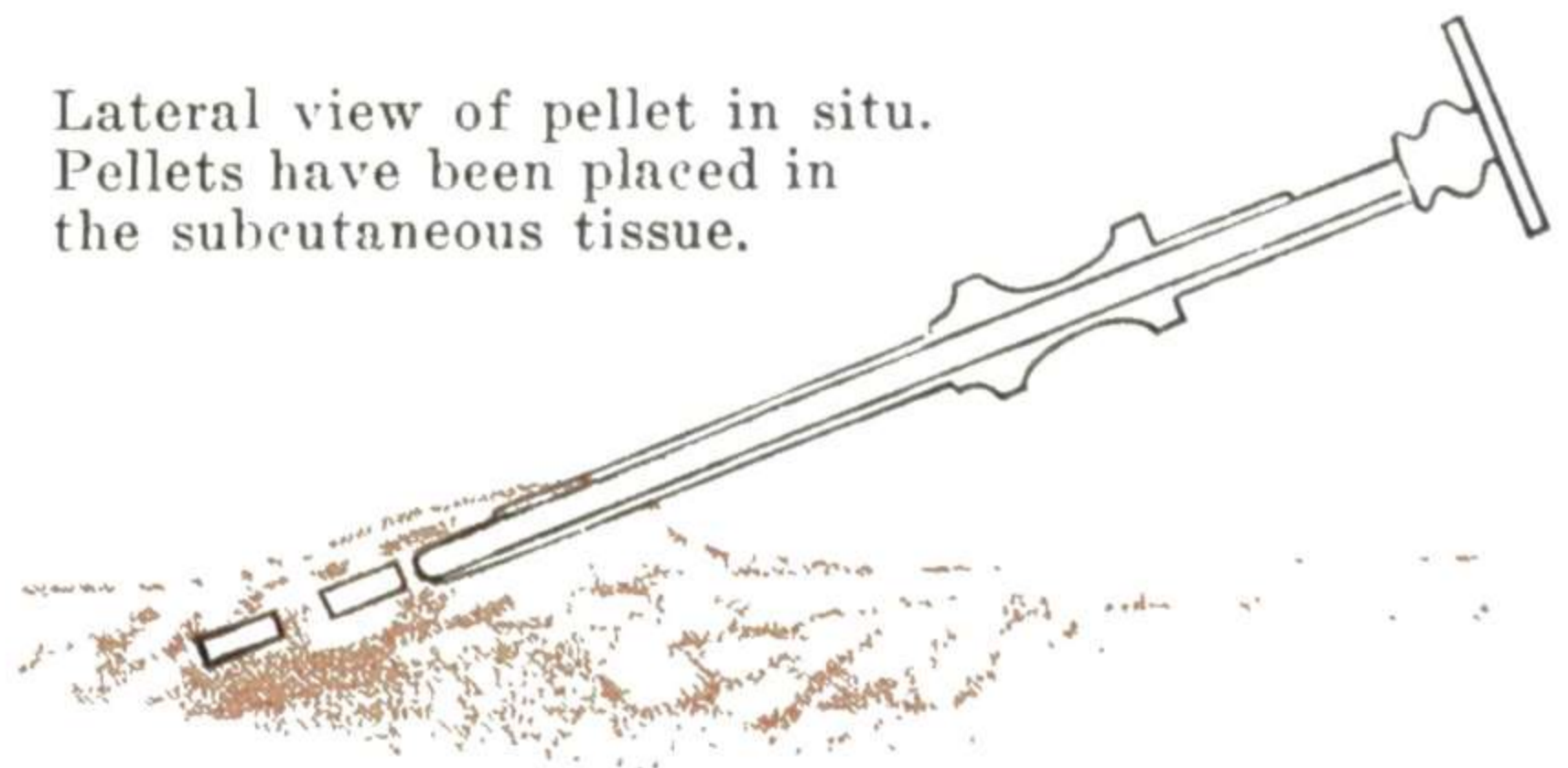


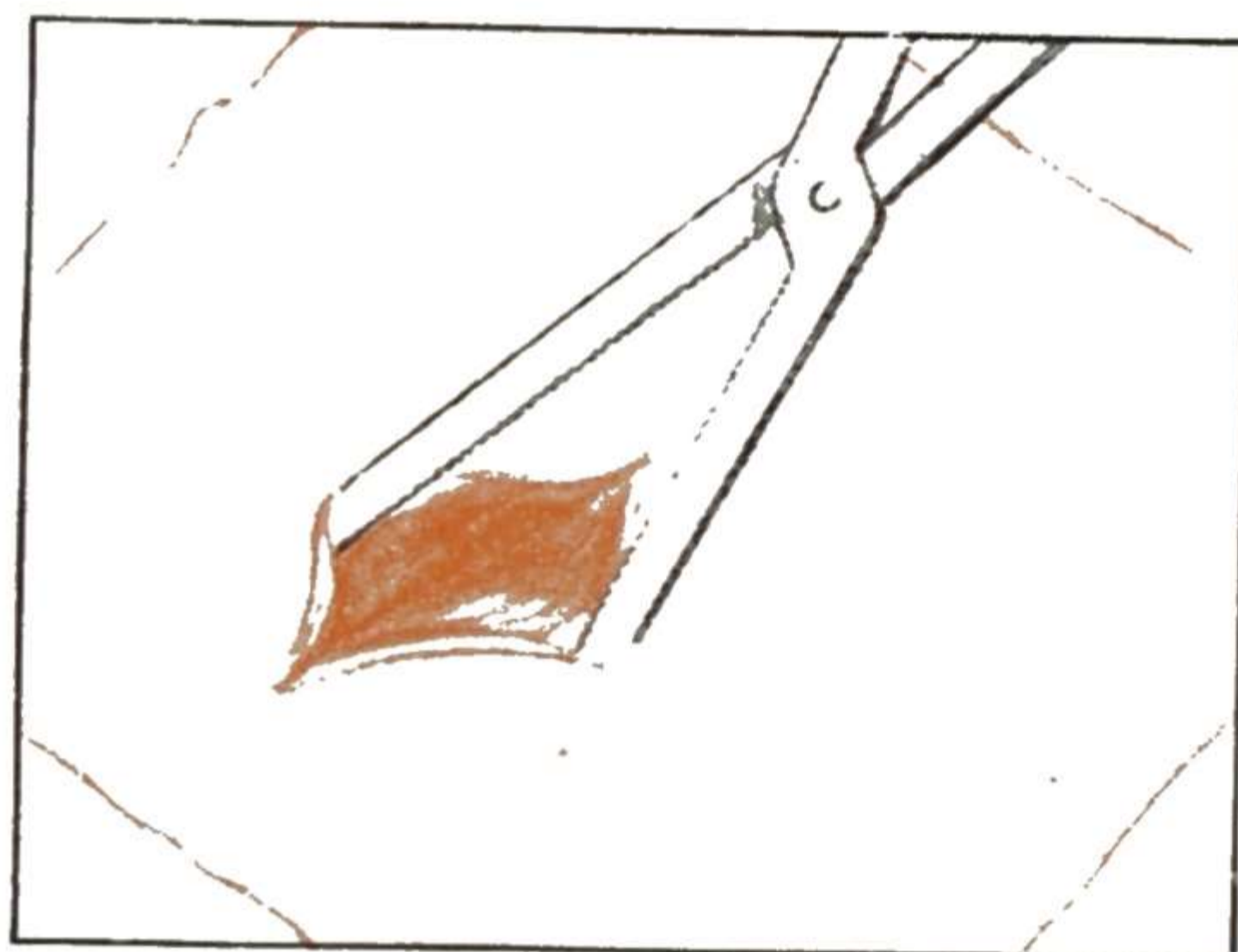
Fig. 337A.—The shape of the pellets adapts them for implantation by injection. The areas usually selected for implantation are the infrascapular region, the lumbar muscle, or the inner aspect of the thigh. The skin is carefully cleaned, followed by iodine and alcohol. The area is infiltrated with procaine 1:200. The needle with sharp plunger in place is inserted either subcutaneously or into the muscle. The sharp plunger is withdrawn and one or two pellets inserted into the needle. The pellets are gently pushed as far as possible through the needle by means of the blunt plunger. One or two pellets are placed at one site, and by partially withdrawing and reinserting the needle additional pellets may be distributed as indicated in the illustration. A later note from Dr. Kearns states that he has found it advisable to deposit all the pellets (even up to six) in one place without shifting of needle. On removal of injector, the small wound may be closed with stitch, skin-clip, or sterile adhesive tape. (From Schering Corporation Bulletin.) (Articles by Dr. W. M. Kearns, J. A. M. A. 112: 2255, 1939; J. Urol. 47: 587, 1942.)

