Oophorectomy and Cardiovascular Tissues

George C. Griffith  479

Hysterectomy: Analysis of 1000 consecutive operations

Walter F. Watts and Robert A. Kimbrough, Jr.  483

Pregnancy at Age of Fifty-Six Years: Report of a case

A. E. Anderson  494

Is Premature Birth Preventable?

Henry L. Tieche, Carl D. Osborn, and John A. Broman  496

Urethral Diverticulum

Lawrence R. Wharton, Jr. and Richard W. Te Linde  503

Cervical Tone and Pain Thresholds: Study in the nongravid human uterus


Harlequin Color Change of the Newborn: Report of a case

M. Lemore Birdsong and Julia E. Edmunds  518

Carcinoma of the Cervix in Pregnancy

Harry Prystowsky and C. Bernard Brack  522

Vaginoabdominal Approach in Pelvic-cancer Surgery

Raymond J. Simmons  527

Stromal Endometriosis

Morton A. Schiffer and Abraham Mackles  531

Tetanus Complicating Pregnancy: Report of a case treated with chlorpromazine with survival of both mother and infant

Allan Singleton and Roger W. Witt  540

Acid Phosphatase of the Endometrium: Histochemical demonstration in various normal and pathologic conditions

Benjamin Goldberg and Howard W. Jones, Jr.  542

Continued on next page
CONTENTS (continued)

Postoperative Staphylococcic Enterocolitis After Antibiotic Therapy: Shock and oliguria after hysterectomy; report of a case with recovery
JOHN A. WALL and JOHN ROGER KELSEY, JR. 547

Spontaneous Rupture of the Liver in Afibrinogenemia During Pregnancy: Report of a case
ARMAND J. PEREYRA and MATTHEW P. LAWLER 552

Cervical and Perineal Lacerations: Studies on the mechanics of labor in relation to cervix, vulva, and perineum
FRIEDERIC R. BEHRINGER 557

Primary Ovarian Pregnancy: Report of a case
DAVID M. FARELL and JEROME ABRAMS 562

Ovarian Cyst in the Mesentery of the Ileum: Report of a case
JOSEPH H. ZEIGERMAN and JOSEPH IMBRIGLIA 565

Cytologic Nomenclature: Method for standardization and recording of data on cells exfoliated in body fluids: I. A record book for the cytology laboratory
MARIA S. BLANCO DE DEL CAMPO 567

Ruptured Interstitial Pregnancy Following Homolateral Salpingectomy: Report of a case
HENRY E. STEADMAN 572

Hospital Departments and Tissue Committees: Their functions in community hospitals
LEON P. FOX 576

After Office Hours: Obstetric-Gynecologic Eponyms
HAROLD SPEERT 582

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OVARIAN CANCER strikes down one woman in every hundred past the age of 40. One way of combating this threat has been the prophylactic removal of the ovaries in such women whenever the opportunity was presented.

Most of us are apt to undervalue or to disregard altogether the extragenital functions of the ovarian secretions. In order that we may understand more fully the effects of oophorectomy, with especial emphasis on its effects on the cardiovascular system, I should first like to outline the influence of ovarian hormones—and deprivation of these hormones—on the body economy as a whole and on other structures in the endocrine system in particular.


From the Department of Medicine (Cardiology), University of Southern California School of Medicine, and the Los Angeles County Hospital, Los Angeles, Calif.

Functions of the Ovary

Regulation of Metabolism

Painstaking investigation by physiologists and endocrinologists is fostering a growing realization that the ovaries are not concerned primarily with the sexual and reproductive life of the individual. Foremost among the functions of the ovary is, rather, regulation of metabolism—notably in the anabolic or nitrogen-retaining effects of estrogen. An example of this function is the promotion of bone calcification through stimulation of
osteoelastic activity. Castration is often followed by decalcification of bony tissue or by the onset of menopausal osteoarthritis, both of which can be halted and in some measure reversed by the administration of estrogens.

**CARBOHYDRATE METABOLISM.** A special instance of the metabolic effects of estrogen is its important role in carbohydrate metabolism, mobilizing the glucose reserves and distributing them to the tissues. The point of action of the ovarian hormone is probably at some stage between extracellular glucose and intracellular pyruvate most probably producing the hexokinase reaction. Like insulin, estrogens facilitate the glucokinase reaction, stimulating both energy production and glycogen deposit. Contrariwise, both the pituitary growth hormone and the glucocorticoid hormone inhibit this reaction, a fact which takes on significance in the discussion of the interrelationship of the pituitary, the ovaries, and the adrenals.

**Protection Against Diabetes**

In the presence of impaired pancreatic activity, ovarian hormones protect against diabetes. Experiments on rats indicate that the presence of active ovaries affords protection against diabetes even if as much as 95 per cent of the pancreas has been removed. Presumably, this protective action may be attributed to the proved ability of estrogen to effect hypertrophy and hyperplasia of the islets of Langerhans and thus to stimulate the production of insulin.

**Protection Against Atherosclerosis**

Even more important from the cardiologist's standpoint is the ability of ovarian hormones to confer relative immunity to atherosclerosis, especially coronary atherosclerosis, in the premenopausal female. Coronary atherosclerosis is from 10 to 40 times as frequent in men under 40 as in women under that age; coronary occlusion is almost unknown in women of this age bracket.

At a recent meeting of the American Heart Association, attention was focused on the efficiency with which estrogen administration lowers cholesterol, increases phospholipids, and progressively decreases the cholesterol/phospholipid ratio—all of which are believed factors in athrogenesis that have been so confirmed in our laboratory. Administered to males, estrogens go far toward correcting the lipoprotein spectrum from an atherogenic condition to immune healthy patterns like those of the premenopausal female, even in middle-aged men who have already suffered myocardial infarction.

Estrogen supplies, either from the adrenals or from residual ovarian activity, were found by a group of University of Southern California investigators to exert a protective influence even in postmenopausal women. The amounts of estrogen in the urine of women who had suffered myocardial infarction were significantly smaller than the amounts present in the urine of women free of cardiovascular signs and symptoms.

What, then, is the effect of operative removal of the ovaries? In a study by Wuest, Dry, and Edwards, women who had undergone bilateral oophorectomy were found to have developed by the age of 50 a degree of coronary atherosclerosis not reached in a control group until they had passed the seventieth year. Decade by decade, the incidence of severe coronary atherosclerosis was between 10 and 45 per cent greater in the oophorectomized women than in the controls. Scattergrams demonstrated that a true increase in average sclerosis had occurred, rather than extremely severe sclerosis in a small number of cases.

The importance of this particular facet of ovarian activity was brought home to me by the frequency with which surgeons include among their published reports a notation that one or more of the patients "died of a heart attack" some 13 or 18 or 20 months after the bilateral oophorectomy. I wonder whether these men are aware that a relation-

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GRIFFITH

Obstetrics and Gynecology

Vol. 1 May 1950
ship exists between these deaths and earlier removal of the ovaries.

INTERRELATIONS WITH OTHER ENDOCRINES

Thus far we have been concerned with the basic, extragenital functions of the ovary, considered separately from the other endocrines. Actually, we must be ever aware of the close interdigitation of the various endocrines, the reciprocal relationship whereby removal of the influence of any endocrine gland from its fellows in the endocrine system causes profound changes in the structure and secretory activity of every remaining member.

Adrenal Cortical Hormones

After oophorectomy, cells in the adrenal cortex hypertrophy and 17-ketosteroid excretion, which is a rough measure of adrenal steroid production, rises under the influence of increased adrenal cortical function. In mice (perhaps in humans as well), cancer-susceptible individuals are prone to develop nodular cortical hyperplasia or adrenal carcinomas following the operation.® Changes occur in local and general water configuration and in water balance. When hypertension follows removal of the ovaries, it usually is an expression of a disturbance in extracellular fluid balance as a result of the sudden withdrawal of ovarian hormones from the endocrine pattern. However, hypertension already present before removal of the ovaries often is accentuated by climacteric symptoms. Under these conditions, but not otherwise, proper substitutive hormone treatment may produce an incidental, mild hypotensive effect.

Pituitary-Influenced Hormones

In isolated cases, hypertrophy of the adrenal cortex under increased stimulation of the anterior pituitary may result in a disproportionate overproduction of mineralocorticoids or glucocorticoids.® If the former steroid is produced in greater quantities, cardiovascular and hypertensive changes may occur. Increased secretion of anterior pituitary growth hormone—which always follows oophorectomy—is in itself able to cause cardiovascular and renal lesions comparable to those produced by overproduction of the mineralocorticoids.

Thyroid Activity

Nevertheless, oophorectomy rarely initiates clinically evident hypertension in the previously normotensive individual, as shown in the study by Taylor, Corcoran, and Page. These investigators examined 200 women, 179 of whom had undergone surgical castration, the remaining 21 having reached the menopause. Ten per cent had been hypertensive prior to the operation (or prior to onset of the menopause); afterward, the percentage rose to only 13 per cent. It is altogether possible that any moderate hypertensive effect which might be due to removal of the ovaries would be masked by the decreased thyroid activity following menopause.

The already mentioned inhibition of the glucokinase reaction by pituitary and glucocorticoid hormones, a reaction aided prior to menopause by ovarian secretion, is one instance of abrupt change to which the body must adjust following castration. Another is the partial suppression of thyroid action by increased supplies of adrenal cortex hormone, through interference with the collection of iodine by that organ. This results in creation of myxedema, at least at a subclinical level, lowering metabolic efficiency and offering a fertile ground for atherogenesis. The structural changes in the pituitary, with consequent changes in function, are fully as severe as those occurring in the adrenals and, once established, may be irreversible.

EFFECTS ON CARDIOVASCULAR TISSUES

Obviously, cardiovascular tissues cannot escape the effects of the profound glandular changes occasioned by oophorectomy. Overproduction of either growth (somatotrophic) hormone of the anterior pituitary and/or mineralocorticoids by the hypertrophied ad-
renal cortex may result in severe cardiac and renal lesions, most commonly as a result of the deposit of hyalin material within the vessel walls.7.8

Not only are cardiovascular tissues robbed of the anabolic stimulation of estrogens but also, because of impaired ability of sclerotic coronary vessels to augment the flow of blood according to the needs of cardiac muscle, nutrition of the heart is interfered with, to the detriment of both cardiac efficiency and cardiac reserve.

THE PROBLEM

Because of its important role in the body economy the ovary should not be removed except for the most cogent of reasons. Experience has taught that control of the artificial menopause is by no means completely successful, and it is sometimes a woeful failure. As yet, we have little knowledge concerning the extent to which ovarian hormones enter into enzymatic reactions in the tissues. Although we have information about the main hormones, we are by no means certain that these account for all of the ovary's effects. It is possible that the ovarian hormone acts as a catalyst in the interreaction of micronutrients and cardiovascular enzymes.

Apart from "incidental" or "prophylactic" operations, a surprising number of oophorectomies betray a misconception of the physiologic relationship between the ovary and other organs. Thus we find extirpation of ovaries plus adrenals in attempts to slow or shrink malignancies in no way supported by estrogen; ovaries alone removed to retard mammary cancer, for example, but with no thought given to estrogen-producing ability of the adrenals; uteri permitted to remain minus necessary ovarian stimulation; or oophorectomy performed because of a patient's mental or emotional aberration. At the time of removal of uteri for benign conditions, some surgeons will wantonly sacrifice one ovary or the greater part of both, in the erroneous belief that the smallest remnant of ovarian tissue will safeguard ovarian activity—unmindful that too little ovarian mass brings on ovarian failure.

As clinicians, our problem is to balance possible beneficial effects of oophorectomy against (1) certain loss to the patient of orderly hormonal interchange, plus (2) certain loss of the protective action of ovarian secretion. Rarely do the benefits outweigh the deleterious effects. From the cardiologist's standpoint, deleterious effects on the cardiovascular system are so important as to outweigh possible beneficial effects, except in the exceptional instance.

REFERENCES


Hysterectomy

Analysis of 1000 consecutive operations

WALTER F. WATTS, M.D., and ROBERT A. KIMBROUGH, JR., M.D.

Since removal of the uterus has become the most common major gynecologic operation,1 hysterectomy has received increasing attention in recent literature. During the past 10 years two types of article on this subject have appeared frequently. The first is the statistical report on the various aspects of relatively large series of hysterectomies performed by one or two men or by an entire hospital staff. The second is the report of investigation into the necessity for the operation. This type follows the lead of Miller who, in 1946, first questioned the justification of many hysterectomies. He presented a relatively small series of patients operated upon in ten Midwestern hospitals during a period of four months: In 17.4 per cent the preoperative diagnosis was not confirmed, and in 33.1 per cent the patients either had no disease or had an illness which contraindicated hysterectomy.

Following Miller’s work, others investigated larger series, attempting to evaluate the difficult question of therapeutic necessity. Diddle, O’Connor, and Winebrenner,6 reporting 889 hysterectomies, either alone or combined with resection or removal of ovaries, found 39.7 per cent justified and the remainder unjustified, partially justified, or undetermined. Doyle, in studying 6248 hysterectomies from 30 hospitals during 1948, found the preoperative diagnosis confirmed in only 54.9 per cent, while a total of 39.3 per cent of the series were considered open to criticism.

There is no question concerning the value of each type of article. However, if the two could be combined, a more valuable contribution might possibly result. A review of the literature failed to reveal any analytical article which attempts to include the delicate question of therapeutic necessity.

It is the aim of this study to present a statistical and critical analysis of 1000 consecutive hysterectomies performed at the Pennsylvania Hospital. It is hoped that the questions of justification and therapeutic necessity may be answered in this group of patients by using acceptable criteria for evaluation.

MATERIAL

The 1000 patients analyzed in this paper were operated upon in the Division of Obstetrics and Gynecology of the Pennsylvania Hospital, a teaching institution affiliated with the Graduate School of Medicine of the University of Pennsylvania. In order to report the 1000 most recent hysterectomies, the authors examined all records from the Department of Pathology starting with December 31, 1954, then working in reverse chronologic order. All specimens that included a uterus were listed for this survey. The hospital record of each patient was examined and only those hysterectomies performed for benign gynecologic conditions were recorded.

From the Division of Obstetrics and Gynecology of the Pennsylvania Hospital, Philadelphia, Pa.

Present address (W. F. W.): 6710 West North Avenue, Chicago 35, III.
Both ward (service) and private patients were included. The ward patients were operated upon by the senior resident in gynecology, after consultation with one or more members of the attending staff. The private patients were operated upon by the attending gynecologists.

All patients were operated upon during a period of slightly less than 45 months—April 10, 1951, to December 31, 1954. The group was divided into 663 private patients, operated upon by 28 attending gynecologists, and 337 ward patients, operated upon by 8 senior residents. At the time of this study, all but 3 of the attending gynecologists were certified by the American Board of Obstetrics and Gynecology. The distribution of patients is shown in Table 1.

### RESULTS

#### Type of Hysterectomy

As mentioned previously this study included only those patients in whom hysterectomy was indicated because of a benign gynecologic condition. All hysterectomies as a planned part of an operation for carcinoma, cesarean hysterectomies, and those indicated for obstetric reasons or complications thereof were excluded. As a result of this elimination, only total abdominal, vaginal, and subtotal (supravaginal) hysterectomies were analyzed. Table 2 shows the number and percentage of these hysterectomies. Total abdominal hysterectomies made up 69.2 per cent of the series, a somewhat higher percentage occurring among the ward patients. Vaginal hysterectomies were done in 25 per cent of all the patients, but in 30 per cent of the private patients. The subtotal procedure, performed 58 times, was 5.8 per cent of the 1000 operations. As might be expected, the incidence of the incomplete operation was more than doubled among the ward patients.

#### Age

Table 3 gives the incidence according to age. As in other reported series, the largest number of patients were in the fourth and fifth decades. In this study 79.2 per cent of the patients were in these two decades. The youngest patient in the series was 19 years of age, and the oldest was 87. The age of

![Image with table and text](https://example.com)
HYSTERECTOMY

the patients who had the vaginal operation was higher due to the greater frequency of prolapse, relaxations, and poorer surgical risks among older patients.

**Table 3. Distribution of Patients According to Age**

<table>
<thead>
<tr>
<th>Age group</th>
<th>No. of patients</th>
<th>% of total</th>
<th>Type of patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-20a</td>
<td>1</td>
<td>0.1</td>
<td>Private Ward</td>
</tr>
<tr>
<td>21-30</td>
<td>51</td>
<td>5.1</td>
<td>21 30</td>
</tr>
<tr>
<td>31-40</td>
<td>345</td>
<td>34.5</td>
<td>180 165</td>
</tr>
<tr>
<td>41-50</td>
<td>452</td>
<td>45.2</td>
<td>342 110</td>
</tr>
<tr>
<td>51-60</td>
<td>105</td>
<td>10.5</td>
<td>88 17</td>
</tr>
<tr>
<td>61-70</td>
<td>41</td>
<td>4.1</td>
<td>28 13</td>
</tr>
<tr>
<td>Over 70b</td>
<td>5</td>
<td>0.5</td>
<td>4 1</td>
</tr>
</tbody>
</table>

a Youngest 19 years.

b Oldest 87 years.

**Previous Operations**

In recording previous operations for this survey, only major surgical procedures in the lower abdomen, pelvis, and vagina were noted. Accordingly, 274 private patients (41.0 per cent) had 366 previous operative procedures. Of the ward patients, 91 (26.0 per cent) had 124 previous operations.

**Preoperative Studies**

An attempt was made to determine the number of patients who had curettage, cervical biopsy, and/or vaginal smears within 2 years before hysterectomy. Such data shown in Table 4, were arrived at by examining all previous records of these patients in the Department of Pathology. Because of the possibility that these examinations might have been done at a different hospital or laboratory a list of each doctor’s patients was formulated, and the preoperative studies were summarized from individual office files.

Curettage at the time of hysterectomy was not included, since it could not be considered as part of the preoperative work-up. It was, however, recorded under associated operations.

There were 347 patients who had a total of 507 procedures. It is of interest to note that a higher percentage of these studies was performed on the ward patients. One explanation for this is that for the last year of the study (January 1, 1954–December 31, 1954) it was a rule of the institution that all ward patients who were to have a hysterectomy must have had at least one negative vaginal smear. A second explanation, while not proved, is that the expense involved might have been a deterrent in having these studies done when hysterectomy first became necessary or advisable.

**Symptoms**

A listing of the primary symptoms of the 1000 women is found in Table 5. These figures and percentages are in agreement with those of other reports. Abnormal menstrual bleeding was the most frequent complaint, followed in order by pain, symptoms...
associated with prolapse, and symptoms of leiomyoma; i.e., pressure, sensation of a mass, etc. It should be noted that 83 patients were asymptomatic. The majority of these were patients with leiomyomas of increasing size or large leiomyomas found on routine physical examination.

Anesthesia

Methods of anesthesia were recorded. However, with the skilled anesthesiologist of today, it is rare that a patient is given only one anesthetic agent. Therefore, the cases were divided into only two categories—801 patients who had received spinal anesthesia (regardless of supplementary agents) and 199 patients who had been given general anesthesia.

Mortality

In this series there was 1 death, an incidence of 0.1 per cent. This 56-year-old ward patient sustained an operative perforation of the uterus at the time of a curettage performed because of postmenopausal bleeding. Cardiac arrest occurred during laparotomy, but the rhythm was re-established after approximately five minutes. A subtotal hysterectomy was rapidly completed. She appeared to be fairly well for a short while, but died 48 hours postoperatively. Post-mortem examination was not obtained.

Morbidity

The febrile morbidity rate in the 1000 cases was 19.9 per cent, determined by the accepted criteria for obstetric morbidity. Recent reports by Smith, Wier, and others have stated that the incidence of morbidity following surgical procedures is high if these rigid criteria are used. For this reason and because the value of such criteria may be questioned in this age of chemotherapy, some new standard of postoperative morbidity is needed. The analysis of postoperative febrile morbidity is summarized in Table 6.

The total febrile morbidity of 19.9 per cent is somewhat lower than that of other series. An interesting finding was the slight difference following each type of hysterectomy, especially in comparing the subtotal and total procedures. In most series, while the rate of morbidity was higher in the private patients, it followed that the ward patients were probably more affected.

The mortality was less than 1 per cent, a similar incidence as in the previous series. Table 6 shows the patients entering each group.
the rates of febrile morbidity were similar, the percentage difference in febrile morbidity following the various types of hysterectomies was greater.

The percentage rates of morbidity by etiology and by the number of days are similar to those of other reports. The higher incidence of febrile morbidity among the ward patients may be attributable to the poorer nutrition of these patients and the

Laceration of the bowel and/or bladder occurred in 6 cases. Ureteral injury was not described in any of the operations.

**POSTOPERATIVE.** This category (Table 8) includes disorders without febrile morbidity but of definite consequence. In cases of urinary retention or difficulty in voiding, only those considered to be major postoperative problems which prolonged the patient’s hospital stay were included. In the 13 pa-

### TABLE 7. INTRAOPERATIVE COMPLICATIONS

<table>
<thead>
<tr>
<th></th>
<th>Private</th>
<th>Ward</th>
<th>Total</th>
<th>% of complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage with shock</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td>38.9</td>
</tr>
<tr>
<td>Hemorrhage without shock</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>22.2</td>
</tr>
<tr>
<td>Laceration of bowel</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>16.7</td>
</tr>
<tr>
<td>Laceration of bladder</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>16.7</td>
</tr>
<tr>
<td>Mismatched blood</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>5.5</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td>7</td>
<td>11</td>
<td>18</td>
<td>100.0</td>
</tr>
</tbody>
</table>

### TABLE 8. POSTOPERATIVE COMPLICATIONS (WITHOUT MORBIDITY)

<table>
<thead>
<tr>
<th></th>
<th>Private</th>
<th>Ward</th>
<th>Total</th>
<th>% of complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary infections</td>
<td>23</td>
<td>18</td>
<td>41</td>
<td>25.0</td>
</tr>
<tr>
<td>Urinary retention (diff. voiding)</td>
<td>19</td>
<td>4</td>
<td>23</td>
<td>14.1</td>
</tr>
<tr>
<td>Wound infections</td>
<td>11</td>
<td>9</td>
<td>20</td>
<td>12.2</td>
</tr>
<tr>
<td>Vaginal bleeding</td>
<td>5</td>
<td>8</td>
<td>13</td>
<td>7.9</td>
</tr>
<tr>
<td>Transfusion reactions</td>
<td>6</td>
<td>6</td>
<td>12</td>
<td>7.4</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>7</td>
<td>3</td>
<td>10</td>
<td>6.2</td>
</tr>
<tr>
<td>Wound hematoma</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td>4.9</td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>4.3</td>
</tr>
<tr>
<td>“Cuff” infections</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>2.6</td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>1.8</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>U. R. I.</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>Others</td>
<td>12</td>
<td>6</td>
<td>18</td>
<td>11.0</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td>98</td>
<td>65</td>
<td>163</td>
<td>100.0</td>
</tr>
</tbody>
</table>

more frequent association with pelvic inflammatory disease, as well as to the difference in surgical experience between the resident and attending staffs.

**Complications**

**INTRAOPERATIVE.** The operative description of each chart was examined and the intraoperative complications were recorded. The most common was hemorrhage, comprising 61.6 per cent of this group (Table 7). Patients with postoperative vaginal bleeding, the quantity of blood lost was sufficient to require resuturing or vaginal packing in each instance. A large percentage of these complications probably would have resulted in febrile morbidity had it not been for antibiotics and chemotherapeutic agents.

**Chemotherapy and Antibiotics**

All patients receiving antibiotics or chemotherapeutic agents, either vaginally or
systemically, were tabulated. It was found that 701 patients had received some vaginal antibiotic or chemotherapeutic agent either preoperatively or postoperatively, more commonly both; 592 patients received some form of systemic chemotherapeutic or antibiotic agent. While evaluation of vaginal antibiotics and chemotherapy has been used by others to determine their effect on the incidence of febrile morbidity, these findings are valid only with the use of standardized medications, adequate controls, and results categorized according to the operative procedure. Recently this method has been criticized in surveys in which the work of a number of surgeons is included in the same report. Vaginal antibiotic or chemotherapeutic agents are almost routine at this institution. However, the agents themselves and the methods of their postoperative use were not standardized. These variations and the lack of controls rendered useless any attempt to determine their effect on the postoperative morbidity in this series.

Associated Procedures

The operative procedures associated with each type of hysterectomy are given in Table 9. In this series there is a relatively low per centage of hysterectomies done without additional operations. This is in part explained by the frequent employment of prophylactic appendectomy at this institution.

Length of Hospital Stay

All charts were examined to determine the number of postoperative hospital days following each type of hysterectomy. Four were excluded: 1 remained voluntarily to undergo deep x-ray therapy; another remained to have a secondary nongynecologic operation; the third was hospitalized 77 days awaiting transfer to a nursing home; and one patient died 48 hours postoperatively.

As seen in Table 10, the longest average hospital stay was among the patients who were subjected to the subtotal procedure. These patients remained hospitalized 0.8 days in the hospital. However, this method of hysterectomy was performed on patients with other conditions or complications so that this might not be applicable to hysterectomy as it is usually used. Further investigation of this operation would be of value in this series. One patient died 48 hours postoperatively.

Pathology

TABLE 9. ASSOCIATED OPERATIVE PROCEDURES

<table>
<thead>
<tr>
<th>Procedure</th>
<th>T. A. H.</th>
<th>S. T. H.</th>
<th>V. H.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hysterectomy alone</td>
<td>692</td>
<td>58</td>
<td>250</td>
<td>1000</td>
</tr>
<tr>
<td>Other procedures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appendectomy</td>
<td>330</td>
<td>10</td>
<td>2</td>
<td>342</td>
</tr>
<tr>
<td>Adnexal removal, complete</td>
<td>276</td>
<td>17</td>
<td>3</td>
<td>296</td>
</tr>
<tr>
<td>Adnexal removal, partial</td>
<td>221</td>
<td>29</td>
<td>13</td>
<td>263</td>
</tr>
<tr>
<td>Ant. and post. colporrhaphy</td>
<td>4</td>
<td>1</td>
<td>166</td>
<td>171</td>
</tr>
<tr>
<td>Posterior colporrhaphy</td>
<td>20</td>
<td>0</td>
<td>43</td>
<td>63</td>
</tr>
<tr>
<td>Dilatation and curettage</td>
<td>30</td>
<td>7</td>
<td>26</td>
<td>63</td>
</tr>
<tr>
<td>Marshall-Marchetti procedure</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Hemorrhoidectomy</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Inguinal herniorrhaphy</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Umbilical herniorrhaphy</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Bartholin cystectomy</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Omentectomy</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Anterior colporrhaphy</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Presacral neurectomy</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td>705</td>
<td>64</td>
<td>264</td>
<td>1033</td>
</tr>
</tbody>
</table>

TABLE 10. HOSPITAL STAY

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. cases</th>
<th>Range</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtotal</td>
<td>57</td>
<td>7-48</td>
<td>11.9</td>
</tr>
<tr>
<td>Vaginal</td>
<td>250</td>
<td>7-21</td>
<td>11.1</td>
</tr>
<tr>
<td>Total abdominal</td>
<td>689</td>
<td>6-45</td>
<td>10.5</td>
</tr>
</tbody>
</table>

a One patient excluded.  
b Three patients excluded.
days longer than the group who had vaginal hysterectomy, and 1.4 days longer than patients who had the total abdominal procedure. While this finding is at variance with other reports previously cited, it is what might be expected. The subtotal procedure is utilized only in cases of extreme technical difficulty or in those patients with intraoperative complications of such a degree that removal of the cervix might jeopardize the patient.

Pathologic Findings

Table 11 details the pathologic findings in the 1000 patients. No record was kept of uteri with diagnosis of chronic cervicitis, as this was an almost universal finding. Uterine leiomyomas without other lesions were found in 415 patients. In 195 other patients leiomyomas were combined with additional pathologic conditions. Those leiomyomas of less than 2 cm. diameter were not included. The total of 610 patients having the pathologic diagnosis of leiomyoma uteri constituted 61 per cent of the series.

There were 157 patients in whom a major pathologic finding was lacking. Of these, 119 had a vaginal operation because of varying degrees of uterine prolapse, with or without relaxation of the pelvic floor. The remaining 38 patients had uteri of normal dimensions, which were removed for a variety of indications. This group is analyzed, both for the indication and therapeutic necessity, in the section Normal-sized Uterus and in Discussion.

Diagnoses

One accepted criterion used in appraising the surgical indication for any operative procedure is to compare the preoperative diagnosis with the findings of the pathologist. The preoperative diagnosis per se is not necessarily the indication for operation. In analyzing the preoperative diagnoses, however, it was found that except for 8 cases the preoperative diagnosis was synonymous with the indication for hysterectomy. These 8 exceptions included 3 perforations of the uterus at the time of curettage, 2 bilateral ovariectomies in cases of carcinoma of the breast, 2 instances of sterilization, and 1 case lacking a preoperative diagnosis.

In this study the preoperative diagnosis was classified as correct, incorrect, or correct but with additional pathologic conditions. Table 12 gives these figures. The preoperative diagnosis was correct in 76.6 per cent and correct but with additional lesions in 13.5 per cent. In 9.8 per cent the diagnosis was incorrect.

Normal-sized Uterus

It was thought that a study of the excised uteri of normal size and weight would be of
value. However, the question of what constitutes a uterus of normal size arose. Conversely, in the absence of pregnancy or definitive disease, what constitutes an enlarged uterus? It will be noted that there are 38 cases of "hypertrophy" of the uterus in Table 11. Quotation marks are used because the term was not employed by the pathologist but by the authors to signify a uterus.

TABLE 12. PREOPERATIVE DIAGNOSIS

<table>
<thead>
<tr>
<th>Preoperative diagnosis</th>
<th>Incorrect</th>
<th>Correct with add. findings</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>98</td>
<td>135</td>
<td>233</td>
</tr>
<tr>
<td>Actual diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvic inflammatory disease</td>
<td>9</td>
<td>65</td>
<td>74</td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>22</td>
<td>19</td>
<td>41</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>21</td>
<td>10</td>
<td>31</td>
</tr>
<tr>
<td>Benign ovarian cysts</td>
<td>13</td>
<td>16</td>
<td>29</td>
</tr>
<tr>
<td>Without pathologic findings</td>
<td>15</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Ovarian carcinoma</td>
<td>4</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Cervical carcinoma (invasive)</td>
<td>2</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Endometrial hyperplasia</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Tubal carcinoma</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Endometrial carcinoma</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Carcinoma in situ (cervical)</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Intrauterine pregnancy</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Incomplete abortion</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

* Correct, 766; not recorded, 1.

definitely larger and heavier than accepted "normals," yet without significant change to account for the enlargement. Acceptable measurements for a "normal" uterus proved difficult to obtain, since different authors vary in what they consider to be average or normal figures. Admittedly, the variation is not large, but in attempting to write a critical analysis, the figures become important. It was decided to use the standards of Saphir, which are averages based on 1000 autopsies and, for the most part, include the figures of other authors.

Using these figures as a base line, there were 38 uteri significantly enlarged in one or more dimensions. In the absence of any demonstrable cause, they were classified as "hypertrophied." In discussing such hypertrophy, Novak states that it is a rare condition. Possibly he along with many other pathologists would consider the majority of these 38 uteri as being within "upper limits of normal."

Again, using Saphir's figures, there were 294 uteri within the "normal" size and weight range. The indications for their removal are given in Table 14, which shows that the majority of hysterectomies were justified. In considering uteri of normal size, the indication of dysfunctional uterine bleeding must have special attention. In such cases, because endometrial hyperplasia is frequently not found by the pathologist, any attempt to question the necessity of hysterectomy becomes difficult. While the condition is a recognized indication, as such it must be qualified. Although almost all authorities list it when considering indica-

TABLE 13. AVERAGE SIZE AND WEIGHT OF UTERI

<table>
<thead>
<tr>
<th></th>
<th>Nulliparous</th>
<th>Multiparous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>7.8–8.1 cm.</td>
<td>8.7–9.4 cm.</td>
</tr>
<tr>
<td>Width</td>
<td>3.4–4.5 cm.</td>
<td>5.4–6.1 cm.</td>
</tr>
<tr>
<td>Depth</td>
<td>1.8–2.7 cm.</td>
<td>3.2–3.6 cm.</td>
</tr>
<tr>
<td>Weight</td>
<td>33–41 Gm.</td>
<td>102–107 Gm.</td>
</tr>
</tbody>
</table>

Data from Saphir.
HYSTERECTOMY

tions, Te Linde maintains that hysterectomy is seldom necessary.

<table>
<thead>
<tr>
<th>Indication for hysterectomy</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protrusio and relaxations</td>
<td>123</td>
<td>41.8</td>
</tr>
<tr>
<td>Dysfunctional uterine bleeding</td>
<td>68</td>
<td>23.1</td>
</tr>
<tr>
<td>Endometriosis and ovarian cysts</td>
<td>48</td>
<td>16.2</td>
</tr>
<tr>
<td>Pelvic inflammatory disease</td>
<td>25</td>
<td>9.0</td>
</tr>
<tr>
<td>Ovarian carcinoma</td>
<td>7</td>
<td>2.2</td>
</tr>
<tr>
<td>None (without pathologic findings)</td>
<td>6</td>
<td>1.9</td>
</tr>
<tr>
<td>Retropulsion</td>
<td>4</td>
<td>1.5</td>
</tr>
<tr>
<td>Tubal carcinoma</td>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td>Uterine perforation</td>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td>Persistent vaginal bleeding</td>
<td>2</td>
<td>.7</td>
</tr>
<tr>
<td>Suspicious biopsy</td>
<td>2</td>
<td>.7</td>
</tr>
<tr>
<td>Leukoplakia</td>
<td>1</td>
<td>.3</td>
</tr>
<tr>
<td>Sterilization</td>
<td>1</td>
<td>.3</td>
</tr>
<tr>
<td>TOTALS</td>
<td>294</td>
<td>100.0</td>
</tr>
</tbody>
</table>

**DISCUSSION**

In attempting to determine in retrospect the therapeutic necessity of these 1000 hysterectomies, predetermined criteria were employed.

The general factors which contraindicate hysterectomy are well known and, if present, render the operation unjustified. Therapeutic necessity, however, is a more subtle term and certainly more difficult to determine. The recent advent of tissue committees has done much to prevent the needless sacrifice of normal tissue and to clarify some of the difficulties in determining the necessity for a surgical procedure.\(^9\) Even so, each case must be individualized. A tissue committee or anyone seeking to make a critical analysis should consider all involved factors and attempt to evaluate the case from the point of view of the clinician.

In order to discover operations that might be unjustified, unnecessary, or open to criticism, all records were screened by asking the following questions: What were the symptoms and their duration? Was the preoperative work-up adequate? What were the pathologic findings? Was the preoperative diagnosis confirmed by the pathologist?

Any procedure that might be criticized according to these criteria was studied further, by considering the patient's age, parity, laboratory findings, and previous therapy. The result of the application of these questions is summarized in Table 15 and in the following paragraphs.

1. Surgery was considered justified in all but 2 of the 83 patients without symptoms. These two patients were operated upon because of an incorrect preoperative diagnosis and are considered under that category.

2. Inadequacy of the preoperative work-up constituted the greatest cause for criticism. As previously mentioned, only 34.7 per cent of the patients had preoperative curettage, biopsy, or vaginal smears. Excluding ovarian malignancy and sarcomatous degeneration of leiomyomas, there were 7 cases of invasive cervical carcinoma, 3 instances of cervical carcinoma in situ, and 2 cases of endometrial carcinoma that might have been diagnosed preoperatively had these studies been performed. The hysterectomies in the cases of invasive cervical

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Vol. 7, No. 5
May, 1956

491
carcinoma were considered unjustified; the others were classified as “open to criticism.”

Dysfunctional uterine bleeding, the most difficult indication to evaluate, must be given special attention in considering preoperative curettage. In this condition an accurate diagnosis is impossible without curettage. This fact, combined with an accepted cure rate of 40 per cent following curettage, leaves no question concerning its need, especially in younger women. In this study the records of patients who had a hysterectomy because of dysfunctional uterine bleeding were examined for age, prior curettage, pathologic findings, clinical evidence of anemia, and previous hormonal therapy. The surgery was considered unjustified in patients under 40 without previous curettage, in the absence of evidence of pathologic change or of anemia and with no record of prior hormonal therapy. In patients over 40, without previous curettage or vaginal smears, the hysterectomy was criticized because of the possibility of an inaccurate diagnosis.

Nine cases of hysterectomy for dysfunctional uterine bleeding were considered unjustified because of age, lack of pathologic alteration in pelvic organs, and failure to attempt to control the bleeding by curettage. There were 4 patients in whom the operation was criticized because of failure to obtain a correct preoperative diagnosis (if not therapeutic success) by means of curettage.

3. Table 14 shows that hysterectomy was considered justified in all but 6 of the 157 patients without major pathologic findings. In these 6 patients, a surgical indication was lacking, the surgery being done on the basis of an incorrect preoperative diagnosis.

4. There were 98 patients with an incorrect preoperative diagnosis and 135 patients in whom the diagnosis was correct, but in whom there were additional undiagnosed lesions. Mistakes made most frequently included pelvic inflammatory disease, leiomyomas, endometriosis, and ovarian cysts. Since such diagnostic errors are reasonable they were not criticized as long as the hysterectomy was still indicated.

Of the 98 patients with an incorrect preoperative diagnosis, 15 were found subsequently to be lacking pathologic lesions sufficient to warrant hysterectomy. The removal of a normal uterus on the basis of an incorrect preoperative diagnosis can be classified only as unjustified. The previously discussed cases of cervical and endometrial carcinoma were also in this category.

Lastly, there were 3 patients who had unsuspected intrauterine pregnancy. Biologic tests for pregnancy were lacking in all, and the operation was considered unjustified.

**SUMMARY**

1. An analysis has been presented of 1000 consecutive hysterectomies done in the Division of Obstetrics and Gynecology of the Pennsylvania Hospital.

2. Total abdominal hysterectomy accounted for 69.2 per cent, 25.0 per cent were vaginal hysterectomies, and 5.8 per cent were subtotal hysterectomies.

3. The age, parity, presenting symptoms, and postoperative complications were in general agreement with those of other series.

4. The mortality was 0.1 per cent, the one death following cardiac arrest.

5. The febrile morbidity was 19.9 per cent. There was no significant difference in the febrile morbidity following the three types of hysterectomy.

6. The hospital stay varied only slightly following the three types of hysterectomy. The longest average period of hospitalization followed the subtotal procedure.

7. The preoperative diagnosis was confirmed microscopically in 76.6 per cent. In an additional 13.5 per cent it was correct, but other undiagnosed lesions were found. In 9.8 per cent the diagnosis was incorrect.

8. An attempt was made to determine the justification for, or therapeutic necessity of, these operations. Hysterectomy was considered unjustified in 3.4 per cent, and was
HYSTERECTOMY

criticized in 0.9 per cent because of failure to perform prior curettage for diagnosis and/or therapy.

9. The small percentage of patients who had preoperative curettage, cervical biopsy, and/or vaginal smears has been noted. It is imperative that all patients who are to undergo hysterectomy should have the benefit of one or more of these diagnostic tests.

REFERENCES


Pregnancy at Age of Fifty-Six Years

Report of a case

A. E. ANDERSON, M.D.

Par turition in a woman over 52 years of age has not been proved," and to occur at 55 "... it must be considered a gross aberration of reproductive physiology." A case is presented of a pregnancy occurring in a woman over 56 years of age.

The patient (A. H. 2535-55) was born in Turkey on September 28, 1898. No birth certificate is available but this date is recorded in the family bible kept by the patient's father (Fig. 1). The patient was married August 16, 1919, at the age of 20 years, which is also recorded in the family bible (Fig. 2). She delivered 2 children, one on February 14, 1924, and one on October 26, 1925 (also recorded in the family bible). The ages of these children at the time of this pregnancy (1955) were 31 and 30 years, respectively. The patient became a naturalized citizen of the United States in 1944, at which time her age was recorded as 45 years (recorded on naturalization papers).

The patient was first seen on July 8, 1955. Pertinent history at that time was that the menarche had occurred at age 14. Normal and regular menses had occurred until March, 1955. No vaginal bleeding occurred in April or May. In mid-June the patient had the onset of...
vaginal bleeding which persisted to the time of her first office visit on July 8, 1955. Pelvic examination on that date revealed a bloody discharge in the vagina. The cervix was clean. The uterus was slightly enlarged and softened. Hemoglobin was 14.0 Gm./100 cc.

abundant necrotic tissue suggestive of placenta. Pathology report included “the presence of recognizable placental villi” (Fig. 3).

The patient was admitted to St. Agnes Hospital on July 19, 1955. Preoperative diagnosis was possible carcinoma of the corpus uteri. Dilation and curettage of uterus yielded

REFERENCE

Is Premature Birth Preventable?

HENRY L. TIECHE, CAPT., M.C., USAR, CARL D. OSBORN, CAPT., M.C., USAR, and JOHN A. BROMAN, CAPT., M.C., USAR

Prematurity is the most frequent cause of fetal and neonatal death. In the United States prematurity now ranks seventh as the cause of death of all ages. Seemingly, if the obstetrician could prevent premature birth he could salvage a large number of infants.

In an effort to determine whether premature birth is preventable, the birth weights of all single, liveborn infants delivered after spontaneous onset of labor were tabulated for a 1-year period in order to determine the incidence of prematurity, and the three most commonly listed causes of premature birth—premature rupture of the membranes, toxemia, and bleeding complications of pregnancy—were recorded for both premature and term infants to ascertain whether the incidence of these complications is really greater in premature birth than would be expected.

INCIDENCE

Figure 1 indicates that a normal distribution curve of birth weights was obtained. The average weight was roughly 7 pounds and the standard deviation 19.3 ounces. By the criterion for prematurity of a birth weight of 5½ pounds or less, of the infants were premature.

That this histogram would not be appreciably altered by the cases excluded can be observed in Table 1. Cesarean sections and inductions of labor were excluded, as most of these cases had not progressed to spontaneous onset of labor; that is, they were interrupted prematurely for obstetric indications. Even so, the premature: term cesarean section ratio of 4:18 is essentially the same as that of the histogram. The single induction of labor is obviously not significant. Stillborns were excluded, as the time between fetal death and delivery may have been considerable and would be reflected in the fetal weight at birth. There was a total of 18 stillbirths, or 1.03 per cent, which if included would not have appreciably altered the normal distribution curve. Multiple births were excluded, as a higher incidence of prematurity is expected in these pregnancies and they are usually considered as a separate class in prematurity studies.

That the histogram here presented represents a normal distribution curve is substantiated by two facts: (1) the two measures of central tendency, the median and the mean, correspond within their probable errors, and (2) 95.5 per cent of the cases occur between two standard deviations from the mean, where the expected is 98 per cent. However, probably the most important observation from the histogram is the confirmation that birth is a biologic event influenced by multiple variables, and would be expected to vary in its criteria in the manner of a normal distribution curve.

CAUSES

It is believed that any retrospective analy-
sis of charts to determine causes of pre-
maturity may be misleading because of the
tendency of physicians to "explain" a birth
frequency of the three most commonly listed
causes of premature labor, as determined by
a review of the literature—premature

Fig. 1. Distribution of birth weights. This histogram differs from a true normal distribution curve in that
in the lower weight ranges cases are encountered down to 1 pound. Theoretically about 100 per cent of
the cases should be within three standard deviations from the mean, or in this graph the lower limit should
be 3 pounds 3 ounces. There are still 26 cases below this lower limit. The explanation offered here for the
presence of these cases in the extreme lower weight ranges is entirely theoretical (See legend for Fig. 2).

in which an infant is premature and may die.
In such an analysis the frequency of compli-
cations causing premature birth may be high

<table>
<thead>
<tr>
<th>TABLE 1. BIRTHS NOT INCLUDED IN HISTOGRAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases</td>
</tr>
<tr>
<td>Cesarean sections</td>
</tr>
<tr>
<td>Inductions of labor</td>
</tr>
<tr>
<td>Stillborns</td>
</tr>
<tr>
<td>Twins</td>
</tr>
</tbody>
</table>

* Less than 5½ lb.

in contrast to the frequency of those com-
lications in births of normal-sized infants.
To eliminate this error of human bias the
rupture of the membranes, toxemia, and
bleeding complications of pregnancy—was
tabulated for both premature and term de-

terminations during the study period.

Rupture of the Membranes

To eliminate those patients in whom rup-
ture of the membranes may be a part of
labor itself, the arbitrary criterion for pre-
mature rupture of the membranes was its
occurrence 12 or more hours before the
onset of labor as determined by descent of
the presenting part or progressive effacement
and/or dilation of the cervix. Table 2 re-
veals that 57 patients had rupture of the
membranes at least twelve hours before the
onset of labor. Thirty-seven term and 20 premature infants were delivered in these pregnancies. If rupture of the membranes had not “caused” labor we would have expected 5 premature infants (8.26 per cent of

### Table 2. Premature Rupture of Membranes

<table>
<thead>
<tr>
<th>Membranes Ruptured 12 or More Hours Before Onset of Labor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. cases</strong></td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Over 5½ lb.</td>
</tr>
<tr>
<td>Premature</td>
</tr>
<tr>
<td>Expected (57 x 8.26%)</td>
</tr>
<tr>
<td>“Caused” by rupture of membranes (20 — 5)</td>
</tr>
</tbody>
</table>

Thus, 15 of these cases of prematurity may have been “caused” by premature rupture of the membranes. Thus 15 of these cases of prematurity may have been “caused” by premature rupture of the membranes.

### Toxemia

The diagnosis of toxemia of pregnancy is based on at least two of three criteria: (1) blood pressure over 140 systolic and/or 90 diastolic, (2) albuminuria, and (3) edema. Table 3 reveals that in this series there were 43 patients with toxemia of pregnancy. Of these pregnancies 36 term and 7 premature infants were delivered. If toxemia of pregnancy had not occurred, 4 premature infants in the total 43 cases would have been expected. Thus, 3 premature infants were “caused” by toxemia of pregnancy.

### Table 3. Toxemia

<table>
<thead>
<tr>
<th>No. cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Over 5½ lb.</td>
</tr>
<tr>
<td>Premature</td>
</tr>
<tr>
<td>Expected (43 x 8.26%)</td>
</tr>
<tr>
<td>“Caused” by toxemia (7 — 4)</td>
</tr>
</tbody>
</table>

Thus, 3 premature infants were “caused” by toxemia of pregnancy.

### Bleeding Complications

Bleeding complications of late pregnancy, notably abruptio placenta and placenta previa, are supposed to increase the frequency of premature birth. Table 4 discloses that in this series there were 29 cases of premature separation of the placenta, some of which may have been lowly. These were subdivided into (1) major abruption, when more than one third of the placenta was involved (by gross observation of the placenta after delivery) and (2) minor abruption, including separation of less than one third of the placenta and marginal separation. Severely, separation of the placenta is correlated with premature labor, particularly a major separation. This resulted in 4 term and 4 premature infants. There were 21 minor separations accounting for 6 premature infants, whereas 3 would have been expected if this complication had not occurred.

### Table 4. Placental Abnormalities

<table>
<thead>
<tr>
<th>Premature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over 5½ lb.</td>
</tr>
<tr>
<td>Abruptio placenta</td>
</tr>
<tr>
<td>Minor</td>
</tr>
<tr>
<td>Placenta previa</td>
</tr>
<tr>
<td>Circumvallate placenta</td>
</tr>
<tr>
<td>Miscellaneous (scarred, infarcted, calcified, fibrotic, etc.)</td>
</tr>
<tr>
<td>TOTALS</td>
</tr>
</tbody>
</table>

21 prematures "caused" by placental abnormalities
IS PREMATURE BIRTH PREVENTABLE?

previa, which was marginal as the infants were delivered vaginally. Both were premature. There was 1 central placenta previa delivered by cesarean section, which is not included in Table 4. This section also produced a premature infant. The low incidence of 3 placenta previas in 1683 deliveries cannot be explained. Seemingly, from this study, placenta previa is not a predominant cause of prematurity, though all 3 cases resulted in premature infants.

As the study progressed, close observation of the placenta after delivery revealed the complications. If these complications had not occurred, only 11 premature infants would have been expected. In other words, 39 minus 11, or 28, prematures may have been caused by these complications, or roughly 20 per cent. Conversely then, about 80 per cent of the prematurity had no cause or was due to causes of less importance.

DISCUSSION

In the contemplation of causes of premature labor, we realize that the causes of all labor still remain unknown. Obstetric

<table>
<thead>
<tr>
<th>TABLE 5. SUMMARY OF CAUSES OF PREMATURE LABOR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Premature</strong></td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Rupture of membranes</td>
</tr>
<tr>
<td>Toxemia</td>
</tr>
<tr>
<td>Bleeding complications</td>
</tr>
<tr>
<td>Abruptio placenta</td>
</tr>
<tr>
<td>Placenta previa</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
</tr>
</tbody>
</table>

28 cases "caused" by 3 complications (20.4% of 137 total prematures)

most common placental anomaly to be circumvallate placenta. Eighty-eight patients were delivered with placentas of this description, resulting in 73 term and 15 premature infants. If this placental condition had not existed 7 premature infants would have been expected. In other words, 8 premature infants may have been "caused" by a circumvallate placenta.

In the last category of placental abnormalities are included the designations "scarred," "infarcted," "calcified," "fibrotic," and so on. There were 23 infants delivered with these placental abnormalities, 7 of which were premature. Without these abnormalities 2 prematures would have been expected.

To summarize then, reconsidering the three leading causes of premature labor, Table 5 reveals that 39 premature infants were delivered in the presence of these complications or changes in the obstetric course may be observed to be followed by labor. However, to establish an obstetric complication as a cause of premature labor it must be shown that (1) this complication occurs with greater frequency than would be expected in premature than in term labors,* (2) this complication must invariably be followed by labor and in a reasonable period of time, and (3) this complication must be such that it can be objectively and accurately determined. The three leading causes of premature labor discussed should, then, be reconsidered.

Effect of Status of the Membranes

Soon after our study was started the lack of scientific accuracy in determining the status of the membranes became obvious.

Some patients with a clinical history of ruptured membranes were found to have in-
tact membranes at the time of delivery, and some patients with no history of ruptured membranes antepartum or intrapartum had ruptured membranes when delivered.

Was the arbitrary criterion of 12 hours between rupture of the membranes and onset of labor too short? Would the ratio of premature to term infants be altered by a longer time interval?

In some patients the time interval between rupture of the membranes and onset of labor was great. One patient in this series had a proved rupture of the membranes 37 days before the onset of labor. Did rupture of the membranes cause labor in her case?

From the above statements prematurity by rupture of the membranes was seemingly increased by 15 in 137 cases. The accuracy of this is questioned, however, because of the inability to determine the status of the membranes and the occasional long interval between rupture and onset of labor.

Role of Toxemia

In toxemia of pregnancy, an increase in blood pressure and the presence of albuminuria are readily and reasonably accurately determined; edema may be missed unless a recent sudden gain in weight is detected. However, the signs and degree of toxemia can be determined with a fair degree of scientific accuracy. In this series only 3 premature infants in 137 cases may have been caused by toxemia, which fact, when considered with the total number of cases of toxemia, suggests that this complication is not a significant cause of premature birth.

Placental Abnormalities: Cause or Effect?

Placental abruption seemingly produced an increased frequency of premature infants. However, does abruption precede labor or does it occur after labor has started? Because the normal mechanism of placental separation is thought to be due to reduction in the size of the placental bed by uterine contractions, thereby shearing the placental uterine attachment, in most cases abruption probably occurs after labor has already started.