## PELLET IMPLANTATION BY SURGICAL METHOD

(All aseptic precautions must be observed)



Incision; 3-7 cm.



Forming of subcutaneous pockets.



Pocket held open by nasal speculum, and pellet placed within.



Wound closure.

Fig. 337B.—The infrascapular region posteriorly is the preferred site for implantation. The area is prepared with iodine and alcohol, and the site of injection is infiltrated with procaine 1:200 solution. A transverse incision 3-7 cm. in length is made a few centimeters below the inferior spine of the scapula. A number of small pockets (depending on the number of pellets), 3-4 cm. in depth, are then prepared in the subcutaneous fat by blunt dissection. The opening of each pocket in the subcutaneous fat is held sufficiently far apart by a nasal speculum to permit pellets to gravitate to the bottom of the pocket without applying force. This is important, for if the opening of the pocket is too small, the pellet may be crushed by being forcibly inserted. Subcuticular sutures of fine black silk may be used to close the wound. After removing the sutures on the fourth postoperative day, the wound should again be inspected several days later for any tendency toward sloughing. There should be no pain at the site of implantation other than that which occurs from the surgical procedure itself. (From Schering Corporation Bulletin.)

## CHAPTER IV

# DISEASES OF THE EXTERNAL GENITALS AND VAGINA

For clinical consideration it is convenient to take up the diseases of the external genitals and vagina in the following order:

### Classification

#### GONORRHEA

OTHER TYPES OF VULVITIS—Intertrigo, Eczema, Herpes, Bacterial Infections, Parasitic Infections, Leucoplakic Vulvitis.

OTHER TYPES OF VAGINITIS—Simple Vaginitis, Diphtheritic Vaginitis, Emphysematous Vaginitis, Trichomonas Vaginitis, Monilia Vaginitis, Atrophic Vaginitis.

ULCERATIVE DISEASES OF VULVA AND VAGINA—Simple Ulcers, Chancroid, Syphilis, Tuberculosis, Granuloma Inguinale, Lymphogranuloma Inguinale, Rarer Ulcerations.

URETHRAL CONDITIONS—Widening of Meatus, Prolapse of Mucosa, Urethral Caruncle, Urethritis (Skene's Glands), Suburethral Abscess.

VULVOVAGINAL GLAND DISEASES—Inflammation, Abscess, Sinus, Cyst, Tuberculosis.

NONMALIGNANT GROWTHS AND SWELLINGS—Condylomas, Stasis Hypertrophy, Tumors, Pudendal Hernia, Pudendal Hydrocele, Varicose Veins, Hematoma, Injuries.

MALIGNANT DISEASES—Carcinoma, Chorionepithelioma, Sarcoma.

MISCELLANEOUS DISTURBANCES—Leucoderma of Vulva, Adhesions of Prepuce or Labia, Hyperesthesia of Vaginal Entrance, Pruritus Vulvae.

(The more pronounced Malformations are considered in Chapter XIII.)

### GONORRHEA

Gonorrhea is inflammation of the genital organs produced by the gonococcus. The term, when not qualified, is understood to mean gonorrheal inflammation of the vulva, vagina, and urethra, i.e., gonorrheal vulvitis, vaginitis, and urethritis. If the process extends into the uterus or fallopian tubes or bladder, it causes complications known respectively as gonorrheal endometritis, gonorrheal salpingitis, and gonorrheal cystitis. Gonorrhea is sometimes referred to as "specific" vaginitis or vulvitis or urethritis.

### Etiology

Gonorrhea is caused by contact of the affected organs with a gonorrheal discharge, usually in sexual intercourse. The infecting germ (the gonococcus) is a diplococcus, easily stained, and is found in large numbers in the pus cells of all acute gonorrheal discharges. In chronic gonorrheal discharges it is not found so abundantly—in fact, in some cases, it is so scarce as to be very hard to find, and may even disappear entirely for a time.

Though the usual cause of gonorrhea is sexual contact with an infected person, it may exceptionally be caused by other means, as by contact with an infected towel or douche nozzle or chamber utensil or closet seat.