If the examining finger is kept out of the cervix, placenta previa with the placenta situated in the noncontractile lower uterine segment theoretically should not cause significant bleeding, when the internal os is closed, until cervical effacement and dilation occur and labor is imminent. Is significant bleeding in placenta previa then a result of normal labor or a cause of premature labor? Are infants in cases of placenta previa "small" because nutrition may be partially impaired by abnormal placationation?

In this series abruptio placentae and placenta previa seemingly caused 10 premature infants in the total of 137. However, the fact that the cause-and-effect relationship may be reversed makes this figure of doubtful value.

Prevention of Premature Labor

Let us consider these three causes of premature labor from a statistical viewpoint. Because a normal distribution curve of birth weights was obtained (see Fig. 1), if we believe that premature rupture of the membranes, toxemia, and bleeding complications of pregnancy cause premature labor, we must also believe that failure of the membranes to rupture, lack of toxemia, and the presence of a normally implanted placenta produce postterm, large infants. Furthermore, we must also believe that if these complications cause premature labor, then labor can be electively induced by the superimposition of these complications in any pregnancy at any time.

Let us consider our normal distribution curve from another statistical viewpoint. Let us assume that one cause of premature labor is known and can be eliminated. By so doing, all premature births will not be eliminated, because all other causes acting as variables will still be present. Moreover, eliminating the one cause will not produce a skewed distribution in the upper weight ranges.

The prevention of labor must be directed to the entire process of labor, and not to the individual components of labor.

If we were to require all deliveries by cesarean section as it is not possible to determine if the primary cause of labor is not labor itself, labor would be eliminated that is 100% preventable.

1 TIECHE ET AL.

Obstetrics and Gynecology

Vol. 7 May 1930
IS PREMATURE BIRTH PREVENTABLE?

ranges but will merely shift the entire normal distribution curve to a higher weight range. Let us further assume, optimistically, that by so doing we raise the birth weight of all infants 4 ounces. Then a larger group, from 5 pounds 4 ounces to 5 pounds 8 ounces, would be eliminated from the premature classification. However, the survival in this group is good. We have done little in the lower weight ranges where the fatalities are greatest, and little in the way of premature salvage has been accomplished.

The only way that all prematurity can be prevented is by the elimination of all causes of labor. Then labor and delivery become entirely an elective event. This is a biologic impossibility.

The prevention of premature birth has not met with success despite the rise in standard of living, the improvement and increased knowledge in nutrition, the development of many labor-saving devices in the home, and the greatly improved antenatal care resulting in the great reduction in maternal and fetal mortality and morbidity. That the incidence of premature birth remains essentially unchanged means either that we have done or can do little to eliminate the causes of premature birth or that the real causes are still unknown.

**Increased Fetal Salvage**

If the assumption that premature birth is largely not preventable is correct, then clinically the obstetric hope for salvage of premature infants depends upon two possibilities: (1) postponement of delivery as long as it is maternally and fetally feasible in obstetric complication, and, probably more important, (2) once labor becomes inevitable, the determination of the obstetric technics that will deliver the premature infant with minimal damage to its vital systems.

**SUMMARY AND CONCLUSIONS**

1. The birth weights of 1683 consecutive, single, liveborn infants was determined. These birth weights produced a normal distribution curve with an incidence of prematurity of 8.26 per cent.

2. The three most commonly listed causes of premature birth were determined for both premature and term infants in this series.

3. Of the 137 premature infants, premature rupture of the membranes may have caused 15 of the premature births, toxemia 3, and placenta previa and abruptio placentae 10, a total of 20 per cent.

![Graph](image-url)
to be the determination of the obstetric technics that will deliver the premature infant in the best possible condition.

1759 Fulton St.
Fresno, Calif.

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Obstetrics and Gynecology
Urethral Diverticulum

LAWRENCE R. WHARTON, JR., M.D., and RICHARD W. TE LINDE, M.D.

The subject of diverticulum of the urethra in the female is scarcely a new one, the first case having been reported in 1805 by Hey, who stated that he had treated his first case in 1786. The second case to find its way into the literature was that of Foucher in 1857. Priestley reported the third case in 1867. Lawsen Tait described a case of "Saccular Dilatation of the Urethra" in 1875. The first reports were of single cases, whereas later reports of multiple cases appeared, such as that of Hunner in 1938. He stated that he had seen probably 12 to 15 cases of urethral diverticulum, including 3 with calculi in the sac.

In spite of these reports the condition has not been generally recognized by the profession, and there is no doubt that many women are unnecessarily suffering from it today, even though they have repeatedly consulted gynecologists and urologists. It seems apparent that whenever the condition is called to the attention of the profession by an article in the literature more cases are diagnosed. Then, after a lapse of time the cases seem to be overlooked again. This point is well illustrated by our experience at the Johns Hopkins Hospital. During the 19-year period 1931-49, 22 cases were diagnosed and treated at the Hopkins Hospital. The cases were reviewed and published by Wharton and Kearns in 1950. In the succeeding 5-year period through 1954, 41 cases were diagnosed.

The present study includes these 63 cases plus 3 others treated at the Johns Hopkins prior to 1931. The average age of our patients was 39.8 years, but the ages ranged from 22 to 76 years. The decade of greatest incidence was the fourth.

Etiology

The mechanism of production of urethral diverticula is not known although there has been much speculation. Congenital suburethral cysts occasionally occur in the newborn, and it has been suggested that such cysts may become infected and rupture into the urethra. It is also possible that the actual diverticulum may be congenital. Occlusion of Skene's or other paraurethral glands with resultant infection and rupture into the urethra is a possibility. Trauma with infection at childbirth has been considered by some to be the etiology but certainly is not the usual mechanism of formation, since many diverticula occur in nulliparous women. The arrest of calculi within the urethral lumen with erosion through the mucosa could instigate an infection, leading to a suburethral abscess.

Bacteriology

Some of the diverticula are epithelium-lined but in several specimens the epithelium, if it ever existed, has been completely destroyed by infection. It is quite possible that some may represent true abscesses. On the other hand we have encountered some diverticula in which the contents were clear mucus and the epithelium-lined walls showed no infiltration by inflammatory cells. In the majority of cases infection can be proved bacteriologically but in several of ours the culture was sterile. It is doubtful whether the number of sterile diverticula is as great as...
indicated by our bacteriologic studies, for it is possible that the organisms may die between the operating room and the incubator. On the other hand, the sterile cultures obtained from the diverticula with clear contents undoubtedly represent the true status of the contents. Recently many patients have had antibiotics or chemotherapy before cystoscopy or operation, and these medications may account for some sterile cultures. The total number of cultured organisms found (Table 1) exceeds the number of cases because of mixed infection in several instances.

**SYMPTOMS**

The symptoms of urethral diverticulum are many and varied. This might be expected because the diverticula vary greatly in size, position, and degree of inflammatory reaction. Dysuria was the most frequent symptom, occurring 44 times among our 66 cases. Frequency was complained of by 27 patients, and urgency by 14. Twenty-six women complained of what they designated as "recurrent" or "chronic cystitis." By this they probably meant dysuria and frequency. Local pain in the vaginal-urethral region was complained of by 24 patients. Eleven women had noted a vaginal mass, hematuria, stress incontinence, and/or dyspareunia. Fifteen patients had seen pus coming from the urethral meatus. A bearing-down sensation was described in 4 instances and an equal number had difficulty in starting the flow of urine. Three women had suffered from acute urinary retention on occasion and 3 were febrile. In 4 patients there were no complaints and the condition was discovered on routine examination.

**Duration**

The symptoms were generally of long duration, and the usual story was that of going from physician to physician without relief. In many instances the patients had been treated for a urinary-tract infection without a specific diagnosis, often in spite of the fact that a complete urologic examination had been done by a competent urologist. Only 2 of the 66 women had had symptoms for 1–2 months. Seventeen had had symptoms for 1 year or less. In 8 cases the duration had been 1–2 years and in 10 the duration had been 2–5 years. Except for 2 in which the duration was not stated in the history, the remaining 24 patients had suffered for more than 5 years and in 8 the symptoms had been present for 15 or more years.

**DIAGNOSIS**

**Physical Signs**

The physical findings upon which an accurate diagnosis of urethral diverticulum may be made are usually quite definite and concrete. A suburethral mass may generally be seen and palpated. In only 8 of our 66 cases could no mass be demonstrated. In 10 cases the mass was estimated at less than 1 cm. in diameter. In a large majority of the cases the mass was 1–5 cm. in diameter but in 4 of our cases the mass was over 5 cm. In 1 case the mass was estimated at 8 cm. in diameter. The position of the mass was quite variable. Twenty-five were in the upper third of the urethra, 10 were in the lower urethra, and 5 were in the vestibule.

## TABLE 1. BACTERIOLOGY IN SIXTY-SIX CASES OF URETHRAL DIVERTICULUM

<table>
<thead>
<tr>
<th>Culture</th>
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</tr>
<tr>
<td>E. coli</td>
<td>4</td>
</tr>
<tr>
<td>Coli aerogenes</td>
<td>18</td>
</tr>
<tr>
<td>Streptococcus fecalis</td>
<td>26 enteric organisms</td>
</tr>
<tr>
<td>γ-Enterococcus</td>
<td>3</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>6</td>
</tr>
<tr>
<td>Staphylococcus albus</td>
<td>8</td>
</tr>
<tr>
<td>α-Streptococcus</td>
<td>2</td>
</tr>
<tr>
<td>β-Streptococcus</td>
<td>1</td>
</tr>
<tr>
<td>γ-Streptococcus</td>
<td>4</td>
</tr>
<tr>
<td>B. subtilis</td>
<td>4</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
</tr>
<tr>
<td>Diphtheroids</td>
<td>1</td>
</tr>
<tr>
<td>Trichomonas vaginalis</td>
<td>1</td>
</tr>
<tr>
<td>No culture</td>
<td>15</td>
</tr>
</tbody>
</table>
of the urethra, 17 in the middle third, and 6 in the lower third. In one instance the mass was very irregular in shape and involved the labia.

One of the most characteristic signs of urethral diverticulum is the expression of pus from the urethral meatus on pressure of the suburethral mass. As a matter of fact, the appearance of pus at the urethral meatus should make one suspicious even when no mass is demonstrable. In 47 of our 66 cases pus could be demonstrated at the meatus. In 7 of our proved cases no pus could be expressed from the meatus. The inability to express pus, however, does not rule out urethral diverticulum because inflammatory edema may temporarily cut off the communication between the urethra and the sac.

Pus in the catheterized urine specimen was found in 35 of the 66 cases. If uncatherterized specimens had been routinely examined, undoubtedly more pus than is usually found in the voided specimen of normal women would have been found in a high percentage of the cases. When the communication with the infected sac is in the outer portion of the urethra there may be no regurgitation of pus into the bladder urine but such pus is washed out on voiding. Blood was found in the catheterized urine in 4 instances; in one of these cases hematuria was a major complaint. A stone or stones in the sac could be felt on palpating the suburethral region. In only 9 cases was tenderness noted on urethral palpation.

Cystoscopy

Although the appearance of pus at the urethral meatus and a suburethral mass are extremely suggestive of urethral diverticulum, the diagnosis should be confirmed by cystoscopy. For several years this has been a routine diagnostic procedure in our clinic in suspected cases, but in the histories of some of the earlier cases no mention is made of cystoscopic examination. One or more communications into the urethra from the diverticulum were demonstrated in 42 of the patients who were cystoscoped, but in 8 no orifice could be seen in the urethra. The failure to demonstrate an orifice within the urethra does not exclude its presence. This is usually due to the fact that a very small opening has been swollen closed by inflammatory edema. The orifice can usually be identified by the appearance of a drop of pus as the Kelly cystoscope is withdrawn. Probably a better opportunity to visualize the orifice is offered by using the water panendoscope; we have located it with this instrument in several instances when we failed with the Kelly scope.

Radiography

The demonstration of the cavity by radiographic means finally confirms the diagnosis. If the intraurethral communication is visualized cystoscopically it can often be catheterized with a small ureteral catheter and the cavity filled with dye for roentgenologic study. Not infrequently catheterization of the cavity is impossible. An easy method of filling the sac with dye which is often successful is illustrated in Fig. 1. The bladder is first filled with a weak solution of dye to outline it lightly. Then the tip of a Foley catheter is tied off proximal to the opening near its end. A second hole is cut in the catheter proximal to the ligature. It is then passed into the bladder and the balloon inflated. Dye is then injected into the catheter until the patient becomes uncomfortable. If there is an appreciable opening into the diverticulum the intraurethral dye will find its way into the diverticulum and outline it as shown in Figs. 2–4.

TREATMENT

The treatment of urethral diverticulum is excision, with the necessary plastic repair of the urethra (Fig. 5). When the sac is sharply outlined the dissection may be very easily accomplished but when the cavity is irregular
it may be difficult to be certain that all the lining is removed. If there is any doubt it is best to deliberately open the sac and complete the dissection with the sac open, methylene blue in order to outline all ramifications. Another advantage of opening the sac is visualization of the opening into the urethra, which minimizes damage to this structure. It is important in searching for the diverticulum orifice to remember that although most diverticula empty into the urethra near the midline posteriorly, some have

(Fig. 5B). If the sac appears to have irregular ramifications (Fig. 6) it is often advantageous to aspirate the contents and refill the cavity with a weak solution of
URETHRAL DIVERTICULUM

lateral urethral communications which must be closed. It is also conceivable that a diverticulum may enter the anterior aspect of the urethra although we have not encountered such a situation.

After excising the neck of the sac the opening into the urethra is closed with interrupted sutures of #00 chromic catgut.

This reconstruction of the urethra may be minimal and very simple, or in some diverticula the opening may be large or multiple

Fig. 5. A, a midline incision is made through mucosa of anterior vaginal wall over diverticulum. B, the diverticulum is opened widely, demonstrating urethral communication; a sound is in the urethra. C, the diverticulum lining is excised. D, urethral defect is closed with mattress sutures and redundant vaginal mucosa is excised. E, the pubocervical fascia is closed, reinforcing urethral repair. F, the vaginal mucosa is closed.
cision of the urethra from the diverticulum to the meatus. We have not yet found this necessary and fail to see the advantage of routinely opening the urethra more than is necessary. The question of more than one opening in the urethra should always be kept in mind while doing the operation to be certain that all openings are closed. In 6 of our cases, two orifices were found and in 1 case there were "multiple orifices." In 3 of our cases no orifice could be demonstrated at operation. This does not exclude the presence of a small orifice and the tissues should be brought together in the midline just as though an orifice were demonstrable. After the first suture line the suburethral pubocervical fascia should be brought together in the midline to reinforce the first suture line and support the urethra. Naturally calculi found in the diverticula should be removed. In 3 of our cases 1 stone was present and in 1 case 17 stones were found.

In rare cases where extensive reconstruc-

RESULTS

The results on the whole have been very gratifying, but there are a few occasional sequelae. Follow-up notes were available in 58 of the 66 cases. In 42 there is a statement in the history that 1–6 months after operation the patient was free from symptoms. In 5 patients there were recurrent urinary-tract infections, a fact not to be wondered at since many of the cases had been chronically infected for years. Five patients subsequently complained of stress incontinence, but 4 of these were cured by "exercises." Small urethrovaginal fistulas were found on subsequent examinations. Three of these were of no clinical importance for there was no incontinence and the other was successfully repaired. There were 3 cases in which stricture of the urethra developed following plastic repair; in one of these the stricture was not sufficient to cause symptoms but it was found on routine postoperative check-up and was successfully dilated; in 2, the stricture was symptomatic but was dilated easily with relief of the symptoms.

SUMMARY

We have recorded our experience with 66 cases of urethral diverticulum in the female. Our reason for making this study is to call
the attention of the profession to a condition which has long since been described but which continues to go unrecognized. The symptomatology is essentially that of recurring or chronic cystitis. Other specific symptoms occurring in some cases include acute retention, the appearance of a sub-urethral mass, the appearance of pus at the meatus, and stress incontinence. Methods of diagnosis are described, such as palpating the mass, expressing of pus from the urethra, visualization of the opening into the urethra by cystoscopic methods, and the demonstration of the cavity by means of x-ray visualization. Treatment by excision and plastic repair of the urethra has been described. Although the treatment is generally successful there are sequelae which may persist or may result from surgery, such as symptoms of persistent bladder infection, urethral stricture, urethral fistula, and, rarely, incontinence from sphincter damage.

REFERENCES

Cervical Tone and Pain Thresholds

Study in the nongravid human uterus

WILLIAM M. PAUL, M.D.,* B. I. GLICKMAN, M.D.,† I. M. CUSHNER, M.D.‡ and S. R. M. REYNOLDS, Ph.D., D.Sc.

OF ALL ASPECTS of uterine physiology, we are least informed concerning that of the uterine cervix. The cervix is the principal source of painful stimuli from the uterus and it acts as a barrier between the uterus and the vagina. The role of cyclical changes in the cervical mucus is well established, but about the variability in cervical tonus and its relation to functional states and pain, we are largely in the dark. The sensory innervation of the uterus at the internal os we know to be up to the level of the tenth thoracic dermatome. Accordingly, this region becomes a crucial one for study as a possible source of pain in essential dysmenorrhea.

PREVIOUS STUDIES

Among the previous studies of the cervix, those of Liesse1, 2, 3 are perhaps the most quantitative. He recorded the exact intruterine pressure necessary to expel through the uterine cervix gas which was introduced into the uterine cavity. He found high cervical tone during the proliferative phase of the cervical cycle and low tone during the secretory phase. High tone was abolished by injection of local anesthesia into the hypogastric plexus, and low tone was augmented by injection of parasympathomimetic drugs. The bubbling of gas through the cervix and induction of uterine contractions may well have influenced the results. The results may show, therefore, how an irritated cervix and active uterus respond to a stimulus.

PRESENT STUDY

We set about to establish in our study less irritative procedures, if possible. We report in a general way our failures along with what success we may have had so that others may be guided by our experiences.

Three experimental approaches were employed. First, localized cervical contractility was recorded about the midzone of the cervical canal by employing a small balloon permitting minimal distention. Second, we developed a technic for determining precisely

510
the force required to draw a balloon of fixed size from the uterine cavity through the cervical canal in order to measure the cervical-traction threshold. Finally, we measured the amount of cervical distention necessary to cause pain by local distention at the level of the internal os, in the midcervical region, and just inside the external os. Our experience with each of these procedures will be described, although it appears that only the last one may be useful in selected cases at its present development.

MATERIAL

For development of the above technics, a cervical-tension clinic was established in Sinai Hospital to work one afternoon each week for five months. Where feasible, certain women were compensated to appear weekly. A group of 4 women made themselves available for extended study. Other women were requested to come to the clinic for isolated observations.

These women selected were, insofar as possible, without any gynecologic or other history likely to influence the observations to be made. Most were parous, and some had been treated successfully for pelvic inflammatory disease. In all, 18 women were studied from 1 to 15 times each.

When the pain-threshold study was developed, it became clear that other subjects ought to be studied on a random basis, in order to compare dysmenorrheic with non-dysmenorrheic women. Accordingly, a second cervical-tension clinic was established in Johns Hopkins Hospital. For the most part, patients were called in from the waiting room where they had come for other than gynecologic treatment. The women with severe dysmenorrhea were referred from the Personnel Health Service during treatment there. In the latter two groups only one set of observations was made. The pertinent data with respect to all of these subjects are summarized in Table 1. The group varied in parity from 0 to 8, and in age from 16 to 43 years. Not included are 2 women recently post partum, 1 with a patulous cervix after operation, 1 who was amenorrheic, 1 with an amputated cervix, and 3 in whom satisfactory observations could not be made. Included are those in whom clear and repeatable end responses could be ascertained.

CERVICAL CONTRACTILITY

Method

Latex balloons, 2.5 × 30 mm.*, were mounted on polyethylene tubes in such a way that a distensible portion of the balloon extended about 4 mm. beyond the end of the tube. The system was completely filled with Zephiran solution, 1:1000, and connected by a three-way stopcock (to permit removal of bubbles of air) to a Statham pressure transducer. This was fed into a Honeywell-Brown recorder in which there were adjustable features so that sensitivity of the system could be varied as needed. When the pressure gauge and balloon were connected, the system was virtually isometric since maximum displacement of the diaphragm of the transducer was only 0.015 inch.

Before use, the volume of the balloon was determined when it was just full. When inserted into the cervical canal, the balloon was empty and was never filled beyond this point. In this manner, the cervix acted upon a very small volume of fluid under no pressure other than that sufficient to bring it against the wall of the cervical canal. Any fluctuations in pressure, therefore, were the result of direct transmission of pressure of the cervix against the fluid inside the balloon. Patients never experienced discomfort from the presence of the catheter when it was in place or of the slight distention of the balloon as described above.

* Obtained from the C. R. Bard Co., Summit, N. J.
### Table 1. Summary of Data on Cervical-Pain Thresholds

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Parity*</th>
<th>Day of cycle</th>
<th>Pain thresholds</th>
<th>I.O.</th>
<th>M.C.</th>
<th>E.O.</th>
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<td>1.6</td>
<td>0.2</td>
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<td>0-1-3-0</td>
<td>7</td>
<td>2.0+</td>
<td>2.0+</td>
<td>2.0+</td>
<td></td>
</tr>
<tr>
<td>V. S. (very tense)</td>
<td>35</td>
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<td>5</td>
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<tr>
<td>C. M. (myomas)</td>
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<td>J. H. (irregular)</td>
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</tr>
<tr>
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<td>23</td>
<td>0-0-0-0</td>
<td>amenorrheic</td>
<td>10 months</td>
<td>0.5</td>
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</tbody>
</table>

### B. Menstrual Discomfort—Occasional or Slight

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Parity*</th>
<th>Day of cycle</th>
<th>Pain thresholds</th>
<th>I.O.</th>
<th>M.C.</th>
<th>E.O.</th>
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</thead>
<tbody>
<tr>
<td>L. J.</td>
<td>20</td>
<td>0-0-0-0</td>
<td>8</td>
<td>1.0</td>
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<td>0.8</td>
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</tr>
<tr>
<td>L. G.</td>
<td>36</td>
<td>1-0-1-1</td>
<td>17</td>
<td>2.0+</td>
<td>0.3</td>
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<tr>
<td>A. J.</td>
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<td>1-0-0-1</td>
<td>18</td>
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<tr>
<td>R. D.</td>
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<td>2-0-0-2</td>
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<tr>
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<td>1-0-0-1</td>
<td>15</td>
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<td>1.8</td>
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<tr>
<td>J. T.</td>
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<td>0-0-1-0</td>
<td>16</td>
<td>1.8</td>
<td>0.7</td>
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<tr>
<td>U. F.</td>
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<td>3-0-0-3</td>
<td>16</td>
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<td>2.0+</td>
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<tr>
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<td>H. H.</td>
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<tr>
<td>J. T.</td>
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<td>2-0-1-2</td>
<td>20</td>
<td>2.0+</td>
<td>1.4</td>
<td>0.6</td>
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<tr>
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<tr>
<td>E. M.</td>
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<td>2.0+</td>
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### C. Menstrual Discomfort—Moderate

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Parity*</th>
<th>Day of cycle</th>
<th>Pain thresholds</th>
<th>I.O.</th>
<th>M.C.</th>
<th>E.O.</th>
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<td>R. P.</td>
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<td>9</td>
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<tr>
<td>N. O.</td>
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<td>7-0-0-7</td>
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<tr>
<td>M. D.</td>
<td>21</td>
<td>3-0-3-3</td>
<td>23</td>
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<td>1.7</td>
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<tr>
<td>O. C.</td>
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<td>1-0-0-1</td>
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</tr>
<tr>
<td>L. E.</td>
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<td>0-0-0-0</td>
<td>25</td>
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<td>0.6</td>
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### D. Menstrual Discomfort—Essential Dysmenorrhea

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Parity*</th>
<th>Day of cycle</th>
<th>Pain thresholds</th>
<th>I.O.</th>
<th>M.C.</th>
<th>E.O.</th>
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<tbody>
<tr>
<td>M. W.</td>
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<td>7.1</td>
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<tr>
<td>L. L.</td>
<td>16</td>
<td>0-0-0-0</td>
<td>8</td>
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<td>0.9</td>
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<tr>
<td>F. S.</td>
<td>18</td>
<td>0-0-0-0</td>
<td>10</td>
<td>0.7</td>
<td>0.3</td>
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<td></td>
</tr>
<tr>
<td>F. M.</td>
<td>18</td>
<td>0-0-0-0</td>
<td>10</td>
<td>1.2</td>
<td>1.4</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>J. B.</td>
<td>16</td>
<td>0-0-0-0</td>
<td>20</td>
<td>1.0</td>
<td>0.2</td>
<td>2.0+</td>
<td></td>
</tr>
<tr>
<td>J. B.</td>
<td>16</td>
<td>0-0-0-0</td>
<td>22</td>
<td>1.5</td>
<td>0.4</td>
<td>1.5</td>
<td></td>
</tr>
</tbody>
</table>

*a Parity described as follows: term births—premature births—abortions—living children.
*b I.O. = internal os.
*c M.C. = midcervical canal.
*d E.O. = external os.
CERVICAL TONE AND PAIN THRESHOLDS

Results

The general nature of the results obtained showed repeatedly in the same woman a pattern which seemed at first to be characteristic. It was found that in the late proliferative phase of the cycle, partial filling of the balloon resulted in recording many small, rhythmic contractions at a relatively high level of pressure. In the latter part of the cycle, the initial high pressure quickly gave way to a sudden, steady relaxation so that a curve of adaptation was obtained. Thus the cervix seemed to accommodate itself to the slight distending pressure.

It was felt that this was a truly functional distinction in cervical states during different parts of the menstrual cycle. One day, however, a new subject was brought in for observation. She was not oriented or prepared for the tests except to the extent that she was told they would not hurt her. She was near midcycle, and was very nervous, tense, and suspicious. She yielded the “typical” high tonus curve with rhythmic contractions. The test was repeated and the observation confirmed. After a period of rest, and still lying on the table, she became visibly relaxed and reassured as well as objectively interested in her record. At this time, the tests were repeated. She now yielded the curve of relaxation or accommodation.

Comment

It became clear that the tension state of the patient had modified the response of the cervix and that previous experience had fortuitously led us to a wrong conclusion about its value as an indicator of hormonal state. If there is such a hormonal influence, careful experiments will have to be made to allow for the effects of adjustment to the conditions of observation and anxiety. The method, or some modification of it, may have some value in psychosomatic studies, or in investigations directed along other lines. We abandoned it for our purposes, however, in view of the uncontrollable psychic element involved.

CERVICAL-TRACTION THRESHOLD

Method

In this part of the work, the same balloon was used as in the previous study. The sterilized balloon was inserted into the uterine cavity and distended to a volume of 2 cc. The polythene tube extending from the cervix was connected to a strong thread which passed over a securely mounted pulley at the end of the table and to a weight pan at the other end.

During a test, weights were added in increments of 5 or 10 Gm., with a pause of about fifteen seconds between each addition of weight. This addition of weights was continued until the tube and balloon passed, slowly at first, then rapidly, out of the cervix. The weight necessary to just dislodge the balloon through the cervix was found to be characteristic on any one day and could be redetermined again and again. At the threshold level, a 5 or 10 Gm. weight was the difference between no movement and movement. The procedure was painless except at the beginning of the movement, apparently as the balloon started to move through the internal os and initially distend the cervix.

Results

In 2 subjects, traction studies were repeated throughout 2 and 3 cycles, respectively. The results are shown in Fig. 1A and B. In one of these subjects there was a point of low resistance on Day 15 of the cycle, but no such low point was seen in the other. All data from each of 4 subjects are shown in Figure 1C. These data show that after Day 15 the threshold for cervical traction was rather narrowly limited to 70–100 Gm. In the first half of the cycle the thresholds were highly variable for the group as a whole.
Comment

No significant conclusions seem to be permissible from these results except, perhaps, that during the presumed luteal phase of the cycle the cervix offers rather uniform resistance to the passage of the balloon through it.

PAIN THRESHOLD

Method

The method of producing localized and limited cervical distention was a natural sequence to the foregoing study. It was necessary, however, to devise a small, special dilator (Fig. 2). The end of the polyethylene tube (2.2 mm. outside diameter) was sealed in heat and trimmed to make a smooth rounded end. Two holes were made about 5 mm. from the end with a hot needle (Fig. 2A). The system was filled with water, the balloon slid over the end of the tube, and all air expelled, as shown in Fig. 2B. Silk ligatures were placed on each side of the hole, about 5 mm. apart. This yielded a small segment of balloon that could be distended at will in the shape shown in Fig. 2C.

Fig. 2. Method of making small cervical dilator for cervical-pain (distention) thresholds: A, sealing end of polyethylene tube and making holes on sides; B, small balloon in place over holes in the tube; C, balloon tied and dilated with fluid.

Insertions of the distensible portion of the balloon were made into the cervical canal to the level of just below the internal os, at the mid-point of the cervical canal, and just inside the external os. This permitted highly localized distention of parts of the cervical canal. The balloon could be distended, within limits, to any desired degree by the 5-cc. syringe to which the tube was connected by a three-way stopcock (Fig. 3).

Fig. 3. Assembly of unit for making cervical-pain-threshold determinations.
CERVICAL TONE AND PAIN THRESHOLDS

Results

The insertion of the balloon was never attended by any sensation except in one tense and nervous woman. After the balloon was in place at the desired level, it was distended at a moderately fast speed up to a maximum of 2 cc., or until the patient said she felt pain. The pain was a sharp, cramp-like pain localized in the midlower abdomen. The volume of distention just sufficient to cause pain was very sharp and repeatable at will in any one woman. As will be seen below, greater distention required to cause pain) in the upper part of the cervical canal in the early part of the cycle. This altered sensitivity was not evident at the level of the external os. This was seen at the midcervical level in Subject R. The internal os was quite sensitive at all times of the cycle.

Dysmenorrheic and Nondysmenorrheic Women

At this point, observations were begun on a larger group of women, with only single determinations in each being made. They were made by another observer. Tests were made routinely in order; from the region of the internal os to the midcervical canal to the external os. In this series (Table 1, A) a relative insensitivity of the entire cervical canal was seen in the early proliferative part of the cycle before the eleventh day (Fig. 5a). There were two exceptions, 1 woman feeling pain on the second day of menstruation, and the same in 1 woman having a myomatous uterus. Later in the cycle all women with no history of menstrual pain had sensitive cervical canals, usually most
sensitive in the midcervical portion and near the external os (Fig. 5b and c). In contrast to the above, women with a history of mild menstrual pain had quite sensitive cervical canals in the early proliferative phase of the cycle (Fig. 5d) but quite variable sensitivity later (Fig. 5e and f). Much the same is also true of women with severe dysmenorrhea (Fig. 5g, h, and i). Early and late in the cycle most such women who have, or have had, menstrual pain exhibited quite sensitive cervical canals or some part that was particularly sensitive (Table 1, C and D).

**CORRELATION BETWEEN CERVICAL PAIN AND DYSMENORREA.** The data were examined and plotted (not shown) for a study of cervical sensitivity and parity. Generally speaking, multiparous women had relatively insensitive cervical canals at the level of the internal os, even when there was a history of menstrual discomfort. On the contrary, the midcervical part of the canal as well as just above the external os in multiparous women with menstrual pain showed marked sensitivity. Among the nulliparous women, only those with a history of no menstrual pain had an insensitive cervical canal early in the cycle. All others had areas of hyperesthesia, most of them quite marked. A majority of the multiparas with no dysmenorrhea had some part of the cervical canal which was quite sensitive. A hyperesthetic area is not of itself pathognomonic of dysmenorrhea but, taken in conjunction with the time of the cycle (e.g., early proliferative phase), there appears to be a rather good correlation between cervical hyperesthesia and dysmenorrhea, especially in nulliparous women.

**COMMENT.** It appears from this study that there is a difference between nondysmenorrheic and dysmenorrheic women with respect to cervical-pain thresholds. In the former the cervix is relatively insensitive early in the menstrual period while in the latter group it is sensitive. This could be related, perhaps, to the role of menstrual clots in causing uterine pain, or it could be that very strong uterine contractions make the hypersensitive cervix of the dysmenorrheic woman contract painfully, while they do not have this effect upon the relatively less sensitive cervix of the nondysmenorrheic woman.

Further studies are indicated immediately before, during, and after menstruation. The shape of the distended balloon should be determined by radiographic means in the two groups of women.

**SUMMARY AND CONCLUSIONS**

1. Three procedures to study cervical tonus and pain thresholds quantitatively have been reported:
   a. Cervical contractility, recorded with minimal distention of the cervix.
   b. Traction by measured forces through the cervix of a small balloon of fixed volume.
Localized pain thresholds throughout the cervix by means of local distention of the cervical canal, just below the internal os, at the midpoint, and just above the external os. Results are highly reproducible in any one woman.

A small group of patients was available for repeated observation at weekly intervals for periods of time ranging from 2 to 5 months. A larger group of patients was available for repeated study by single observations on cervical-pain thresholds. This group consisted of nulliparous and multiparous women, some of whom either had histories of menstrual discomfort or essential dysmenorrhea.

Psychosomatic factors affected uterine tonus sufficiently that recording of cervical contractions without “control” of such factors tended to render observations difficult to interpret.

The force required to draw a balloon of fixed volume through the cervical canal was relatively constant at 70–100 Gm, during the secretory phase of the menstrual cycle, but during the proliferative phase was variable.

Local cervical-pain thresholds are affected by parity and phase of the menstrual cycle. In general, the cervical canal is least sensitive to painful stimulation during the first 10 days of the cycle. The multiparous cervix tends to be relatively insensitive throughout to the stimulus employed. Women with a history of menstrual discomfort (nulliparous and multiparous) tend to have sensitive cervical canals throughout part or most of the length and during all phases of the menstrual cycle. One woman with no history of menstrual discomfort had a sensitive cervix on the second day of menstruation, as well as one with a myomatous uterus during the early part of the cycle.

While the methods employed are not perfectly suited to evaluation of hyperesthesia, it appears that they may be useful to evaluate the role of various drugs and psychotherapeutic procedures on pain of uterine origin in nongravid women.

REFERENCES

Harlequin Color Change of the Newborn

Report of a case

McLEMORE BIRDSONG, M.D., and JULIA E. EDMUNDS, M.D.

NELIGAN AND STRANG in 1952 reported a syndrome called the harlequin color change of the newborn in 28 infants. All but 2 of the infants were prematures weighing less than 5 pounds. These authors state that they had not found any previous description of this phenomenon. Recently we have had an opportunity to observe a similar case at the University of Virginia Hospital, and in view of the rarity of this syndrome, we present the following case report.

DELIVERY

Baby boy P (#382392) was born on April 9, 1954, of a full-term pregnancy. He weighed 3350 Gm. Delivery was accomplished from an L.O.T. position with the aid of midforceps, after a total labor of approximately thirteen hours. The physical examination at admission had been completely normal.

The infant appeared to be in good condition. The circumference of his head was 51 cm., the chest 34.5 cm., the abdomen 33 cm., the anterior fontanel 2 x 2 cm., and the posterior fontanel 0.25 x 0.25 cm.

ONSET OF COLOR CHANGE

Approximately twenty hours after delivery, the infant appeared to have a definite color change consisting of diffuse redness of the entire left half of the body, with a sharp line of demarcation extending through the center of the forehead, nose, chin, and trunk (Plate 1). Closer observation revealed the infant to be reclined in the bassinet with the left side of the body barely dependent. A physical examination of the infant at this time revealed no other abnormalities. The vital signs were likewise normal.

SUBSEQUENT OBSERVATIONS

It was observed during the examination, however, that the condition was flexible and that gravity must be the aggravating factor, for on placing the infant with the right half of the body slightly dependent, the left half of the body became blanched and the right half became markedly erythematous. The attacks could be precipitated readily and were demonstrated on several subsequent occasions for the two following days. The color change occurred within 1 minute after a positional change and persisted for variable lengths of time, none of which was recorded. The color change could be avoided, however, by placing the infant perfectly flat on his back. By the fourth day, at which time mother and baby were discharged from the hospital, it had become difficult to precipitate the attacks.

DISCUSSION

In the cases studied by Drs. Neligan and Strang, a series of 250 newborns was observed in the Princess Mary Maternity Hospital and the Department of Child Health, King's College, New Castle under Lyme. This study included all newborns weighing 5 pounds or less and those above 5 pounds who showed clinical evidence of cerebral
Plate 1. Harlequin color change in 20-hour-old male; photograph was taken immediately after he had been lying on his right side.
HARLEQUIN COLOR CHANGE OF NEWBORN

damage or whose obstetric record suggested the liability of its development. Of the 250 infants observed, only 22 showed one or more of these attacks, and in only 3 of these was the attack observed in the first 48 hours of life. The majority of the attacks appeared to occur on the third or fourth day of life, but 1 of the 22 infants had an attack as late at 21 days after delivery. Likewise, the frequency of the attacks varied from one attack to several attacks per day, the highest being 12 per 24 hours.

In the infant observed at the University of Virginia Hospital the first attack was observed within the first 24 hours of life. The attacks were continuous as long as the infant was placed on one side or the other. On the fourth day, the day of discharge, it was quite difficult to precipitate an attack of color change in this infant.

It would appear that these attacks have no pathologic significance and will tend to disappear as the infant grows older. The infants do not appear to have any distress during the attacks and although the mechanism is not definitely known, it would be reasonable to assume that they are caused by some instability of the nervous system at the upper level.

SUMMARY

1. A case report of an infant with the harlequin color change is presented.
2. From a review of the literature it would appear to be a self-limited disturbance and causes no discomfort or damage to the infant.
3. The cause is not known but would appear to be an instability of the central nervous system at a high level.

REFERENCE

Carcinoma of the Cervix in Pregnancy

HARRY PRYSTOWSKY, M.D., and C. BERNARD BRACK, M.D.

REPORTS FROM THE LITERATURE

Incidence and Distribution

ALTHOUGH THERE are many reports in the literature on the subject of carcinoma of the cervix uteri in the nonpregnant, there is a relative dearth of data on carcinoma of the cervix in pregnancy. Eastman reviews the literature thoroughly up to 1950. Other authors report the following widely varying incidences:

New York Hospital, 1:14,000 cases (3 in 41,457 pregnancies); Willson at Chicago Lying-In, 1:6620; and Danforth, in a review, 1:3100.

The actual incidence is probably somewhere between these two extremes, possibly 1:7000.

The disease is said to be most common between the ages of 30 and 40, two thirds of the cases occurring within this decade. Most of the patients have had previous pregnancies, and the greatest incidence is in those who have given birth four or five times.

Effect on Pregnancy and Prognosis

Carcinoma of the cervix influences pregnancy very unfavorably, abortion occurring in 30-40 per cent of the cases. If the patient reaches term the dangers of labor are greatly increased (1) because of the risk of intrauterine infection from the infected carcinoma, (2) because the carcinoma may interfere with dilatation of the cervix, with possible spontaneous rupture of the lower uterine segment, and (3) because of the danger of hemorrhage from laceration of the tumor. In general, the mortality has been higher in the carcinomas treated in the second half of pregnancy.

The prognosis is said to be the same as in the nonpregnant woman, Emge reporting 5 cures in 6 cases, Richman 3 in 4, and Maino reporting a 30 per cent 5-year survival rate in 20 cases treated at the Mayo clinic.

Therapy and Results

Eastman recommends deep x-ray therapy followed by radium therapy in the first half of pregnancy and recommends miniature cesarean section if abortion does not occur within 3 to 4 weeks after completion of treatment. In pregnancy beyond the sixth month, with the fetus alive but still nonviable, the same author recommends radium therapy followed by cesarean section with deep x-ray therapy being given after delivery.

Willson in 1945 recommended prompt and thorough investigation of bleeding during pregnancy. He believes that radical surgery has no place in the treatment of carcinoma of the cervix in pregnancy, since the results from combined irradiation therapy are equally good. He recommends deep x-ray therapy and a dilatation and curettage if abortion does not occur during the third week of treatment. Five thousand milligram hours of radium therapy is then given to the cervix.

Jones and Neill reported a series of 11
patients treated with irradiation at the Kelly Hospital. Eight of these patients were treated by them alone and 3 received a portion of their treatment elsewhere. They attempted to give repeated small doses of radium therapy during pregnancy and to allow as many of the mothers as possible to go to term. Four of the eleven mothers survived 5 years, for a 5-year survival rate of 36 per cent. There were 7 living children, 5 of whom were normal. Two of the children had microcephaly.

Among the more recent reports is that of Newton, giving a small series of cases with inadequate follow-up, and of Hirst, who recommends radical surgery for carcinoma of the cervix in pregnancy. Cosbie reports a series of 20 cases treated by radiation, including 4 of his own, in which the survival rate was lower than for nonpregnant patients. Brown and Jernigan report a 3-year survival rate of 60 per cent. Most of their early cases were treated with x-ray and radium therapy without hysterotomy. In late pregnancy hysterectomy accompanied cesarean section in 3 of the cases.

Maier and Klein report 4 cases in which all the patients were treated with irradiation. Three were dead at the time of the report, and the fourth was terminal. Thornton reports 5 cases, 4 treated by means of the radical Wertheim operation and 1 by deep x-ray. One of the patients died from pulmonary embolus and the remaining 4 were alive after 3 years. Hudgins reports 4 patients treated with irradiation, 2 of whom died. The remaining patients were well, but only 1 had been followed more than 5 years.

MATERIAL

Our present series of cases consists of 11 patients divided into four groups. During the period when these 11 cases occurred, there were approximately 20,000 deliveries at Johns Hopkins Hospital, making an incidence of 0.5 per cent. When the incidence is compared to the number of carcinomas of the cervix treated during this period, the incidence is 2.4 per cent. The average age of our patients was 32.4 years. Two were pregnant for the first time. Most of the remainder had had multiple pregnancies. Five were classified as International Classification Stage I. There were 4 Stage II carcinomas and 1 was classified as Stage III carcinoma of the cervical stump. Two of our patients were asymptomatic, the carcinomas having been detected on routine examination. Nine complained of bleeding of varying amounts. In 2 of these the bleeding was associated with incomplete abortion and in 1 it occurred postcoitally. Only 3 of the 11 complained of leukorrhea.

TREATMENT

In treating this group of patients we have attempted to treat them promptly and vigorously regardless of the duration of the pregnancy, according to our usual routine for the nonpregnant. Of the 11 patients, 10 were treated with a combination of radium and deep x-ray and 1 by means of a radical Wertheim operation. Our usual irradiation technic has been described elsewhere. Briefly, it consists of 2 radium treatments of 2400 mg. hr. each given at an interval of two weeks, half intracervically half contracervically. It is our custom to give the radium treatments first in Stage I and II cancer since we have the clinical impression that the patients do better if the radium therapy is given first. The radium therapy is followed after two weeks by a course of deep x-ray therapy over four pelvic fields at either 250 or 400 kv. From 2500 to 3000 r is delivered to the skin over each field. This technic is calculated to deliver 20,000 r to the cervical canal, 8000 r to Point A and just less than 4000 r to Point B. More recently, an attempt has been made to increase the dosage at Point B by increasing the deep x-ray therapy.
RESULTS

Group 1: Early Treatment

Our first group comprises those patients treated early in pregnancy at 17, 19, and 15 weeks, respectively. All were treated with the combination of radium and deep x-ray therapy outlined above. One radium treatment was given. A hysterotomy was performed a week later, and this was followed after another week by a second radium treatment. All were then given deep x-ray therapy. The results of the treatment in this group, Cases 1, 2, and 3, are shown in Table 1. All of these patients are well 6 months, 3½ years, and 6½ years after the treatment.

Group 2: Late Treatment

The second group of patients comprises 2 patients who were diagnosed and treated late in pregnancy. The first patient had a very large cervical lesion which was classified as late Stage II. She was 32 weeks pregnant. A cesarean section was done and a living child obtained, but upon attempting to apply radium to the cervix 10 days after the cesarean section, the lower uterine segment was perforated and only contracervical radium could be applied. This accident delayed the patient's treatment, and although she was fully treated, the total duration of irradiation therapy was prolonged. The patient died of persistent carcinoma 10 months after treatment. This was our only cancer death.

The second patient in this group was treated with cesarean section followed by x-ray therapy, and then by two radium treatments according to our usual routine. She was well 6½ years after treatment, but died of a stroke 6 months later. These cases #4 and 5, are summarized in Table 2.

Group 3: Postpartum Diagnosis and Treatment

Our third group includes patients who developed symptoms shortly after delivery and in whom the carcinoma was certainly present.

### Table 1. Group 1: Early Treatment

<table>
<thead>
<tr>
<th>Case #</th>
<th>Clinical classification</th>
<th>Duration of pregnancy (wk.)</th>
<th>Treatment (in sequence)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>I.C. I</td>
<td>17</td>
<td>Radium, hysterotomy, radium, x-ray</td>
<td>Well 6 mo.</td>
</tr>
<tr>
<td>2</td>
<td>I.C. I</td>
<td>19</td>
<td>Radium, hysterotomy, radium, x-ray</td>
<td>Well 3½ yr.</td>
</tr>
<tr>
<td>3</td>
<td>I.C. I</td>
<td>15</td>
<td>Radium, hysterotomy, radium, x-ray</td>
<td>Well 6½ yr.</td>
</tr>
</tbody>
</table>

### Table 2. Group 2: Late Treatment

<table>
<thead>
<tr>
<th>Case #</th>
<th>Clinical classification</th>
<th>Duration of pregnancy (wk.)</th>
<th>Treatment (in sequence)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>I.C. II</td>
<td>32</td>
<td>Cesarean section, radium (perforation), radium, x-ray, radium</td>
<td>Dead 10 mo.</td>
</tr>
<tr>
<td>5</td>
<td>I.C. I</td>
<td>32</td>
<td>Cesarean section, x-ray, radium, radium</td>
<td>Well 6½ yr. Died stroke, 7 yr.</td>
</tr>
</tbody>
</table>
CERVICAL CANCER IN PREGNANCY

ent during pregnancy. There are 4 of these, 1 of whom was treated by a radical Wertheim operation, and 3 with a combination of radium and deep x-ray therapy. All of these patients are well 1½ to 9½ years after hysterectomy had to be done. The cervix was not biopsied on this obstetric admission. Three years after the original diagnosis of questionable intraepithelial carcinoma, she appeared on the gynecologic service with treatment. This group, Cases 6, 7, 8, and 9, is summarized in Table 3.

**Group 4: Delayed Treatment**

The fourth group consists of two patients in whom intraepithelial carcinoma of the cervix was diagnosed prior to pregnancy. In Stage III carcinoma of the cervical stump. She was treated with deep x-ray therapy and 3 radium treatments, one of the radium treatments being an interstitial application of radium needles to the cervix and left parametrium. This patient is well after 1¾ years.

**Table 3. Group 3: Postpartum Treatment**

Carcinoma of Cervix and Pregnancy

<table>
<thead>
<tr>
<th>Case #</th>
<th>Clinical classification</th>
<th>Postpartum Interval (wk.)</th>
<th>Treatment (in sequence)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>I.C. I</td>
<td>5</td>
<td>Radical Wertheim</td>
<td>Well 1½ yr.</td>
</tr>
<tr>
<td>7</td>
<td>I.C. II</td>
<td>8</td>
<td>X-ray, radium, radium</td>
<td>Well 5½ yr.</td>
</tr>
<tr>
<td>8</td>
<td>I.C. II</td>
<td>24</td>
<td>Electrosurgical excision, radium, x-ray</td>
<td>Well 7½ yr.</td>
</tr>
<tr>
<td>9</td>
<td>I.C. I</td>
<td>14</td>
<td>X-ray, radium, radium</td>
<td>Well 9½ yr.</td>
</tr>
</tbody>
</table>

**Table 4. Group 4: Delayed Treatment**

Carcinoma in Situ and Pregnancy

<table>
<thead>
<tr>
<th>Case #</th>
<th>Original diagnosis</th>
<th>Interval until made (mo.)</th>
<th>Clinical classification</th>
<th>Treatment (in sequence)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Intraepithelial carcinoma</td>
<td>24</td>
<td>I.C. II (Heyman)</td>
<td>Radium, radium, x-ray</td>
<td>Well 3 yr.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Case #</th>
<th>Original diagnosis</th>
<th><a href="http://www.cmich.edu">www.cmich.edu</a></th>
<th>Clinical classification</th>
<th>Treatment (in sequence)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Intraepithelial carcinoma</td>
<td></td>
<td>I.C. II (Heyman)</td>
<td>Radium, radium, x-ray</td>
<td>Well 3 yr.</td>
</tr>
</tbody>
</table>

*Original diagnosis made at The University of Maryland Medical School.

The first patient, Case 10, admission to the hospital for a sharp conization of the cervix had been recommended for diagnostic purposes after a cervical biopsy showed questionable carcinoma in situ, but the patient refused to come in and was lost track of. She next appeared on the obstetric service where a cesarean section was done. Because of injury to the uterine artery a subtotal

In Case 11, the carcinoma progressed in 24 months from an intraepithelial carcinoma to a Stage II of the cervix with extension to one vaginal fornix. The patient was treated with radium and deep x-ray therapy and is well 3 years after treatment. A summary of this group is shown in Table 4.

Of the 11 patients in our series 9 are
living and well after 6 months to 9 1/2 years since treatment. One patient died of persistent carcinoma, and a second patient died of a stroke 7 years after treatment. The absolute 5-year cure rate in the 7 patients treated 5 years or more is 86 per cent (Table 5). The absolute 5-year cure rate in all cases of carcinoma of the cervix treated in this clinic during the same period is 40.7 per cent (see Table 5).

CONCLUSIONS

1. The prognosis in carcinoma of the cervix uteri in the pregnant woman is as good as or better than in the nonpregnant, provided prompt and thorough treatment of the carcinoma is given.

2. Patients in whom the diagnosis of carcinoma in situ or questionable carcinoma in situ has been made before or during pregnancy must, if the carcinoma has not been treated, be followed extremely carefully in the postpartum period.

REFERENCES

2. Cosbie, W. G. Discussion in Hirst.8
Vaginoabdominal Approach in Pelvic-cancer Surgery

RAYMOND J. SIMMONS, M.D.

Most operations for gynecologic cancer in this country are done entirely transabdominally. However, Bastiaanse in Holland, Mitra in India, Navratil in Austria, and others continue to treat cancer of the cervix successfully by radical vaginal hysterectomy, according to the method of Schauta. This vaginal operation allows wider resection of the vagina, paravaginal tissue, and parametrium, but of course does not provide opportunity for removing the pelvic lymph nodes which drain the uterus. The abdominal operation has a disadvantage in that the lowermost dissection is less efficient than in the Schauta operation. This is especially true in the presence of obesity and a narrow deep pelvis, and in cases requiring removal of a considerable length of vagina or a total vaginectomy.

Little mention is made in the literature of a combined vaginoabdominal approach in the surgical treatment of cancer of the cervix, uterus, or vagina. Brunswig described a vaginal phase, using it "when the cancer of the cervix is large and fungating or appreciable spread into the vagina has occurred." A vaginoabdominal approach is not mentioned in Meig's recent text Surgical Treatment of Cancer of the Cervix.

Advantages of Combined Surgical Approach

It would appear that in all cases where resection of a wide cuff of vagina is desirable, it could be done more efficiently and easily, under direct vision, through the vagina than through the abdomen. In this way, a wider dissection of paravaginal and paracervical tissue can be accomplished. Also, the operator then knows exactly how much of the vagina is being removed, whereas when this deep dissection is done transabdominally he has to depend on palpation rather than visualization. If too much of the vagina is removed in resection for an early cancer of the cervix, intercourse becomes difficult and often impossible; and if only a narrow length of vagina is left attached to the cervix, there is likelihood of recurrence in the vaginal cuff.

Facility of Low Transection

In very obese patients and in those with a deep, narrow pelvis the lowermost dissection through the abdomen is the most difficult part of the operation for cancer of the cervix. Even in thin patients with a roomy pelvis the dissection of the paravaginal tissue and the low transection of the vagina are tedious, time-consuming, and technically difficult procedures. However, it is surprisingly easy to effect en bloc removal of these structures through the abdomen after they have been mobilized through the vagina.

Decreased Spillage of Tumor Cells

Another distinct advantage of the vaginal phase is that there is less likelihood of spillage of tumor cells, since the vaginal vault
distal to the tumor has been packed and securely sutured transversely.

No Vaginal Clamping

No clamping of the vagina is necessary, and this promotes better healing of the distal cuff. Even with the aid of long right-angle clamps and long right-angle scissors, there is always difficulty in transecting the vagina distal to the clamps.

Improved Suturing

Accurate placement of sutures in the distal cuff is often not possible from above, and requires traumatic retraction of the bladder, ureters, pelvic veins, and so on, to visualize the contracted vaginal edges. The likelihood of postoperative bleeding from the vaginal cuff, especially at the lateral angles, is small when the sutures are accurately placed without tension in the preliminary vaginal phase of the operation.

Symmetrical Excision

Another advantage of the vaginal mobilization is that a symmetrical length of vagina can be removed. In vaginal transection from above, the operator often is dismayed to find a shorter anterior wall than posterior, or that one side of the resected vagina is considerably shorter than the other.

Fig. 1. Vaginal incision.

PROCEDURE

Vaginal Phase

The vagina and perineum are cleansed and an indwelling catheter is inserted into the bladder. A circular incision is then made around the vaginal wall (Fig. 1), at a level selected according to the individual circumstances of the case. If there are vaginal metastases, or in a primary cancer of the vagina, the incision is made just within the introitus, so that the entire vagina is removed with the uterus. In an early cancer of the cervix or endometrium, the incision is made...
VAGINOABDOMINAL SURGERY IN PELVIC CANCER

in the middle third of the vagina. Dissection upward around the vagina in a lateral plane within the paravesical space on each side is then done, up to the level of the parametrium (Fig. 2). Separation from the urethra and bladder is carried out in the vesico vaginal space, and separation from the rectum is readily accomplished in the rectovaginal space, where there is an excellent cleavage plane. The vagina is thus mobilized as a cylindrical structure, and a tight gauze pack is inserted. The proximal vaginal cuff is tightly closed with a running lock suture. The distal vaginal cuff is closed without tension, using interrupted sutures. No drainage is necessary. The abdominal phase is then begun and, in cancer of the cervix, proceeds according to the method of Meigs and Brunschwig.

Abdominal Phase

The pelvic lymph nodes, broad ligaments, and parametrium, with the uterus, are mobilized in continuity. The dissection from above meets that from below, and the entire specimen is readily removed. Peritonealization of the pelvic floor is then done. If a large amount of peritoneum is removed with the specimen, this step is not necessary.

RESULTS AND DISCUSSION

This vaginoabdominal approach has been used by the author in 16 Stage I and 22 Stage II cancers of the cervix during 1949–54. Two cases of primary cancer of the vagina and 8 cases of cancer of the endometrium, 1 of which had metastases in the vaginal vault, have also had this type of combined approach. No prolapse of the vaginal vault has occurred since surgery, probably as a result of paravaginal scarring. Except in 6 cases where the entire vagina had to be removed, intercourse was possible after surgery, and in cases not preceded by radium application the vaginal walls remained quite elastic. No postoperative bleeding from the vaginal cuff has occurred, and there have been no recurrences in the vaginal cuff.
Sufficient time has not elapsed for a long-term follow-up on these cases; 5- and 10-year survival rates will be reported at a later date.

SUMMARY

Advantages of a combined vaginoabdominal approach in the surgical treatment of cancer of the cervix, endometrium, and vagina are described. These include:
1. More effective removal of vaginal and paravaginal tissues.
2. No need for clamping the vagina, thus allowing for better healing.
4. Less possibility of spillage of tumor cells during removal of the tumor.
5. The technical advantage of being able to do the deepest dissection under direct vision, rather than by palpation from above in the depths of the pelvis.

This approach is applicable in early and moderately advanced cancer of the cervix and endometrium, in primary cancer of the vagina, and in cancer of other pelvic organs with vaginal metastases. In this way, certain advantages of the Schauta radical vaginal operation are utilized to improve the efficiency of the abdominal approach.

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REFERENCES

Stromal Endometriosis

MORTON A. SCHIFFER, M.D., and ABRAHAM MACKLES, M.D.

STROMAL ENDOMETRIOSIS is a tumor-like change within the myometrium composed of endometrial stromal cells. According to Hunter, many terms have been used to describe this lesion: perithelioma, fibromyosis, endometrioma interstitiale, endolymphatic stromal myosis, stromatosis, endometrial sarcoid, and others.

REVIEW OF THE LITERATURE

Hunter collected 54 examples of this lesion from the literature through 1953. Both he and Goodall independently suggested that many other examples were neither recognized nor reported. Goodall labeled these lesions endometrioma interstitiale and stated that all his older cases were originally reported as sarcoma. Goodall's series of 14 cases is the largest individually reported group. Hunter's 10 cases and Henderson's 7 cases comprised the next largest series. Other publications on the subject contain 1–3 cases in any single report.

The endometrial stromal cell is a remarkable cell and has a great potential for differentiation. It comes as no surprise to find that this cell or its precursor can give rise to tumor formation. It varies greatly in its own natural habitat and when growing rapidly may simulate sarcoma very easily. Goodall stated, in discussing the appearance of stromal cells in this lesion, "when it pervades fixed tissues and surrounds the preformed blood vessels, these latter retain their pristine thick walls, but where the new growth builds its own lymph and vascular channels the interstitial cells abut upon the channels and not infrequently invade them." This statement partially explains the vascularity of these tumors and also the arrangements of cells so often seen dipping into lymphatic and venous channels as well as into surrounding small vessels on many occasions.

Park, in reviewing 43 cases from the literature, notes the association of ectopic endometriosis in 7 cases and typical adenomyosis in only 4 cases. These associated lesions may be present, but are not necessary for diagnosis. In the majority of the 43 cases studied by Park, the new growth merged with the endometrium, although in several instances no connection could be found in the serial sections made. Six cases showed some significant concurrent endometrial pathology.

Theories on Origin and Development

Henderson believes that stromal endometriosis is an entity distinct from endometriosis and has shown that the former may recur many years after primary removal. Te Linde, in discussing Henderson's paper, noted that stromal endometriosis may occur after the menopause or castration and also that stromal endometriosis does not show cyclic bleeding into its substance, forms large tumors, and spreads in a fashion not at all similar to endometriosis.

On the basis of the above points Park states that stromal endometriosis is not a variant of ordinary endometriosis, and further states that "the theory that the diffuse overgrowth of stromatoid tissue which characterises stromatous endometriosis as a
direct development from the endometrial stroma depends to a great extent on the analogy with adenomyosis." He also states that adenomyosis is not a variety of true endometriosis and that stromal endometriosis is analogous in many respects to adenomyosis or really to its stromatous analogue. The absence of glands and the neoplastic nature of stromal endometriosis proved to him that they are not completely analogous. There is, however, enough similarity to suggest that they develop in like fashion. In reaching these conclusions Park refers to Henderson; Novak; Curtis; and Hunter, Smith and Reiner.10

INVASION AND LATENT POTENTIAL. According to Park the following possibilities may explain the presence and origin of the stromal tissue in the myometrium:
1. Direct invasion from basal endometrial stroma.
2. Unifocal or multifocal development from undifferentiated precursor tissue in situ.
3. Lymphatic or venous embolism from the endometrium.

He discounts the embolic process as a possibility and believes that direct invasion or development from precursor tissues are the two main possibilities. It is those examples of stromal endometriosis in which there is no direct connection between the surface endometrial stroma and the tumor tissue that pose the problem as to the origin of the tumor. Park quotes Gruenwald as follows: "No morphologic terms and characteristics can serve to indicate the developmental potencies of cells." Gruenwald is also quoted as saying, "In terms of morphology of adults these facts mean that the non-epithelial layers of the uterovaginal canal, including the lamina propria, the muscularis and the subserous tissues, originate at least partly from the cells which had been part of the inner or the outer epithelial lining." Therefore, nonepithelial tissues may arise from epithelial tissues or the converse may be true.

The foregoing statements indicate that tissues with potencies to form stromal cells may be present throughout the uterus. Further, those tissues may be stimulated to growth and tumor formation by whatever stimulant —humoral, physical, or otherwise—that causes tumors to develop and grow.

Lock, in discussing a paper by Hellman on proliferation of reserve cells in the human cervix, states: "The endometrial stroma is an excellent example of the persistence after birth of large masses of incompletely differentiated cells of embryonal type."

It is not surprising, therefore, to see this tissue express under certain circumstances latent developmental potencies, especially since endometrial stroma resembles mesenchyme.

From the foregoing facts and hypotheses it is believed by Park, others, and ourselves that stromal endometriosis is a tumor which develops in the uterine wall. The tumor originates from either unifocal or multifocal areas of stromal anlage or from the endometrium proper.

CASE REPORTS

Case 1

First Admission. Mrs. T. K., a 31-year-old white para 2-O-O-2, was admitted to the private service of Dr. S. A. Wolfe at The Jewish Hospital of Brooklyn on May 16, 1948, with the chief complaint of meno-metrorrhagia of 1 year's duration. Past history was noncontributory.

EXAMINATION. Physical examination was negative except for pelvic examination which revealed an anteriorly placed uterus enlarged to the size of an 8–10 week gestation with a symmetry in the left cornual area. The adnexal areas were negative. The preoperative diagnosis was fibromyomata uteri.

LAPAROTOMY. On May 17, 1948, a laparotomy was done and the uterus was described as being slightly enlarged and soft, with a submucous myoma the size of a walnut arising from the left lateral posterior wall. There were marked varicosities of the broad ligament. The oviducts and ovaries presented no gross pathology. A longitudinal incision was made over the latter and the myoma was removed.
the left fundal wall and the submucous myoma was removed. The patient’s postoperative course was uneventful.

**PATHOLOGIC FINDINGS.** Gross examination showed an irregular, soft, pink-red portion of tissue measuring $3 \times 2.5 \times 1$ cm. The cut surface was pink-gray, soft, and slightly trabeculated.

Microscopic examination. There were areas at the periphery of the myoma in which the endometrial surfaces were covered by columnar cells and in which endometrial glands were seen. The stroma was cellular and composed of closely packed spindle cells and many thick-walled arterioles.

**Second Admission.** On June 26, 1953, five years after her first admission, Mrs. T. K. was readmitted to the hospital with a chief complaint of persistent lower back pain. She stated that since the previous operation her periods had been regular and with no menometrorrhagia, but that the periods gave rise to very severe back pain. The last normal period was on June 13, 1953. Physical examination was negative, except for the pelvic findings.

**PELVIC EXAMINATION.** The uterus was slightly enlarged, irregular, firm, and in the anterior position. The adnexa were negative. The clinical diagnosis was recurrent myomas and adenomyosis.

**SURGERY.** On June 29, 1953, laparotomy was performed and the uterus was found to be enlarged to the size of a 10-12-week gestation.
Fig. 2. The polyp consists of endometrial glands and stroma. A profusion of spiral-like arterioles is present at the base. (X 95) (Figs. 2-6 are of Case 1.)

Fig. 3. Topographic view of polyp, mural mass, and smaller nodules lying within spaces. Endometrial glands are present in one quadrant of mural mass near polyp. Distal portion consists entirely of stroma and vessels, and appears to serve as a spearhead. (X 87)

Fig. 4. Portion of mural mass showing glands and profusion of spiral-like arterioles. There is continuity of stromal cells within the endometrium and the stromal cells of the mural mass. (X 87)

Fig. 5. Nuclear details and basket-like pattern of collagenous fibers about individual cells.

Fig. 6. Adjacent to portion of mural mass and within spaces in the myometrium are nodules composed only of stroma. (X 98)
STROMAL ENDOMETRIOSIS

consisted of few tubular glands separated by relatively large amounts of compact stroma. At the base of the polyp groups of thick-walled arterioles were noted (Fig. 2). The largest intramural mass was just beneath the endometrium (Fig. 3) and on one section stromal cells and blood vessels appeared to be continuous with the polyp overlying the mass (Fig. 4). In one upper corner of the large intramural mass a collection of endometrial glands was seen. The vast bulk of the mass consisted of cells with leptochromatic oval, or plump, spindle-shaped nuclei (Fig. 5). Each cell was surrounded by a delicate wavy collagenous fibre. Apparent small satellite nodules, often within endothelial lined channels, lay in the vicinity of the main mass. These nodules (Fig. 6) consisted entirely of the spindle cells, fibres, and blood vessels. The deepest penetration of the tumor was at the junction of the middle and outer thirds of the myometrium.

The oviducts and the right ovary were not unusual. The left ovary contained a recent corpus luteum.

Diagnosis. Endometrial polyp with a large stromal component and underlying area of stromal endometriosis with a single focus of endometrial glands. Normal ovaries with recent corpus luteum in left ovary.

Case 2

Mrs. L. S., a 42-year-old-white para 3-0-0-3, was admitted to the private service of Dr. F. Moskowitz at The Jewish Hospital of Brooklyn on July 30, 1953, with the chief complaint of continuous vaginal bleeding of 4 months’ duration. Past history was irrelevant. Physical examination was negative, except for the pelvic findings.

Fig. 7. Case 2. Mural mass bisected. Upper arrow points to wormlike area pulled out of channel. Left lower arrow points to smooth rounded polyp pulled out of channel indicated by lower right arrow.
Fig. 8. Case 2. Polypoid projections from vessels of broad ligament.

PELVIC EXAMINATION. The uterus was irregularly enlarged to the size of a 12-week gestation, with multiple, firm, nodular areas. The adnexa were not felt. The preoperative diagnosis was multiple fibromyomas.

SURGERY. On July 31, 1953, a laparotomy was performed. The uterus was irregularly enlarged to the size of a 3-month gestation, with numerous subserous and intramural myomas. The largest myoma measured 6 cm. in diameter. Several soft polypoid masses were noted within the vessels of the broad ligament. The adnexa did not appear abnormal. A total hysterectomy and appendectomy were performed. The adnexa were left in place. The patient had an uneventful postoperative course.
PATHOLOGIC FINDINGS

**Gross.** The specimens consisted of a total uterus and an appendix. The appendix showed no feature of note. The uterus measured 14 × 9 × 6 cm. The cervix presented little of note apart from a patulous, linear external os and several nabothian cysts. A scattering of intramural and subserous myomas was noted, as well as a few leiomyomas.

The endometrial surface was smooth and thin except where it showed an irregular soft, thin lining. The mucosa was usually smooth and thin, but in some places there were scattered protuberances. The endometrium measured 2.5 cm in greatest thickness. The glands were soft, tubular, and in some areas lined with a thin epithelium. The muscle layers were smooth and thin. The stroma was quite sparsely cellular. There was no subserosal or serosal involvement. The cervical canal contained some metastatic tumor, and there was a dense lymphocytic infiltration of the connective tissue about the ureteral orifices. The ovaries were of normal size and color.

**Microscopic.** The endometrium was hyperplastic, with scattered small islands of endometrial tissue. The myometrium was composed of dense, fibrous tissue with scattered smooth muscle fibers. There were no abnormalities of the vascular system.

**Fig. 9.** Tiny endometrial polyp. Note superficial adenomyosis. (X 86) (Figs. 9-12 are from Case 2.)

**Fig. 10.** Details of nuclei within a nodule. Collagenous network is relatively delicate. (X 342)

**Fig. 11.** Case 2. Nodules within myometrial channels (X 4.5)

**Fig. 12.** Case 2. A mass of stromal cells lying free within a myometrial channel. (X 86)

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*Obstetrics and Gynecology*
STROMAL ENDOMETRIOSIS

as a submucous leiomyoma 0.6 cm. in diameter. The endometrial cavity was 5 cm. long and the endometrial surface was congested, irregular, and finely granular, with an absence of the usual smoothness. The left lateral wall was thickened to 4 cm. and on section there was an irregular, soft area 5.5 cm. in length and 2.5 cm. wide. It was separated completely from the endometrial surface. This area consisted of soft, silky, white tissue in which several long thin blood vessels were noted. In one area a strand of such tissue could be pulled out of a smoothly lined channel. In another place within this area, a smoothly lined polyoid mass could be easily pulled out of a distended smoothly lined channel (Fig. 7). Apart from pallor, the myometrium was not unusual. Soft polyoid masses projected from the open ends of thin-walled vessels in the left lateral wall (Fig. 8). Nine such polyoid masses composed of the same soft white tissue as in the mural mass were noted. The external polyoid masses and the mural mass were continuous.

Microscopic. The endometrium was generally thin and contained many minute polyoidal excrescences. Glands were relatively few and of the straight tubular. In several sections endometrial glands lay between muscle bundles of the superficial myometrium (Fig. 9). Sections from the irregular mural mass and the external masses showed them to consist of rather closely packed, moderate-sized cells with round, oval, or spindle-shaped nuclei which were generally leptochromatic (Fig. 10). There were fine, wavy collagen fibres. The smaller masses lay within vascular channels (Figs. 11 and 12). A moderate number of blood vessels were noted.

Diagnoses. Stromal endometriosis with extension into veins of the left broad ligament. Multiple minute endometrial polyps and superficial adenomyosis, leiomyomas. Normal appendix.

DISCUSSION

Pathologic Features

The pathologic features of this condition have been very adequately described in several previous publications, particularly those of Hunter; Park; and Henderson.

Grossly, the uterus is enlarged and globular. The freshly sectioned myometrium has a coarse, nodular surface. There is a tendency within the endometrial cavity to polyoid formation, usually broad-based and smooth-surfaced, with a yellow color on cut section. Rubberly, cordlike areas frequently extend into the broad ligament. These cords of tissue are extensions of the tumor tissue into the vascular and lymphatic channels of the uterus.

The microscopic appearance is that of closely packed endometrial stromal cells of the late proliferative type. The cell pattern is uniform; numerous thick-walled arterioles are frequently, but not necessarily, present. Strands of tumor cells may be seen apparently pushing their way into lymphatic or other vascular spaces and covered by a single layer of endothelial cells. Mitoses may be present, but are few in number. The cells are uniform in size, shape, and staining characteristics. Giant-cell formation is not present. Another characteristic finding microscopically is that seen with the aid of a reticulum stain. The endometrial stroma possesses a basketlike reticulum which is also present in growths arising from the stromal cell. The lesion may or may not have a direct connection with the endometrium.

Diagnosis

It is not unusual to diagnose these cases as sarcoma, and this is frequently done by the pathologist who is not familiar with this lesion. In a previous study,17 we described another case of stromal endometriosis which was originally diagnosed as hemangioendothelioma.

Knowledge of the gross features will enable the correct diagnosis to be made in the operating room. If involvement of the veins and lymphatics of a broad ligament is present, the diagnosis is possible before the uterus is opened; otherwise, the correct diagnosis can be made only after the uterus is opened and the tumor bisected.

Connection with Endometrium

In both cases reported here, the endo-
metrium showed an abnormality. In Case 1 a large sessile polyp was present directly above the mural lesion, and in Case 2 the endometrium was granular in appearance due to its being thrown up into folds by numerous tiny polyps. The uterine bleeding in this case resulted from endometrial change and not to the presence of the mural and extramural lesion.

In Case 1 the mural lesion was continuous with the stroma of the endometrial polyp. In case 2 there was no connection between the mural mass and the overlying endometrium, a feature previously reported in other cases and discussed at length by Park and Tennant.¹⁶

**Malignancy**

In view of the fact that metastases and recurrences have been reported by Park and Hunter, despite a relatively benign histologic appearance, this lesion must be viewed as one of low grade malignancy. Novak states, and we concur with him, that if there is histologic evidence of malignancy the lesion should be classified as endometrial sarcoma.

**Histologic Features**

The histologic features of both cases reported here show a striking similarity. In these cases the mural lesions, and in Case 2 the extraterine extensions, showed the following characteristics:

1. The cells were in solid masses and the individual cells possessed poorly defined cytoplasmic borders. Nuclei were of moderate size and round, oval, or of plump spindle type. Leptochromatism was a prominent feature. The uniformity of appearance of the cells was striking. Mitotic figures were conspicuously absent.

2. Prominent wavy collagenous fibres formed a "basket-weave" pattern because of their encirclement of each individual cell. Although this feature was striking when the tissue was stained by the Wilder method for reticulin or by the elastic Van Gieson method the collagenous fibers were prominent enough in the routine hematoxylin-eosin stain to be detectable. The use of special stains does, however, eliminate the possibility of confusing the stromal cells with smooth-muscle fibers.

3. Blood vessels of the arteriolar type were numerous in both cases, particularly in Case 1. Because of the appearance of the vessels, their size and the frequent occurrence in clusters, the resemblance to spiral arterioles was striking.

4. There was tumor within endothelium-lined spaces and it was impossible to determine whether these spaces were lymphatic or blood vessels.

5. Tumor lay within the myometrium.

6. Degenerative changes were conspicuously absent.

**Clinical Findings**

The symptoms and signs of stromal endometriosis are not specific or pathognomonic. There may be irregular bleeding with increase in menstrual flow, shortening of cycles, or intermittent bleeding. Pressure symptoms due to formation of a mass also may be present. The physical findings in all cases are those of an irregular pelvic mass indistinguishable from a mass due to fibromyomas. The diagnosis can be made at surgery by the appearance of an enlarged uterus with extension of worm-like masses into the vessels of the broad ligaments. These masses may be stripped out of the spaces within which they lie.

**Treatment**

The treatment of stromal endometriosis is total hysterectomy and bilateral salpingo-oophorectomy.

**Factors in Prognosis**

Our two cases are alive and well with no evidence of local recurrence or metastases. Both patients have been followed only 1½
STROMAL ENDOMETRIOSIS

Two cases of stromal endometriosis have been reported. The cases have been reviewed in detail and the pathologic features have been presented, with accompanying photographs. The theories and facts as to the origin and pathogenesis of this lesion have been discussed. We believe that these tumors arise from endometrial stromal cells or their precursors.

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Tetanus Complicating Pregnancy

Report of a case treated with chlorpromazine with survival of both mother and infant

ALLAN R. SINGLETON, Jr., M.D., and ROGER W. WITT, M.D.

IN HIS TEXTBOOK of obstetrics, Eastman mentions a case of tetanus in pregnancy reported by Archambaud, but a survey of the English literature between 1880 and 1955 failed to reveal a case of tetanus complicating pregnancy in which both mother and infant survived. For this reason, the following case seems worthy of reporting.

A 29-year-old Negro housewife, gravida VII, para VI, was admitted to Charity Hospital in New Orleans on February 16, 1955, with the complaint of being unable to open her mouth. Seven days prior to admission she sustained a small laceration of the left elbow as a result of being struck by a chip of wood. Two days prior to admission, the patient noticed some stiffness of the left arm with gradual onset of stiffness of the muscles of the jaw. Systemic complaints, past history, and family history were noncontributory. The last menstrual period and the date of confinement were not known. She assumed that she was approximately 7 months pregnant but had not received prenatal care. Six previous pregnancies had been uneventful.

PHYSICAL EXAMINATION

Physical examination revealed a well-developed, well-nourished Negro woman. The patient was ambulatory but appeared to be in acute distress, exhibiting a masklike facies and classical risus sardonicus. Her temperature was 98.6° F., pulse 130 per minute, respirations 32 per minute. There were generalized spasticity and partial flexion of the left arm. Overlying the head of the left radius was an edematous punctate laceration measuring 5 mm. in diameter. Heart and lungs were normal.

Abdominal palpation revealed intrauterine pregnancy of approximately seven and one-half months gestation. Active fetal movements could be felt, and fetal heart tones were of good quality at 140 per minute. The deep tendon reflexes were hyperactive bilaterally, and a moderate degree of opisthotonos was present.

Diagnoses on admission were: (1) tetanus with systemic manifestations, (2) localized tetanus of the left arm, and (3) intrauterine pregnancy of 7½ months.

LABORATORY DATA

The following laboratory data were obtained on admission: hematocrit 29 per cent, white blood cells 14,000, with 90 per cent polymorphonuclears and 10 per cent lymphocytes. Urinalysis was negative. Blood glucose was 90 mg./100 cc., BUN was 8 mg./100 cc., serum chlorides were 101.1 mEq./L., and CO₂ combining power was 12.1 mEq./L.

A spinal tap was performed upon admission. Spinal fluid was clear, and a pressure of 90 mm. of water was obtained. Microscopic examination failed to reveal any cells or organisms, and culture was negative.

Surgical débridement of the laceration and tracheotomy were performed. A Levin tube was inserted into the stomach for feeding.

Medication

On admission, the patient received 50,000 units of tetanus antitoxin intramuscularly, 50,000 units in slow intravenous drip, and thereafter 10,000 units daily intramuscularly.
TETANUS COMPLICATING PREGNANCY

for five days. Eight million units of aqueous penicillin and 2 Gm. of streptomycin were administered daily. Phenobarbital, gr. 2, and mephenesin (3), Gm. 2, were administered every 4 hours for sedation, the doses being staggered in order to avoid respiratory depression.

COURSE OF DISEASE

On the second day after admission, the patient developed generalized clonic convulsions, which occurred every 3 to 5 minutes. Fetal heart tones remained constant and of good quality throughout her entire hospital stay.

Two weeks after admission, bronchopneumonia developed on the left side. In addition to penicillin and streptomycin, she was now also given tetracycline, 300 mg. daily intramuscularly. The pneumonic process did not clear completely until about 5 to 6 days postpartally. She remained febrile during almost her entire hospital course, with temperatures ranging from 100° to 102° F.

DELIVERY

Twenty-four days after admission the patient was in questionable labor. Vaginal examination at that time revealed the cervix to be dilated 7 to 8 cm., with the membranes ruptured and the fetus in the right occiput transverse position at a plus 2 station.

Two hours later, the patient's cervix was fully dilated with the head on the perineum. At this time the patient was observed to be completely exhausted, all voluntary abdominal effort having been expended. Left mesiolateral episiotomy was performed under pudendal block, and low forceps was applied in occipito-anterior position. A living infant was lifted across the perineum without incident. The patient lost approximately 300 cc. of blood. Postpartum course was uneventful, and antibiotics were discontinued on the fourth day.

On the third hospital day chlorpromazine (thorazine) (3, 1) was added to the plan of sedation because, despite administration of phenobarbital and toslerol, the patient continued to have clonic convulsions. Initially, these were dramatically controlled by intravenous administration of chlorpromazine, 40 mg., given slowly in divided doses. Thereafter, 25 mg. of chlorpromazine was given intramuscularly every 4 hours. From the third to the twelfth hospital day the patient received the following sedation daily: 12 gr. phenobarbital, 12 Gm. mephenesin, and 150 mg. chlorpromazine. Thereafter, sedation was gradually reduced.

Thirty-six days after admission the patient was discharged in an ambulatory state with an apparently normal infant.

SUMMARY

The first known case in the English literature of tetanus complicating pregnancy with survival of mother and infant is reported. Tetanus was caused in this 7½-months pregnant woman by a small laceration on the left elbow sustained 1 week prior to admission. Management included surgical débridement of the laceration and tracheotomy, administration of 50,000 units of tetanus antitoxin intramuscularly, 50,000 units intravenously, and thereafter 10,000 units daily intramuscularly for five days, as well as 8,000,000 units of penicillin and 2 Gm. of streptomycin daily. Sedation was accomplished by phenobarbital, mephenesin, and chlorpromazine. Her hospital course was complicated by the development of pneumonia, for which tetracycline hydrochloride was added to the therapeutic regimen. Twenty-four days after admission the patient was delivered of a living infant by low forceps and episiotomy under pudendal block. The patient was discharged 36 days after admission in an ambulatory state with an apparently healthy baby.

REFERENCES

Acid Phosphatase of the Endometrium

Histochemical demonstration in various normal and pathologic conditions

BENJAMIN GOLDBERG, Ph.D., and HOWARD W. JONES, JR., M.D.

This paper describes the histochemical acid phosphatase activity in the endometrium during the menstrual cycle and in selected abnormal states.

MATERIALS AND METHODS

All tissues were obtained by curettage from the gynecologic operating rooms of the Johns Hopkins Hospital in Baltimore. In all cases the material was frozen as promptly as possible in gasoline or isopentane, which had previously been chilled to just about freezing with liquid nitrogen.

Subsequent storage, handling, cutting, incubations, and so on, followed technics previously borrowed or devised. All results reported here (unless otherwise stated) were obtained with sodium $\beta$-glycerophosphate as a substrate (0.01M) at pH 5 in the presence of lead acetate (0.004M) in sodium acetate buffer (0.05M). Frozen sections were cut at 15 $\mu$ and incubated for various periods of time (from a few minutes to a few hours) in order to evaluate more clearly the relative activities, but, for purposes of uniform basis for comparison, descriptions and photographs refer to material incubated for 1 hr. at 37°C.

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RESULTS

Menstrual Cycle

Our material appears to indicate an increase in activity of acid phosphatase in the endometrium with the menstrual cycle. The phenomenon primarily concerns the glands. In the early part of the cycle, as shown in a 5-day specimen in Fig. 1, the activity is primarily confined to the luminal border of the glandular epithelium. As the cycle progresses (Figs. 2, 3, and 4, which represents...
15-, 24-, and 27-day specimens, respectively) pronounced activity is extended basalward in the glandular epithelium. Thus by the end of the cycle the entire glandular cell layer becomes sharply delineated by heavy precipitation of the indicating salts, though

Fig. 2. Fifteen-day endometrium showing activity of entire cytoplasm of glandular epithelium. (× 65)

Fig. 3. Twenty-four-day endometrium, showing very reactive glandular epithelium. (× 65)

Fig. 4. Twenty-seven-day endometrium, showing very reactive glandular epithelium. The stroma also shows increased activity. (× 65)

Fig. 5. Decidua at 9 weeks, showing reactive glandular epithelium and some activity in decidua cells. (× 65)
the free border still retains the initial higher activity.

There is appreciable stromal activity, which seems confined to cell membranes, as cytoplasm or nuclei are seldom noted. There

![Image 6. Chorionic villi at 8 weeks, showing very reactive trophoblast. (X 65)](image)

![Image 7. Atrophic endometrium 1 year postmenopause, showing very little activity. (X 65)](image)

![Image 8. Endometrial hyperplasia showing activity in glands confined to luminal border. (X 65)](image)

![Image 9. Endometrium of patient with functional uterine bleeding and Stein syndrome, showing activity of glands confined to luminal border with more prominent activity in stroma. (X 65)](image)
ENDOMETRIAL ACID PHOSPHATASE

seems to be some increase in activity premenstrually.

As can be seen in Fig. 4, blood vessels are relatively inactive.

Pregnancy

The endometrium in pregnancy shows considerable acid phosphatase activity (Fig. 5). The glandular epithelium in the basalis and just above is quite active but tends to diminish in activity in the compact zone bordering the uterine cavity. The decidual cells show much more activity than the stromal cells of the normal cycle and suggests an intensification of the activity noted premenstrually.

The trophoblastic layer of the chorionic villi is very active. Its activity is probably at least as great as the greatest activity of endometrial glandular epithelium encountered, and seems to be present in the luminal border as well as in the basal regions of the trophoblast. As may be seen in Fig. 6, some of the cells in the stroma are quite active.

Atrophic Endometrium

This presents by far the weakest reaction encountered (Fig. 7). Both glands and stroma are quite inert.

Endometrial Hyperplasia

In this condition (Fig. 8) the glands react as they do in the early part of the cycle (see Fig. 1). There is primarily luminal border activity. The stroma appears moderately active.

Stein Syndrome with Functional Bleeding

The endometrium from this anovulatory patient resembles the activity found in the early part of the cycle (Fig. 9). The stroma may be more active than in the normal cycle or in uncomplicated hyperplasia.

Estrogen Therapy

Endometrium was available from a patient who had been treated for over 2 years with high-dosage estrogen for carcinoma of the breast (Fig. 10). There was luminal
border activity of the glands and moderate stromal activity.

Adenocarcinoma of the Fundus Uteri

In the 2 cases observed the activity was only moderate in amount and again confined to the luminal regions (Fig. 11). Unlike the physiologic states where this same distribution was noted, the activity was not confined so precisely to the luminal border but appeared in rather coarse masses in the general region of the lumen of the glands. The scant stroma is only moderately active.

DISCUSSION

Acid phosphatase activity appears to fluctuate in the endometrium in a cyclic manner related to the ovarian steroid pattern. In the absence of ovarian steroid hormones the atrophic endometrium shows little or no reaction in either glands or stroma. During the preovulatory phase in the menstrual cycle the brush borders of the endometrial glands react but the cells are otherwise unreactive as are the stromal cells. Indicative that this is typical of estrogenic stimulation is the observation of similar findings in a case of endometrial hyperplasia as well as the endometrium of a patient who had received large amounts of estrogen. As progesterone begins to dominate the cycle, acid phosphatase appears in heavier concentrations in the glandular and stromal cells, being greatest in the premenstrual phase. The decidual cells in pregnancy are extremely rich in the enzyme, as are both the syncytial and Langhans cells of the cytotrophoblast. In the cases of endometrial carcinoma the reaction resembled an estrogenic effect in that the acid phosphatase was present in a minimal amount, and was found in the brush borders of the cells.

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Postoperative Staphylococcic Enterocolitis After Antibiotic Therapy

Shock and oliguria after hysterectomy; report of a case with recovery

JOHN A. WALL, M.D., and JOHN ROGER KELSEY, JR., M.D.

During the past few years there has been considerable interest in the incidence of micrococcic enterocolitis and, consequently, much speculation about possible etiologic factors. Some investigators have suggested that the pathogenesis of the lesion is in some way related to the use of antibiotic agents. Surgeons are especially concerned with the frequent reports of micrococcic enterocolitis as a fatal complication in postoperative patients. Although the lesion is relatively rare as a complication after surgery, the mortality rate among patients who develop shock secondary to micrococcic enterocolitis has been comparatively high. Speare recently reviewed from the literature 22 cases, in which there were 5 deaths. Most of these patients were postoperative and all had received antibiotic therapy. The purpose of this paper is to report a case of micrococcic enterocolitis which developed after hysterectomy, complicated by shock and oliguria, in which there was complete recovery.

CASE REPORT

K. S., 45 years of age, over a period of four years had recurrent episodes of suprapubic and bilateral lower-quadrant soreness and pain, associated with high fever. The patient received 300,000 units of penicillin in oil on January 30, 1954, and no further antibiotic therapy except that which is detailed below was ever administered. The latest period of suprapubic pain had begun three days before her visit on April 30, 1955.

Pelvic Findings and Therapy

The results of physical examination were normal except for the pelvic findings. There was typical pelvic inflammatory disease with bilateral tubo-ovarian masses filling the cul-de-sac and extending to the pelvic walls on each side. A smear of the purulent material from the cervix showed gram negative intracellular diplococci. Hospitalization was advised and 300,000 units of penicillin with 0.5 Gm. of streptomycin twice daily were administered over a 5-day period. After discharge on May 4, 1955, the patient received tetracycline, 250 mg. orally 4 times a day for 5 days. Ferrous sulfate, 0.3 Gm., was administered 3 times daily.

Surgery

The patient was admitted to the hospital on May 24, 1955, 15 days after discontinuation of all antibiotic therapy. A total abdominal hysterectomy and bilateral salpingo-oophorectomy and appendectomy were performed for bilateral purulent hydrosalpinx with small abscesses in the pelvis. After exposure of the mass in the pelvis, aspiration of the purulent hydrosalpinx was performed under sterile precautions. Beta-Staphylococcus aureus and gamma-strepto-
coccus were subsequently reported in cultures of the purulent tubal contents.

Postoperative Course

Convalescence was apparently uneventful and no antibiotic was given postoperatively. The patient was taking a soft diet and was able to go to the bathroom on her second postoperative day. Seventy-two hours after the operation there was a rather sudden onset of lower abdominal pain, nausea, vomiting, and severe watery diarrhea. The pulse rate was 150 and respiration 30. A shock syndrome was apparent and was associated with a rising temperature. The blood pressure fell to about 80 mm Hg systolic and 40 diastolic, and respiration increased to 60 plus per minute. The abdomen remained soft. The clinical appearance was that of a severe "food poisoning." Gram stain of fetal smears showed a great predominance of staphylococci.

DIAGNOSIS AND THERAPY. A presumptive diagnosis of staphylococcal enterocolitis was made. Erythromycin and Hydro-Cortone were given intravenously and Chloromycetin intramuscularly. The patient was isolated and Wyamine and intravenous fluids were given to control the shock symptoms. Medications during the course of this illness are tabulated in Fig. 1. In the 12-hour period after the erythromycin, Chloromycetin, and cortisone therapy was instituted, the patient became afebrile and blood pressure returned to a normal level. Wyamine was discontinued. Oliguria developed shortly after the onset of shock and persisted for several days. The total output of urine varied from 175 cc. to 300 cc. per day until the eighth postoperative day, when diuresis was established. There was adequate fluid intake by mouth, and the patient was able to be up and about. Mild diarrhea continued but was controlled by bismuth and paregoric. On the sixth postoperative day the antibiotics were discontinued and the patient was started on Lactinex tablets. She was discharged on the twelfth postoperative day, and the convalescence from that time was uneventful.

DISCUSSION

The first description of the enterocolitic syndrome was reported by Finney in 1893. This occurred in a patient who had successfully survived a gastroenterostomy but died on the fifteenth postoperative day of "diphtheritic colitis." Additional reports of pseudomembranous enterocolitis appeared in the literature before the advent of the antibiotic drug to which the staphylococci were sensitive.
drugs. There has been some controversy as to whether these early cases of pseudomembranous enterocolitis are identical to the instances reported since the use of antibiotics. Penner and Duckerman have described 9 cases, 8 of which occurred postoperatively. In a summation of their necropsy findings, the authors concluded that this process was secondary to an intense compensatory vasospastic phenomenon which occurred during shock. Dixon and Weisman were unable clinically to confirm the hypothesis of circulatory deficiency, because the interval which occurred between the state of severe shock and death was, in their experience, too brief to allow extensive development of pseudomembranous lesions.

Kleckner, Bargen, and Baggenstoss reported fourteen cases of pseudomembranous enterocolitis in which the onset of the disease was not preceded by operation. In 7 of these cases, enterocolitis was thought to be the primary cause of death. Further, in their opinion, neoplastic obstruction of the large intestine, and the existence of infection were contributory to development of this process. These investigators concluded that antibiotic therapy was not implicated in this disease, since the incidence before and after the era of antibiotic therapy was essentially the same.

Dixon and Weisman's experiences in postoperative cases did not confirm this impression. From their findings it appears that during the period from 1940 to 1947 covered in their study, there was a concomitant increase both in the use of antibiotics and in incidence of pseudomembranous enterocolitis.

Alteration of Normal Bacterial Balance

The normal antagonism between microorganisms is commonly maintained in a precarious balance, and antibiotics are known to disturb the normal bacterial flora of the intestines. Smith, in a classical presentation in 1952, described the disorganization of normal bacterial flora which occurs after administration of the newer antibiotics. Dearing and Heilman, in 1953, described micrococcic enteritis as a complication which occurs after antibiotic therapy and reported clinical observations on 44 patients. They found that despite intensive antibiotic preoperative preparation of the colon, pure cultures of microorganisms could be obtained from the surgical material in some patients. In these patients gastrointestinal symptoms could be prevented by administration of erythromycin. Another group in which large numbers of micrococi were found developed severe gastrointestinal and systemic reactions that were responsive to erythromycin therapy. Seven patients who developed pseudomembranous enterocolitis and did not receive erythromycin died. Oettingen comments in an excellent review that severe gastrointestinal disturbances from superinfections have resulted from all antibiotics, most frequently from the use of chlortetracycline, oxytetracycline, and chloramphenicol. Death has resulted not only from micrococcic superinfections but from Candida albicans and other candidal organisms.

Etiology

It appears that an overwhelming superinfection may occur in the intestinal tract as a result of a number of agents that affect the bacterial flora. Probably the most common of these agents are broad-spectrum antibiotics. Other possible etiologic factors which may influence development of this syndrome are alterations in bowel function, such as occur in obstruction, and the effects of irradiation. In addition, some undetermined effects of surgical procedures may be contributory.

Staphylococci in Oviducts

There is little in the literature pertaining to bacteriologic studies from purulent material in hydrosalpinges. It is of particular
interest that staphylococci were isolated from the pyosalpinx in this patient. Purulent material obtained from a pyosalpinx is usually sterile, and certainly a predominance of staphylococci is an unusual occurrence. This finding may be indicative of the presence of a staphylococcal septicemia at the time of surgery. It is also of interest that this patient had a normal convalescence until midnight of the second postoperative day, 16 days after cessation of antibiotic therapy. To our knowledge, this is the only reported instance of development of the syndrome so long after discontinuation of antibiotics.

Mode of Infection and Prophylaxis

Patients are known to harbor antibiotic-resistant staphylococci in the nasopharynx for protracted periods. The fact that this syndrome developed two weeks after cessation of antibiotic therapy suggests that the patient may have secreted staphylococci within the nasopharynx. The antibiotics administered preoperatively may have caused the patient to become a "carrier." Other factors to be considered are cross-infections from other patients who also may be "carriers," and use of clean but not aseptic anesthetic masks. Materials used for intubating the airway of the patient may also have served as a source of contamination, with trauma sufficient to allow invasion with antibiotic-resistant staphylococci. Theoretically, the surgical procedure could have helped to precipitate this syndrome. Consequently, a culture of the stool before surgery would have demonstrated the abnormally high count of microorganisms present. This information would have afforded indications for prophylactic administration of the proper antibiotics during the postoperative period.

Superinfection

This syndrome has been compared with the clinical entity which occurs in staphylococcal food poisoning. In simple food poisoning, there is only one dose of enterotoxin produced by the micrococci present in the food. Although large numbers of the micrococci are ingested along with the toxin, the organisms apparently do not multiply and produce more enterotoxin in the intestinal tract. However, in micrococcic enterocolitis that occurs after antibiotic therapy, the possible suppression of normal flora by the drugs may permit development of an "antibiotic-resistant food poisoning strain of micrococcus." Obviously, under these conditions, the production of enterotoxin could be continuously perpetuated within the host, often with fatal results.

CONCLUSIONS

From a review of the literature and observation of this particular patient a number of conclusions have been reached regarding diagnosis and management of patients who develop this syndrome. The systemic reactions that develop during a supervening micrococcic enterocolitis are potentially fatal and should be regarded as a possible complication in any patient who receives sulfonamide drugs, streptomycin, or compounds of the tetracycline group (Aureomycin, Terramycin, Achromycin, etc.). The features of this case have suggested to the authors some possible preventive and emergency measures to reduce morbidity and mortality in similar instances.

1. The development of diarrhea after administration of antibiotics, either with or without surgery, should be carefully observed and studied for the onset of shock symptoms. Any patient with preoperative antibiotic therapy should have a fecal smear, and possibly a study of the nasopharynx to determine the presence of staphylococci before operation is undertaken. Surgery should be postponed in cases in which there is a predominance of these organisms; or, in instances in which immediate surgery is mandatory, the proper antibiotic therapy should be instituted before or immediately after operation.

2. The syndrome should be considered in all patients who receive any antibiotic therapy, particularly those in whom an "antibiotic-resistant strain of micrococcus" is found.

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11. The syndrome should be considered in all patients who receive any antibiotic therapy, particularly those in whom an "antibiotic-resistant strain of micrococcus" is found.
ENTEROCOLITIS FOLLOWING ANTIBIOTICS

2. The possibility of cross-infection should be considered and isolation technic should be employed when this syndrome is recognized.

3. The possibility of this complication should be suspected in any patient who has received antibiotics. Fecal smears should be examined immediately, and if gram-positive micrococci are found the empirical use of parenteral injections of erythromycin and chloromycetin must be instituted immediately. Then, sensitivity tests can be made and the appropriate antibiotic can be given.

4. Combating the shock by use of pressor drugs, such as Wyamine or Levophed, and by parenteral fluid adjustments is an integral part of the emergency care.

5. The onset of oliguria or anuria must be anticipated so that accurate fluid intake and output determination may be begun immediately and preparation made to restore fluid balance.

6. The adrenocortical steroids are important in the treatment of patients with this syndrome, as some of the toxic effects can be alleviated by their use.

7. Recognition and study of the syndrome are especially important in order to establish whether there are actually two different groups of cases presenting the same clinicopathologic appearance, but with different etiologies. Intensive study of the case when this complication occurs may reveal the factor or combination of precipitating factors.

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Spontaneous Rupture of the Liver in Asfibrinogenemia During Pregnancy

Report of a case

ARMAND J. PEREYRA, M.D., and MATTHEW P. LAWLER, M.D.

Spontaneous rupture of the liver is a surgical emergency requiring early recognition and prompt treatment. Its occurrence during pregnancy is a very rare and grave complication. The 14 previously reported cases associate the condition with varying degrees of toxemia, mostly in the third trimester. The object of this paper is to present a case of spontaneous rupture of the liver in pregnancy following afibrinogenemia preceded by toxemia and abruptio placentae.

The etiology of spontaneous rupture of the liver in pregnancy is not known. That the liver is particularly susceptible to pathologic changes in certain complications of pregnancy is recognized. Rademaker postulated that high blood pressure plus sudden muscular effort may cause rupture of the hepatic blood vessels rendered pathologic by toxemia. Burton-Brown and Shephard felt that trauma to the liver could result from violent contraction of the diaphragm and abdominal muscles during labor. Haller et al. considered that the strain occurring with convulsions in toxemia could be traumatic to the liver. Sanes and Kaminiski suggested that the strain in moving the patient, pressure of any type on the abdomen, and the increased intra-abdominal tension occurring with vomiting in labor might prove sufficient to cause subcapsular hemorrhage and rupture of the liver in a patient with a pathologic organ. Speert and Tillman state that the combination of hypertension, convulsions, and vomiting is apparently adequate to raise the intra-abdominal pressure to the point of rupture of Glisson's capsule by a hematoma resulting from lesions of toxemia in the liver. Kramish et al., in presenting 1 case, reviewed the 13 reported spontaneous ruptures in pregnancy, only 4 of which were at term. In 10 of these cases eclamptic lesions constituted the primary cause of subcapsular hemorrhage and capsular rupture. In the case of Kramish et al. the rupture occurred without premonitory trauma or preeclamptic symptoms and following a normal term delivery.

CASE REPORT

Mrs. A. M., a 34-year-old white para 8-2-5-4, was admitted to the U.S. Naval Hospital, Corona, at 4:00 A.M. on October 16, 1953, in active labor after a 50-mile auto ride. She gave a history of regular contractions and lower-back pain beginning at 2:30 A.M. on that date. Her last menstrual period occurred on February 9, 1953, and the estimated date of confinement was November 16, 1953.

Prenatal Course

The prenatal course was uneventful except for a moderate unsustained hypertension first recorded at 132/82 in June, 1953, with a maximum of 142/96 in July. Her total weight gain was 552 lbs. Kahl, Kalk, and Pascale reviewed the blood chemistry on October 16 and 17, 1953, and hospital records revealed an enlarged uterus, 15 weeks' size, with some heartburn. General physical examination revealed a healthy, well-nourished woman.
LIVER RUPTURE IN AFIBRINOGENEMIA IN PREGNANCY

gain was 10 pounds. She was Rh positive, Kahn negative, and repeated urine examinations were negative for albumin throughout. Blood counts were within normal limits. On October 11, 1953, she was admitted to the hospital in false labor and was discharged after an 8-hour period of observation. The fetal heart was active at the time of discharge, the head was floating, the membranes were intact, and there was no dilatation of the cervix.

Past History

The past history revealed 2 early spontaneous abortions, followed by 5 pregnancies carried to term, the last one terminated by cesarean section in 1951, at which time she was delivered of a hydrocephalic infant that subsequently died. Except for pneumonia at 5 years of age, there had been no serious illnesses and no other surgery.

Examination on Admission

Examination at the time of the present admission revealed strong uterine contractions occurring every 5 minutes. Neither vaginal discharge nor bleeding was present, and the membranes were intact. The fetal heart could not be heard. The vertex was presenting at a minus 1 station. The cervix was 50 per cent effaced and showed a 2-cm. dilation. The blood pressure was 150/100. A catheterized urine showed a 3 plus albuminuria.

The patient was given 8 cc. of a 50% solution of magnesium sulfate intramuscularly. At 6:00 A.M., tetanic, boardlike contractions of the uterus became evident. A catheterized urine revealed gross hematuria. Irrigation of the bladder with saline solution did not support the possibility of uterine rupture into the bladder, and surgical intervention was deferred.

Blood-clotting Tests

At this time, ecchymoses were noticed on the skin of the abdomen at the site of application of the fetoscope. A sample of venous blood was obtained and was observed for clot formation in a test tube, according to the method described by Weiner et al. No clot formed and the blood remained completely fluid after 30 minutes. Blood was drawn for type and cross-matching. A second specimen of blood taken 1 hour later again failed to show any clot formation in the test tube after one hour of observation. Additional areas of ecchymosis were noted on the skin of the upper extremities. No laboratory facilities were available for determining the fibrinogen level of the blood. Prothrombin time (Lee-White method) was 5 minutes, with a control of 14 seconds.

Diagnosis

A presumptive diagnosis of severe abruption of the placenta with hemorrhage and afibrinogenemia was made, and the patient was transferred to the operating room for pelvic examination and possible rupture of the membranes.

Surgical Procedures and Findings

In the operating room, the patient suddenly went into deep shock, the pulse became weak and rapid, and the blood pressure was not obtainable. Abdominal examination revealed evidence of intra-abdominal fluid with distention in the epigastrium. Transfusion with citrated blood, which was started on arrival in the operating room, was speeded into the veins in each arm, and an emergency laparotomy under local anesthesia was performed on the assumption that uterine rupture and hemorrhage had occurred.

On opening the abdomen, a large amount of unclotted blood was encountered in the peritoneal cavity. The uterus showed a large intramural hemorrhage and discoloration on the left anterior wall. The pelvic organs otherwise were pale, and no source of active bleeding could be demonstrated, although a small rent in the serosa covering the left lower lateral uterine wall and extending into the broad ligament was observed below the uterine hematoma.

The uterus was opened through a classical incision and a moderate amount of unclotted blood was released. A stillborn near-term female infant was delivered. Because of the intramural hemorrhage and incontractility of the uterus, a subtotal hysterectomy was performed. The rent into the left broad ligament was repaired. The bladder wall was examined and found to be intact. The critical condition of the patient did not permit further exploration of the abdomen and the abdominal wall was closed.

Postoperative Course

Following surgery the patient rallied, and the blood pressure rose to 110/70, the pulse remaining rapid but fuller. She was given re-
peated fresh, whole-blood, direct transfusions as rapidly as donors could be obtained. Levophed* was administered by intravenous drip and oxygen was given by nasal catheter. Abdominal distention again became evident at 5:00 P.M. and the patient had difficulty in breathing. An opening was made at the lower end of the abdominal wound by releasing sutures and a considerable amount of dark unclotted blood drained from the abdomen. Blood drawn at 7:00 P.M. revealed a clotting time of 8 minutes, a hematocrit of 18, and a prothrombin time of 32 seconds, with control of 18 seconds. An anuria developed and persisted throughout the postoperative period. Efforts to obtain fibrinogen proved unavailing. Fresh-blood transfusions and supportive therapy were continued but the patient lost ground gradually and died at 9:45 p.m. on the day of admission. A total of 18 pints of blood were transfused into the patient.

**Postmortem Examination**

Postmortem examination revealed massive intra-abdominal hemorrhage and a large subcapsular hematoma (15 × 17 × 4 cm.) of the liver, with a tear and separation of Glisson's capsule on the diaphragmatic surface. The pathologic diagnoses were:

1. Intra-abdominal hemorrhage, massive, recent
2. Subcapsular hematoma of liver, massive, recent
3. Congestion of lungs with edema
4. Pleural effusion, bilateral
5. Surgical absence of uterus, recent
6. Focal fibrosis of cervical stump
7. Subcaliceal hemorrhage of kidneys

**DISCUSSION**

Rupture of the liver in the absence of trauma is an extremely rare accident in pregnancy. Its occurrence in association with afibrinogenemia has not been reported previously. In all cases, toxemia of pregnancy, varying in degree from subclinical to eclamptic, has established the background for rupture.

In the case reported here, events occurred in the following sequence: The patient had a mild toxemia which, except for a transient hypertension, did not become manifest until the onset of labor. Severe abruption of the placenta with intrauterine hemorrhage and death of the fetus happened early in labor. With escape of blood from the uterus prevented by intact membranes and a closed cervix, intrauterine pressure mounted, forcing thromboplastic material from the uterus into the maternal circulation. Evidence of bleeding into the body tissues generally became manifest and the incoagulability of the blood was demonstrated to establish a state of afibrinogenemia. Intrahepatic bleeding occurred as a part of this hemorrhagic disease and proceeded to the point of rupture of the liver capsule. Massive hemoperitoneum, shock, and death followed.

**Factors in Placental Abruption and Rupture of Liver**

Two extrinsic factors may have contributed to this course of events: First, the long, hurried auto ride to the hospital while the patient was in active labor. Secondly, the strain of transferring the patient to the operating table. The effects of these incidents on placental detachment and rupture of the liver respectively is conjectural, yet they cannot be dismissed in view of the pathologic condition of these organs which rendered them increasingly susceptible to injury by any ordinary trauma.

**Persistence of Bleeding**

Eclamptic lesions could not be demonstrated in the liver, and the bleeding here and throughout the body is attributed to the afibrinogenemia, which was unmodified by removal of the pathologic uterus and was improved only slightly and transiently by the multiple blood transfusions. Shock and exsanguination dominated the picture throughout and were the cause of death in this patient.

**Diagnostic Considerations**

The most important factor in the diagnosis of spontaneous rupture of the liver is an awareness of the possibility of this accident.
occurring in toxemia of pregnancy. Kramer et al. have described severe right costal and epigastric pain radiating to the shoulder as characteristic in this condition. In the case reported by them in which rupture and hemorrhage followed delivery, these symptoms were prominent. However, in the presence of an enlarged gravid uterus undergoing painful contractions, such symptoms are too unobtrusive to direct attention to the hepatic involvement. The difficulty of clinical diagnosis is attested by the fact that none of the cases reported in the literature was diagnosed prior to surgery or autopsy. Because of the toxemia present in each case and the prominence of the pregnant uterus in the picture, this organ invariably has been implicated in a clinical consideration of the cause of the ensuing intra-abdominal hemorrhage.

In the present case, the afibrinogenemia with generalized bleeding, the severe abruptio placentae with intramural and intruterine hemorrhage, and the tear into the broad ligament explained the hemoperitoneum to the operator. The incision made in the lower abdomen to permit emptying and removal of a known pathologic uterus did not allow visualization of the torn liver. In consequence of the shock and the lowered blood pressure, surgery was carried out with the patient in Trendelenburg position, and whatever bleeding from the liver occurred during the operation in this position and state of circulatory collapse escaped observation. In the final analysis, a lack of anticipation of this disastrous complication was the primary factor in overlooking the rupture of the liver.

Availability of Fibrinogen

The afibrinogenemia developed in this patient was severe and uncontrollable with transfusions of blood alone. The development of afibrinogenemia is attributed to the placental detachment and massive intrauterine hemorrhage. The mechanism whereby the afibrinogenemia, or the toxemia preceding it, produced liver damage and rupture is uncertain. Whether the hepatic hemorrhage could have been controlled with fibrinogen remains open to question. Had this been obtainable and coagulability of the blood been restored, it is probable that further surgical exploration would have been attempted. The importance of having fibrinogen immediately available for the treatment of this condition cannot be overstressed.*

Justification of Surgery

It is generally recognized that surgery in the presence of an uncontrolled afibrinogenemia is contraindicated. However, under the conditions presented in this case and the preoperative findings suggesting a ruptured uterus with hemorrhage, surgery appeared justified. The operation performed is not considered to have influenced the fatal outcome except for the failure to recognize and repair the torn liver. Even had this damage to the liver been noted, it is questionable whether the critical condition of the patient at the time of surgery would have permitted the further operative procedure required.

Treatment of Ruptured Liver

The treatment of rupture of the liver begins with an awareness of the possible development of this complication, particularly in late pregnancy with toxemia. Active treatment is surgical and includes the use of fascial strip sutures, Oxycel or fibrin-foam packs, incorporation of omental or muscle tissue in the tear for hemostasis, and electrocoagulation. Surgery, however, should not be undertaken until shock is overcome and normal clotting of the blood is restored.

* Since the occurrence of the case presented here, 3 other pregnant patients with afibrinogenemia, proved by laboratory test, but without rupture of the liver, have been admitted to this hospital and treated successfully with fibrinogen supplied by the American National Red Cross. This gives an incidence of 4 cases in 9876 deliveries in the past 34 months since the opening of the U. S. Naval Hospital, Corona, to maternity patients.
SUMMARY AND CONCLUSIONS

1. A case has been reported of spontaneous rupture of the liver during labor at term in a patient with afibrinogenemia.

2. The literature has been reviewed, and the conditions producing pathologic changes and susceptibility to rupture of the liver in pregnancy have been discussed.

3. The difficulty in making the diagnosis and the circumstances tending to obscure this site of hemorrhage at surgery in the case presented have been brought out. The most important safeguard for the obstetrician is an awareness of the possible development of this rare but grave complication, whenever afibrinogenemia or toxemia occurs in late pregnancy.

4. It is well to recognize that, while the advent of fibrinogen has greatly enhanced the possibility of saving patients developing afibrinogenemia, certain other complications such as acute renal failure, central nervous system damage, and rupture of the liver with hemorrhage may result from this condition.

REFERENCES


The Mechanics of birth brings into a relationship the force of labor, the uterine contents, and the birth canal. The process of birth is explained by applying mechanical laws, and in this consideration we will exclude any teleologic thinking such as giving the birth act primary consideration as a physiologic process. In the following discussion we shall attempt to show the relationship of the mechanics of birth to secondary pathologic changes of the birth canal.

We have to keep in mind that the reaction of the tissues of the birth canal during the process of delivery cannot be explained on only a mechanical basis. During the first and second stages of labor, however, the action of the fetus on these tissues has a direct influence in possible resulting pathologic changes.

Cervical Lacerations

Cervical lacerations are reported to occur during labor in 15–90 per cent of all cases.* The difference in incidence is due to different material used in these studies as well as the various classifications of lacerations which are applied. It is interesting that the percentage of cervical damage is not higher with larger fetuses, but it is higher in cases of prolonged labor, in older age groups,®:7 and in occipit-posterior positions.

The cervix, the pelvis, and the presenting fetal part under labor force have to be considered in an attempt to explain the etiology of cervical lacerations.

The Cervix

With the exception of the isthmic part the histologic structure of the cervix is composed predominantly of fibrous connective tissue. Smooth-muscle elements constitute 10–15 per cent of the cervical tissue, and elastic connective tissue fibers constitute less than 1 per cent. During pregnancy hypertrophy and hyperplasia of fibrous connective tissue and muscle bundles take place.3

From the above investigations we can assume that the histologic structure of the cervix is uniform regardless of the exact percentage of the different structural elements. We also assume that changes of the cervical tissue during pregnancy will thus alter the cervix uniformly.

The main factors contributing to the suspension of the cervix are the cardinal and uterosacral ligaments. The insertion of these ligaments is above the portio vaginalis of the cervix. During pregnancy softening of these ligaments occurs. Although the suspension of the cervix is effective during the first stage of labor, and is probably important during the retraction of the dilated cervix over the presenting fetal part, the dilatation of the cervix itself is not influenced by its suspension.

In the upright position the weight of the

From the Allentown Hospital, Allentown, Pa.
fetus causes pressure on the cervix. Labor force acts on the fetus, transmitting pressure on the cervix in an axial line extending through the fetus from the fundus to the midpoint of the presenting part at the cervix. During the phase of cervical dilatation, the axial pressure may be thought of as radial vectors originating from the midpoint of the presenting part and acting on the cervix laterally. When rotation of the vertex occurs another component of the axial force is dissipated in direction of rotation of the vertex. The important direction of pressure in regard to cervical lacerations is the radial or diametral pressure. It is useful to consider each cervix as having a certain tolerance to force. The cervical tissue is subjected to this force during the first and second stages of labor. Ischemia and edema of the cervix will lower its tolerance to force.

The cervix must be considered to be a passive factor during labor.

The Pelvis

The bony pelvis with its muscular coat, the lower uterine segment, the cervix, and vagina, and vulva form the birth canal. The fetus passes through this canal by a maneuver which can be explained on a mechanical basis, the factors being the labor force exerted on the fetus, the shape of the pelvis, and the flexibility (Biegungsfacililum, Biegungsdifiicillium) of the fetal spine. The first step on entering the birth canal is the engagement of the presenting part. It has been shown that the occiput-posterior position occurs more frequently in the pelvises of the android and anthropoid types. As will be seen later this position with the associated extension of the fetal head is interesting in considering the etiology of cervical lacerations. The shape of the pelvis and its muscle coat is partially the cause for rotation of the presenting fetal part under the force of labor. In cases of cephalopelvic disproportion a prolonged first and a second stage of labor will result.

Thus, on the basis of malflexion or malrotation of the presenting part, we consider the pelvis to have an indirect influence in causing cervical lacerations.

The Presenting Fetal Part Under Labor Force

Labor force acts on the cervix either by the pressure exerted by the amniotic sac or the pressure exerted by the presenting fetal part. The following discussion on the mechanism of cervical dilatation is based on the premise that the membranes have ruptured and the fetus presents as a vertex.

If during the first stage of labor normal flexion of the fetal head takes place the widest planum which passes the cervix is the planum suboccipito-bregmaticum. This plane, having an average circumference of 32 cm., is practically circular. If we consider the fetal head to be a body of uniform consistency a uniform pressure will be exerted upon the cervical tissue transmitting the labor force of the uterine musculature. Pressure on the cervix causes a force in the cervical tissue. Since the pressure is equal along each radius (i.e., \( r_1 - r_2 \)) of a circular plane the resulting forces \( \left( F_1 - F_2 \right) \) in the cervical tissues must be uniform. The greatest force on the cervix will be exerted when the widest plane passes the cervical brim.

Different circumstances exist when any degree of deflexion is present. Deflexion in this consideration means that the widest plane which has to pass the cervix is larger than in a normally flexed vertex presentation and its circular plane. We will consider here the occiput-anterior presentation the first degree of deflexion. The circumference of the widest plane in this presentation (planum fronto-occipitale) has an average measurement of 34 cm. This larger circumference is due to an enlarged anteroposterior diameter; the biparietal diameter remains the same as in a normal vertex presentation. The average anteroposterior diameter of the planum
CERVICAL AND PERINEAL LACERATIONS

fronto-occipitale measures 11.5 cm.; the bipparietal diameter has an average length of 9.2 cm. The planum fronto-occipitale, therefore, has an elliptoid shape (Fig. 2). When the widest plane in a deflexion passes the cervical brim the pressure exerted by this plane will not be uniform and neither will the forces be uniform which result in the cervical tissue. Figure 2 shows that the force \( F_1 \), is greater than the force \( F_2 \). The higher incidence of cervical laceration in occiput-posterior position can be explained on this basis. This position is nearly always found to have some degree of deflexion. The widest plane which has to pass the cervix is ovoid. The effect of such a plane on the cervix is explained in Fig. 2.

\[
\begin{align*}
F_1 &= 2pr_1 \\
F_2 &= 2pr_2 \\
F_1 : F_2 &= r_1 : r_2 \\
p &= \text{pressure} \\
r_1, r_2 &= \text{radii} \\
F_1, F_2 &= \text{forces per unit width of cervical tissue}
\end{align*}
\]

\[
\begin{align*}
F_1 &= pd_2w \\
F_2 &= pd_1w \\
F_1 : F_2 &= d_2 : d_1 \\
p &= \text{pressure} \\
d_1 &= \text{biparietal diameter} \\
d_2 &= \text{antero-posterior diameter} \\
w &= \text{unit per width of cervical tissue}
\end{align*}
\]

**Fig. 1.** Labor force in normal flexion.

**Fig. 2.** Labor force in deflexion (occiput-posterior position).

LACERATIONS OF THE VULVA AND PERINEUM

The factors which one has to consider in an attempt to explain the etiology of vulvar and perineal lacerations are in principle the same as those in cervical lacerations. The anatomy of the outlet of the birth canal does not allow us to assume that there is a uni-
form histologic structure. The outlet of the birth canal is composed anteriorly of the commissure of the labia minora, laterally by the labia minora and majora, and posteriorly of the commissure of the labia majora. It is obvious that these tissues have no uniform tolerance for force. The perineum with its centrum tendineum is composed of different tissue elements. During pregnancy these tissues undergo changes leading to a greater distensibility.

We shall now consider the delivery of a fetal head in the occiput-anterior position.

In this position the head reaches its maximal degree of flexion upon reaching the pelvic floor. Labor force is transmitted along the fetal spine, the head exerting pressure against the pelvic floor. When the occiput has reached the symphysis, extension of the head begins. The pressure acting at this moment is exerted along the pelvic curve and transmitted through the fetal head against the perineum. The second component is the diametral pressure exerted on the vulva by the fetal head, effective in a similar way to that in cervical dilatation. A frictional force is caused by the extension of the fetal head in the tissues of the perineum and the posterior commissure of the vulva. This frictional force is probably negligible because of the lubrication of the birth canal by amniotic fluid and the vernix caseosa.

It is stated that in a normal vertex presentation the planum suboccipito-bregmaticum is the widest plane which has to pass the outlet of the birth canal. This would be true if we consider the outlet to be a plane limited anteriorly by a line somewhere at the symphysis, laterally by the corresponding vaginal tissue, and posteriorly by the commissure of the labia majora. This assumption, however, is not correct. The anterior limit of the outlet of the birth canal is the commissure of the labia minora, the others being as mentioned before. The suboccipital area, acting as a fulcrum, causes extension of the fetal head; thus the fronto-occipital plane or the occipito-mental plane must be the greatest plane to pass the vulva during birth. These planes are elliptoid in shape. The forces which exist in the perineal tissue and at the posterior commissure of the labia majora at a certain stage of birth of the fetal head in the occiput-anterior position are demonstrated in Fig. 3. An addition of forces takes place at the posterior commissure.
CERVICAL AND PERINEAL LACERATIONS

sure of the vulva ($F_3$): the vectors being caused by the pressure of an elliptoid-shaped plane as the fetal head passes the vulva outlet ($a$) are added to the force vectors resulting from pressure exerted by the fetal head on the perineum and the posterior commissure of the vulva at the same moment ($y$). This is caused by relative fixation of the occiput in relation to the symphysis. The force which exists at the posterior commissure of the vulva will under these conditions always be considerably higher than at other places at the outlet of the birth canal. Thus a tear will occur wherever the tolerance limit for force in any one of the tissue parts is exhausted. From this it can be explained why most tears occur posteriorly.

**SUMMARY**

An attempt has been made to explain the etiology of lacerations of the cervix, vulva, and perineum during birth in vertex presentations, considering only the mechanics of birth.

The pressure components effective on the birth canal were discussed.

It was shown that the resulting forces and the distribution on the tissue of the cervix, vulva, and perineum have a direct relation to the size and shape of the presenting fetal part.

**REFERENCES**

Primary Ovarian Pregnancy

Report of a case

DAVID M. FARELL, M.D., and JEROME ABRAMS, M.D.

The first observation of a primary ovarian pregnancy seems to be that of Saint Maurice of Perigord, France, in 1682. Saint Maurice's patient was a para 9-0-0-8 who died after several hours of severe right lower quadrant pain. Autopsy revealed the peritoneal cavity filled with blood and a 2-month-old fetus somewhat free and unattached; the "right ovary was torn longwise" while the left ovary, the uterus, and both tubes were intact. Although subsequently there were published several reports of ovarian pregnancy, it was not until 1878, when Spiegelberg published his four criteria for ovarian pregnancy, that the majority of the medical profession began to look upon primary ovarian pregnancy as a pathologic entity. The Spiegelberg criteria, which it is generally agreed must be met in each case of primary ovarian pregnancy, are as follows:
1. The tube on the affected side must be intact and separate from the ovary.
2. The gestation sac must occupy the position of the ovary.
3. The sac must be connected with the uterus by the ovarian ligament.
4. Ovarian tissue must be demonstrable in the wall of the sac.

REVIEW OF THE LITERATURE

In 1932 Wollner reviewed the world's literature and discovered that only 48 out of 87 reported cases could be authenticated. Strother-Stewart estimated that there were at least 125 cases in the English literature alone in 1953. Baden and Heins reviewed approximately 90 of the reported cases of primary ovarian pregnancy; they noted that the average age was 30 and that 43 per cent of the patients had not been pregnant previously.

Scheffey, in an analysis of 82 consecutive cases of ectopic pregnancy, found that only 19.5 per cent had not been pregnant previously. In a subsequent review of 75 consecutive cases Farell and Scheffey revealed that "twelve patients (16%) had never conceived before."

Of the 90 cases of primary ovarian pregnancy studied by Baden and Heins, 75 per cent terminated by the end of the first trimester, 12.2 per cent terminated in the second trimester, and 12.2 terminated in the third trimester. Of this last group of 11 cases, 7 were stillborn and 4 were alive at birth, although two were grossly malformed. The difficulty involved in editing and authenticating the reported cases of primary ovarian pregnancy becomes particularly apparent when presented with cases that have progressed beyond the sixth month of gestation.

Isbell and Bacon reported 1 case of primary ovarian pregnancy out of 110 cases of ectopic pregnancy at the Free Hospital for Women in Brookline, Mass. Eckerson reported 1 case out of 339 ectopic pregnancies at St. Luke's Hospital of New York City. Kuzma and Lillie reported 3 cases of
primary ovarian pregnancy out of 206 cases of ectopic pregnancy at the Milwaukee Hospital. On the basis of these three investigations, the incidence of primary ovarian pregnancy among ectopic pregnancies varies from 0.3 per cent to 1.5 per cent.

In this article there is presented the second case of primary ovarian pregnancy out of 308 cases of ectopic pregnancy observed in the gynecologic ward service at Jefferson Medical College Hospital, the first case having been reported by Porreca in 1950.

CASE REPORT

History

Mrs. D. G., age 31, gravida I, para I, was married at age 22. Her general health was good and she had had no serious illnesses. Her menses had their onset at age 16, and occurred every 30 days, lasting 4 days. She has had difficulty in conceiving. She had a full-term pregnancy in 1948. A Rubin test in December, 1950, showed tubal spasms.

Because of infertility, the patient had a curetage performed at Philadelphia Naval Hospital August 28, 1952. This was followed by pelvic inflammatory disease for which she was hospitalized and treated with antibiotics from August 30 to September 6, 1952. Patient seen by one of the authors (D.M.F.) on December 6, 1952, at which time she complained of lower abdominal pain, more marked on the right side. This pain was sudden in onset, occurring while she was bathing.

Last menstrual period was on November 29, 1952. This was the expected date but the menses were scanty. Previous menstrual period was November 1–8.

Physical Examination

Examination elicited no signs of acute distress. Heart and lungs were clear, and breasts normal. There was some muscle guarding present in the abdomen and the right lower quadrant was tender.

Pelvic examination revealed normal external genitalia. Skene’s and Bartholin’s glands were free of evident infection. Vaginal outlet was normal, the perineum was firm, and the cervix was parous and healthy in appearance. The uterus was anterior in position and normal in size. The adnexa were palpably enlarged and tender on the right side and not felt on the left.

Temperature, pulse, respiration, and blood pressure were within normal limits. Blood count was 3,400,000 R.B.C., 13,100 W.B.C., and hemoglobin was 10 Gm.

Fig. 1. Ovary containing embryo.
Tentative Diagnosis

Tentative diagnosis of intact tubal pregnancy was made, and the patient was admitted to Jefferson Hospital. The next morning, December 7, 1952, patient felt somewhat better, and had less pain. However, repeat blood count showed 2,980,000 R.B.C., 11,000 W.B.C., and 9 Gm. hemoglobin. Two-hour pregnancy test was reported as positive.

Because of her history of scanty menses at the expected period, lower abdominal pain, palpable right adnexa, positive pregnancy test, and drop in hemoglobin and R.B.C., a diagnosis of ectopic pregnancy with tubal abortion was made.

Laparotomy and Findings

Laparotomy disclosed about 50 cc. of free blood in the abdominal cavity. The uterus and both fallopian tubes were grossly normal. At the superior border of the right ovary there could be seen a cystic enlargement the size of a walnut, from the lateral border of which was coming a trickle of blood. The under-surface was transparent and the embryo could be seen lying in the cystic mass (Figs. 1 and 2). Right oophorectomy was performed.

Patient had an uneventful postoperative course and was discharged from the hospital on December 15, 1952. Histologic diagnosis: primary ovarian pregnancy.

SUMMARY

A case of true ovarian pregnancy has been reported which satisfied all the criteria of Spiegelberg.

REFERENCES

Ovarian Cyst in the Mesentery of the Ileum

Report of a case

JOSEPH H. ZEIGERMAN, M.D., and JOSEPH IMBRIGLIA, M.D.

THE PATIENT, C. V., was a 34-year-old single, white waitress who came to the endocrine clinic of the Graduate Hospital, University of Pennsylvania, on October 17, 1950, complaining of severe disabling dysmenorrhea of many years' duration, in addition to episodes of pain in the lower abdomen, constipation, diarrhea, and rectal bleeding. Her medical history revealed that she had been to numerous clinics and hospitals over a period of many years with the same complaints. Recently she was given psychotherapy. She had five previous operations: appendectomy in 1944; right salpingo-oophorectomy in 1945; laparotomy for adhesions in 1947; hemorrhoidectomy in 1949; and partial left oophorectomy in 1950.

Pelvic examination revealed an adherent cystic mass in the cul-de-sac and induration of the uterosacral and left broad ligaments. This was diagnosed as pelvic endometriosis. The diagnoses by the gastroenterologist and the neuropsychiatrist were a functional change in the colon which was induced premenstrually, mental deficiency, and an anxiety state.

Sixteen months later she was admitted to the St. Agnes Hospital in Philadelphia with the same complaints. She had received medical care in the interim, consisting of diathermy, sedatives, laxatives, various diets, and injections, without any improvement. The pelvic findings and the symptoms remained unchanged.

Exploratory laparotomy revealed that the omentum was adherent to the uterus and to the left ovary. The left ovary was cystic and three times normal in size. Total hysterectomy and left salpingo-oophorectomy were performed. On routine abdominal exploration a large cystic mass was found in the mesentery of the ileum; it was the size of a large orange and was round and firm in consistency. The mesentery and the ileum were stretched by the enlarging mass. There were no adhesions or other evidence of previous injury at this site.

Attempted enucleation of the cyst proving unsuccessful, resection of the cyst and the involved loop of the ileum was necessitated, and a side-to-side anastomosis created. The patient made an uneventful recovery and was discharged in good condition on the ninth postoperative day.

On microscopic study, the muscular coat of the ileum was found to be intimately attached to ovarian tissue (Fig. 1). The ectopic ovarian tissue was cystic and was the seat of hemorrhage both old and new. There was no evidence of endometriosis.

DISCUSSION

This case illustrates the difficulty encountered in the diagnosis and treatment of an unsuspected ovarian cyst in the mesentery of the ileum. It had not been diagnosed roentgenologically and had not been discovered during the previous surgical procedures.

The pain syndrome had existed for many years; the character and the site of the pain determined the course of treatment. Severe episodes of intestinal distress had led to in-
tensive intestinal studies. During a recent episode of such intestinal distress, the opinion was expressed that the symptoms were due to the existence of a functional change in the colon induced premenstrually, and that there was also a mental deficiency and an anxiety state.

The lesions necessitating previous opera-

tive interference were cystic ovaries, adhesions, chronic pelvic inflammatory disease, and suspected endometriosis. The extent of abdominal exploration during previous laparotomies could not be determined. It is assumed that the upper abdomen had not been explored.

It is difficult to determine whether the mesenteric cyst was the result of her previous operations, whereby one or more pieces of ovarian tissue had been liberated into the peritoneal cavity and by a process of invagination had formed this unusual mesentero-ovarian cyst, or represented a congenital anomaly in the developmental position of the ovary.

It is our belief that this case was one of an unusual congenital anomaly in the developmental position of ovarian tissue. This is supported by the fact that the ileum and its mesentery were free of adhesions, the serosa was normal in appearance, and there was no evidence of previous insult to that area. The mesentero-ovarian cyst was solitary, filled with fluid, and independent of other surrounding structures.

Periodic examinations during the past 3½ years revealed that the patient was in good physical condition. Her only complaints were the discomfort from the symptoms of the menopause.

REFERENCE


Fig. 1. Section of ileum and ovary. 1, mucosa of ileum. 2, submucosa of ileum. 3, muscularis of ileum. 4, fat. 5, fibroconnective tissue. 6, ileo-ovarian fusion. 7, atretic follicle. 8, hemorrhagic cyst of ovary. 9, another atretic follicle.
Cytologic Nomenclature

Method for standardization and recording of data on cells exfoliated in body fluids: I. A record book for the cytology laboratory

MARIA S. BLANCO DE DEL CAMPO, B.S., M.T., M.S.

In the new field of exfoliative cytology each worker has developed a method for recording and describing microscopic findings and diagnostic impressions. There is confusing multiplicity in classifications. In reviewing the diagnoses given by different experts there are often various interpretations of the same material. Clinicians with little knowledge of exfoliative cytology are consequently at a loss as to the course to be followed.

To standardize impressions obtained from cytologic smears, the method for recording designed in this laboratory has proved useful. This record book is recommended to students and screeners, who, by filling out the corresponding columns, can better classify smears and submit an impression. It should also be useful to the pathologist or cytologist who can recheck with ease the screener's observations at the same time that he renders his diagnosis. Thus the book facilitates accurate and efficient recording of observations by the screening technician, swift reporting of material encountered by the pathologist, and mass survey of cytologic smears.

THE RECORD BOOK

Description

The record book can be easily sketched by hand. It contains in bound form essential data on each case and allows for simple detection of available information. It can be readily interpreted by any member of the working staff familiar with the system and abbreviations.

In this laboratory we use standard composition books of hard covers spotted with white dots in a black field, measuring about 8” wide × 10½” long. They contain approximately 200 pages of 25 lines each, are light and not overly bulky, and cost about 50 cents each. Each book will carry entries of 2500 cases.

Entry of Data

IDENTIFICATION. The data furnished in the requisition when the smears are collected are entered on the left-hand page of the book. It has been found convenient to distribute this information in tabular form (Fig.
DEL CAMPO

1). These columns include the case number, age of patient, last menstrual period, date smears were collected, name of person who took the sample, date smears were received at the laboratory, date smears were processed and interpreted and by whom, and quality of smears in terms of collection and staining. It will be noticed that Column 10 leaves little space for longhand writing of between cytologic vs. histologic interpretations.

**CYTOLOGIC FINDINGS.** Cytologic findings appear on the right-hand page which has 50 horizontal lines while there are but 25 on the left (see Fig. 1). This is to permit recording 2 smears to each case. If one is from the cervix and the other from the vagina, there will be different cellular structures

<table>
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<th>Date of Last Menstruation</th>
<th>Date Smears Collected</th>
<th>Name of Person took Sample</th>
<th>Date Smears Received at Laboratory</th>
<th>Date Smears Processed and Interpreted</th>
<th>Quality of Smears</th>
<th>Clinical Findings</th>
<th>Cytology Suggestions</th>
<th>Biopsy Report</th>
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<td>None</td>
<td>Repeat</td>
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<td>1951</td>
<td>1943</td>
<td>2021</td>
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<td>2021</td>
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</tr>
<tr>
<td>9974</td>
<td>25</td>
<td>1970</td>
<td>1975</td>
<td>1995</td>
<td>Dr. Garcia</td>
<td>1995</td>
<td>Blood Thin</td>
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<td>None</td>
<td>Repeat</td>
<td>Chronic cervix x</td>
</tr>
<tr>
<td>9975</td>
<td>55</td>
<td>1945</td>
<td>1960</td>
<td>2000</td>
<td>Dr. Smith</td>
<td>2000</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Repeat</td>
<td>Chronic cervix x</td>
</tr>
<tr>
<td>9976</td>
<td>49</td>
<td>1955</td>
<td>1980</td>
<td>2005</td>
<td>Dr. Smith</td>
<td>2005</td>
<td>Poor</td>
<td>None</td>
<td>None</td>
<td>Repeat</td>
<td>Chronic cervix x</td>
</tr>
</tbody>
</table>

**Fig. 1.** Key to abbreviations and symbols: ab.-abundant; ab. c.-abundant cocci; abn-abnormal; A. M.-atrophic menopause; anuc.-anucleated cell; at. c.-atypical cell; B. P.-basophilic cell Ë pyknotic nucleus; B. V.-basophilic cell Ë vesicular nucleus; B. v.-bacillus vaginalis; c-cocci; Z-white Ca. in S-carcinoma in situ; C.I.C.-cervical-irritation cell; cl.-cluster or clumps; cor.-cornification; cx.-cervical; disc.-discrete arrangement; dysk.-dyskaryosis; Em.-endometrial cells; E.P.-eosinophilic cell Ë pyknotic nucleus; E.V.-eosinophilic cell Ë vesicular nucleus; Ex.-endo- or exocervical cells; gr.-in groups; I.L.-Intermediate layer cells; inf.-infection; L-loads; ma-many; mbf.-mixed bacterial flora; N-nucleus; n.s.-not seen; O.B.L.-outer layer cells; oc.-occasional; the clinical findings. One must design a code or key of abbreviations to record signs and observations reported by the physician.

**OTHER INFORMATION.** Column 11, Cytology Suggestions, is of value in classification of material specially analyzed in those laboratories used as teaching facilities. In this space one can indicate if slides are suitable for photography, teaching purposes, or further researches. Column 12, Biopsy Report, is of great help in correlating studies in each and they should be recorded separately. There are instances in which the vaginal smear may show no malignant or suspicious cells while the cervical scraping is characterized by a malignant pattern. In this event separate reports should be given by the screener, leaving room for the cytologist to decide as to the final classification. Another reason for subdividing each case is that there may be a satisfactory vaginal smear but the cervical may be unsatisfac-
tory, and vice versa. Such a condition should be noted.

**CELLULAR ELEMENTS.** Figure 1 shows the distribution in tabular form of the possible cellular elements observable in smears. Coloring the rulings facilitates locating the cellular structure in question. The various colors in the right-hand page represent an attempt to indicate the staining qualities of the cellular elements by color. Thus, columns for wandering nuclei and bacteria which stain either in dirty gray or blue-black are in black or violet pencil columns. Histiocytes usually stain pale blue, so the column is in pale blue. White blood cells are either gray-black or blue, so the lines are dark blue. Red blood cells are between two red lines. Trichomonads and mucus are recorded either in gray, black, or dark blue. Superficial cells which are basophilic and have a large vesicular nucleus lie between two blue columns, but those with pyknotic nuclei are between blue and red. Superficial cells of the eosinophilic type with vesiculated nuclei are in red, as are truly cornified cells. All of the other cells—those from the intermediate layer (I.L.) or the outer basal layer (O.B.L.)—are in blue. Endometrial and endocervical cells, when in clumps, or be-

### Table: Distribution of Cellular Elements

<table>
<thead>
<tr>
<th>Superficial Cells</th>
<th>Columns for Various Elements</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wandering Nuclei</td>
</tr>
<tr>
<td>Vesicular nucleus</td>
<td>Blue</td>
</tr>
<tr>
<td>Pyknotic nucleus</td>
<td>Blue</td>
</tr>
<tr>
<td>Vesiculated nuclei</td>
<td>Red</td>
</tr>
</tbody>
</table>

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**APPLICATION**

**Morphology and Quantity of Cells**

An example of the application of this right-hand page is furnished by Fig. 1. Standardized symbols and abbreviations have been used successfully at this labora-
tory to describe in the small space available the morphology and quantity of the cell structures observed. The symbols have been borrowed from mathematics so that the sign > represents "greater than" normal if referring to size of nucleus; :::, which means "equal," and is used to indicate that the amount of basophilic and cornified cells is almost the same; ≠ meaning "not equal to" has been designated for atypical cells. (The term "atypical cells" refers to any epithelial cells that vary from normal morphology but not sufficiently to be considered malignant.) Examples are the superficial cells frequently observed in trichomoniasis showing a peri-or para-halo around the nucleus, and the so-called "Ayre's cervical-irritation cell." Other symbols are indications of quantity as: +, present; ++, present in moderate numbers; ++++, present in great numbers; ++++++, present in huge numbers. X is used to represent abnormal nucleus, 2X more than one nucleus in the cell; \(\neq\) signifies presence of given cellular structure and 0 its absence, and so on.

Among the abbreviations in use at this laboratory B.v. means Bacillus vaginalis; Er, erosion; D, vaginal discharge; P, polyp; S, satisfactory smear; Uns, unsatisfactory smear; Cx, smear from cervix; V, vaginal smear, and so on. A further paper will be presented dealing with this shorthand method found convenient in describing the clinical symptoms of the patient and for reporting the histologic and cytologic impressions and quality and morphology of the smears.

Other Uses

1. For follow-up smears. Exactly the same type of clinical data is requested as for the original smears, but they are not repeated under Clinical Findings, the cytologist's diagnosis only being recorded.

2. For body fluids. Add a column on the right-hand page with the heading "Type of Body Fluid."

Modifications

1. Private cases are entered in different coloring from clinic patients.

2. Heavy lines are drawn under the last case entered at the end of the day or the week to facilitate location of a case by date.

3. Different colors may be used to designate material from those physicians who send in a large amount of work or material for immediate diagnosis.

4. Each screener may be given a number so that his books can show continuity or use a particular mark so that each one can be made responsible for his diagnoses. An extra column could be added for this purpose.

ADVANTAGES

1. At a glance one may extract any number of cases for further study from either a clinical or cytologic point of view.

2. A double check is provided for the re-examination of controversial smears.

3. Correlation between clinical, pathologic, and cytologic observations can be easily obtained.

4. Suggestions as to the additional use of the smear, such as reporting for teaching purposes, photography, checking of stain, and checking physician's collections of material can be entered.

5. Isolated facts group together and make obvious the need for a particular emphasis in research.

6. The system allows for a minimum of difference in microscopic observations, such as one due to personal variations and differences in interpretations of observations.

7. Accuracy of individual reporting as compared to the reports of consultants can be evaluated, and the source of differences of opinion on morphology or diagnostic interpretation of smears can be indicated.

8. Screening can be carried out with minute attention to recordable data, hardly a significant detail being left out.

9. Cytologic detail reporting may be
standardized to avoid mixing different systems of smear classification.

10. The screening time is cut in half.

11. Because smears are entered by a given case number and the name of the patient is not known by the screener, objective reading is increased.

12. When a monthly report of laboratory work is submitted, the record book facilitates the separate listings of total numbers of new cases from the clinic, those from the private offices of physicians using the facility, distribution of follow-up cases, as well as smears satisfactorily diagnosed, or those not diagnosed. The collection of smears versus the technical handling of specimens can be correlated. The number of suspicious and positive cases are easily picked out and comments may be added in regard to the accuracy of the screener compared to the cytologists, the cytologist to the pathologists, and the clinician to the consultant.

13. Date that smears were received in the laboratory, date stained, and date of diagnosis are exact.

14. Proper classification of slides for filing at a later date is aided.

**SUMMARY**

In cytology there is great need for standardizing diagnoses and recording data that can be easily located and evaluated. A book for recording microscopic data and cytoclassification has been designed and has been presented herein.

**REFERENCES**


Ruptured Interstitial Pregnancy Following Homolateral Salpingectomy

Report of a case

HENRY E. STEADMAN, M.D.

ECTOPIC PREGNANCY recurs, according to Lingenfelder in a review of the literature in 1950, in 4–5 per cent of the women who are able to conceive again. He further states that recurrent ectopic pregnancy in the site of previous salpingectomy for tubal pregnancy is, however, exceedingly rare. His report covered 37 cases in the literature with 1 additional case of his own. In a more recent paper in 1955, Ladas states that recurrent ectopic pregnancy occurs in about 2 to 3 per cent of patients who have previously undergone surgery for an ectopic pregnancy. He adds that recurrent ectopic pregnancy occurring in the stump of the tube which has been left in place following salpingectomy is so rare that only 40 cases were reported in the literature to 1953. He adds 1 case of his own. It is assumed that these cases included various-sized stumps of incompletely removed tubes as well as true interstitial, intramural, or cornual tubal pregnancies. Buerger and Weinstein made a thorough historical review of interstitial pregnancy from 1801 to 1948. In another report, Frankel in 1948 stated that interstitial pregnancy is rare, occurring in from 0.65 to 2 per cent of all extrauterine pregnancies. He found 25 cases reported in the literature up to 1940. His paper concerned 4 additional cases of interstitial pregnancy following homolateral salpingectomy and included cases in which the tubes were removed because of infection as well as pregnancy.

The extreme rarity of true cases of interstitial pregnancy in homolateral tubal stump salpingectomy is made clear from these reports. The case presented here is the only case of recurrent ectopic pregnancy occurring in the homolateral tube following salpingectomy in the recorded history of the Georgia Baptist Hospital.

CASE REPORT

Mrs. C. H. Mc. (Case A-45148) was admitted to the Georgia Baptist Hospital emergency room at 4:00 A.M. on August 8, 1947. She was in shock and had some generalized abdominal pain which was not severe. A diagnosis was made of intra-abdominal hemorrhage, probably due to ectopic tubal pregnancy.

PAST HISTORY

Patient stated that menses had begun at age 16, that they had never been regular, and that they often lasted 10–14 days. She had moderate dysmenorrhea.

In March, 1946, she had had a left salpingectomy for ectopic pregnancy and an appendectomy. The pathologist’s report read “Ectopic tubal pregnancy—not ruptured. Chronic catarrhal appendicitis.” The tube removed was 8 cm. in length and 2 cm. at its thickest point (the operating surgeon had made it a rule to remove such tubes very close to the uterus to avoid recurrent tubal pregnancy). Recovery from this operation was uneventful. A hystero-
INTERSTITIAL PREGNANCY IN SALPINGECTOMY SITE

Salpingogram made on June 2, 1948 showed a normal uterine cavity, but the tubes did not visualize.

PHYSICAL EXAMINATION

Physical examination on admission revealed the patient to be cold, clammy, pale, and sweating profusely. Pulse rate was 140, respiration 26, temperature 99, blood pressure 60/30. The abdomen appeared slightly distended, with slight tenderness and rigidity. Bimanual examination revealed a soft cervix which was tender on movement. Uterus was soft and slightly enlarged and freely movable. Right adnexa felt normal but left adnexa could not be palpated.

LABORATORY REPORTS

Urine was normal. Blood examination showed R.B.C. 2,650,000, hemoglobin 50 per cent, W.B.C. 34,000, polymorphonuclears 88 (1 juvenile, 7 stabs, and 80 segs), lymphocytes 12. Kahn was negative, type II-A.

TREATMENT AND FINDINGS

Glucose, 1000 cc. of 10 per cent solution, was begun at once and 500 cc. whole blood was given, after which the patient's blood pressure was 100/65. Sodium Pentothal intravenously and cyclopropane were used as anesthesia. The left cornu was bleeding and there was a ragged cavity oozing fresh blood where the tube should be. This was clamped to control the profuse bleeding. The bleeding area was cut out to obtain clean surfaces for approximation and sutured with #1 chromic catgut. A sac, 1 X 1.7 cm., was found floating in the peritoneal blood. When opened, it was found to contain a small fetus. The blood was aspirated, the clots were removed manually, and the peritoneal cavity irrigated with saline solution. Two units of plasma and another 500 cc. whole blood were given. At the end of the operation blood pressure was 110/70, pulse rate 100, and respiration 16.

POSTOPERATIVE COURSE AND SUBSEQUENT PREGNANCIES

Recovery was uneventful except for daily rise in temperature to 100° F. for 7 days, which was probably due to the blood in the peritoneal cavity. The patient was discharged on August 15, 1947, and dismissed as completely recovered after 6 weeks.

The patient came to the office on December 17, 1953, with signs of pregnancy. Her last menstrual period was on October 13, 1953. The fundus was enlarged to a 2-month pregnancy. Prenatal care was routine with no complications. On July 18, 1954, patient was delivered of 3714-Gm. normal female child. On April 23, 1955, she again came to the office, giving her last menstrual period as December 3, 1954, making due date approximately September 10, 1955. She was found to have a normal intrauterine pregnancy, and her prenatal progress was normal and routine. On October 16, 1955, the patient was delivered of a normal male child. The patient had evidently been in error as to the date of the last menstrual period.

DISCUSSION

Diagnosis

The diagnosis of interstitial pregnancy may be difficult and often is made only after rupture and laparotomy. It is difficult to palpate the gestative mass until it is fairly large because it is surrounded by myometrium and is usually in the middle of the isthmic portion of the tube. The mass is usually tender and most often points anteriorly. The fetus may attain considerable size before rupture. When rupture occurs, bleeding is more profuse than the rupture of the tube free in the peritoneal cavity; therefore, shock occurs rapidly and is more profound. Like other rare conditions, the diagnosis will be made more often if the possibility is considered in the differential diagnosis of any woman of childbearing age with a history of alteration of normal menstrual period. If pregnancy is suspected and there is a palpable cornual mass with a broad base, one should consider pregnancy in the interstitial portion of the tube or in a rudimentary uterine horn which may or may not have an opening into the main portion of the uterus. If the mass grows at a fast rate, cornual pregnancy should be the most likely diagnosis. If the patient is first seen in a state of shock, the history suggestive of tubal ectopic pregnancy

Vol. 7, No. 5 May, 1956

573
may help preoperatively in giving a clue to the etiology of the shock.

*Treatment*

The ruptured cornu may be sutured or packed. Suture is better when possible to stop the bleeding. In some cases with profuse bleeding of a large opening into vascular beds, or hematoma, hysterectomy may be mandatory. Removal of blood and clots is routine. Ballantyne stated that Kelly advocated curettement of the pregnancy and suture or packing of the cavity, at one time even making a diagnosis of interstitial pregnancy and then closing the abdomen to remove the products of conception by curettement through the cervix. He did not advocate such treatment after 1940. Chabrut in 1929 reported a recurrence of interstitial pregnancy in the same side following curettement.

*Mortality*

Ruptured interstitial pregnancy has a much higher mortality rate than does rupture in an external portion of the tube. As previously stated, hemorrhage is more vicious in interstitial pregnancy and contributes to cause of death.

*Etiology*

The etiology of recurrent homolateral ectopic pregnancy is interesting. Lingenfelder gives three possible modes of transmigration: (1) internal migration of an ovum which has been fertilized in a normal tube and crossed the fundus, finding its way up into the opposite cornu which was partially or completely canalized; (2) external migration of the ovum and implantation in a pocket of the tube which has regenerated or recanalized; and (3) external migration of an ovum, fertilized by a spermatozoon which has ascended through the patent tube, with nidation occurring in a pocket of the tube at the site of previous operation. A fourth possibility has been postulated by Buerger and Weinstein of a fistulous tract which may develop between the uterus and the peritoneal cavity due to trauma or infection. The evidence in favor of internal transmigration in humans is scanty, though Forman, Buerger and Weinstein, and Andrews present convincing evidence of internal transmigration in their cases. Recurrences in cases where a wedge was cut out of the cornu or where the cut tube was inverted and peritonealized are likely to be of this type. Corner has demonstrated that transmigration of the ovum in animals with long bicornuate uteri and many litters, such as pigs and cows, is by internal migration. It is believed that patency is regained by some process of recanalization. Richardson and D’Errico claim that patency is regained by the process of regeneration even though the cornual portion of the tube has been completely removed.

The evidence in favor of external transmigration is more conclusive in cases presented by Frankel, Richardson and D’Errico, Ballantyne, Murray and Fraser, Leopold, and Ladas. Frankel states that many cases of extrauterine pregnancy are evidence of external migration of the ovum since the corpus luteum of the ovary is on one side and the pregnancy is in the opposite tube. D’Errico cites the case of DuJarier, who removed the left tube and right ovary of a woman who subsequently had a full-term intrauterine pregnancy. Evidently this has occurred in other cases. Kelly excised a diseased left ovary and right tube, leaving the normal right ovary and left tube in place. Fifteen months later this patient gave birth to a full-term child, and 17 months after that the remaining tube was removed for a ruptured tubal pregnancy. The etiology in any particular case is questionable and makes prophylaxis uncertain. However, the best procedure is a cornual excision of any tube removed for any cause and, even so, a few cases will result in failure, as did one of Nache.
INTERSTITIAL PREGNANCY IN SALPINGECTOMY SITE

SUMMARY

A case has been presented of recurrent tubal pregnancy of interstitial type in homolateral site of previous salpingectomy for unruptured ectopic pregnancy.

REFERENCES

Hospital Departments and Tissue Committees

Their functions in community hospitals

LEON P. FOX, M.D.

The subject alluded to in the program would suggest that the speaker might be an expert in this field. Factually, this is untrue; therefore, I must qualify myself in the very beginning.

I am an obstetrician-gynecologist who practices in a rapidly growing community in two open staff hospitals, which provide far fewer beds than are needed. It has been my lot to be actively interested in the organization of both medical staffs and to observe the many changes and evolutions over a period of seventeen years. During this time both hospitals have usually maintained accreditation by the College and now the Joint Commission.

Rather than attempt to give you authoritative definitions of functions for departments and tissue committees in the hospitals, I hope to bring to you our experiences in my community. Most of the information given will necessarily concern the field of obstetrics and gynecology and its department in our hospitals. However, much of it can be applied to other departments as well.

At this point I wish to quote our Chairman of this section, Dr. John I. Brewer, as he spoke before the Sixth American Congress in Obstetrics and Gynecology in December, 1954:

The Joint Commission has done a grand job in correcting the defects in interpretation of the rules. Much of the credit goes to the Director, Doctor Kenneth B. Babcock, who has been most understanding of our problem and who has been most desirous of making things right. I wish to thank him publicly. The fear of undue action against our specialty has been removed.

This expresses the feelings of each of us toward the Joint Commission. We are here today to continue our efforts to work in harmony with one another, by the highest standards established by our profession. Many problems exist in every part of our country in hospital staff organizations, and it is imperative that we pool our ideas of solution and present them to our accreditation groups.

REQUIREMENTS OF THE JOINT COMMISSION

The Joint Commission’s ideal has been quoted by Doctor Babcock as “better quality care in the hospitals of the United States and Canada.” We are certainly in accord with this goal, but we must advance in a sensible and unencumbered manner.

In many instances, it has been proved that general rules and regulations must be molded to the situation before detailed application is possible. So it is with the requirements of the Joint Commission for Accreditation of Hospitals in this hemisphere.
HOSPITAL DEPARTMENTS AND TISSUE COMMITTEES

Often these standards are made to fit large metropolitan hospitals and areas where a physician need only be a member of a single hospital staff; no allowance is made for the small community where bed shortages, sphere of practice, and terrain prevent the so-called ideal situation from existing. Each medical organization must necessarily be worked out well within the expected standards set up by our approving Boards, and to our own satisfaction, practically and generally.

RAPID GROWTH OF COMMUNITY. We have had serious difficulties arise in my own community, concerning staff organizations in hospitals, for the reasons mentioned. It will be necessary to present some Chamber of Commerce statistics to give some details concerning our growing pains. I hope to show you the problem of a rapidly growing community, large influx of physicians, and static hospital facilities.

Table 1. Population Increases

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Santa Clara County</td>
<td>219,000</td>
<td>403,900</td>
</tr>
<tr>
<td>San Jose trade area</td>
<td>175,000</td>
<td>341,150</td>
</tr>
<tr>
<td>San Jose (city)</td>
<td>84,650</td>
<td>112,645</td>
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</tbody>
</table>

Table 1 shows a ten-year population growth in the area of my experience. You will note the 100 per cent population in-
crease in our local trade area, which is dependent upon our two approved hospitals for standardized hospitalization (Fig. 1). We do have another fifty-bed hospital in the area which is not approved and not supported by the major segment of our physicians.

INADEQUATE INCREASE IN BEDS. Table 2 reflects the almost static hospital bed situation. It merely shows the inadequate increase in approved hospital beds in our community. This small increase has been made possible by matching Hill-Burton funds. Plans are afoot to add substantial numbers of beds to these in the next few years.

HOSPITAL STAFF ORGANIZATION. Table 3 demonstrates the influx of physicians in this ten-year period. The Medical Society has reported that one new physician has come to our county every 5 days. This totals about a 130 per cent net increase in the period studied. The other interesting point in this table is the changing trend toward specialization. In 1944, 42 per cent of our physicians were specialists and 58 per cent general practitioners. In 1954, 65 per cent were limiting their practice to a special field and 35 per cent to general practice. According to recent statistics published in the Education issue of the J.A.M.A. about one third of new physicians were limiting their practice to a specialty; one half to general practice; and one sixth to part-time specialty.

Table 4 pinpoints our specialty trends in the two hospital staffs mentioned before. The numbers indicate individual physicians who may be members of both staff organizations. Duplications are not indicated.

Table 5 shows the number of obstetric deliveries in the two hospitals and who is conducting them. At this point I might say that a recent six-month sampling of statistics indicates that 48 per cent of all gynecologic surgery is done by specialists in gynecology, 12 per cent by specialists in general surgery, and 40 per cent by general practitioners.

Necessity has been a good provider, and we have been able to establish two working staff organizations, which comply with the requirements of accrediting agencies. We have proved that there can be coexistence, in a friendly manner, of general surgeons, general practitioners and obstetrician-gynecologists working in two hospitals on an equal basis. It has been shown that most physicians are honest, capable, ethical, and...
amenable to suggestion, much as was found in a maternity hospital in Hawaii.

Phillips and Nishigaya have presented the experience of staff activities in the Kapiolani Hospital in Hawaii. Their open-staffed hospital has shown a steady improvement in standards of practice without arbitrary rules limiting general practitioners in our field. Demonstrably, it can be done.

All members of our County Medical Society are eligible for active membership on the staff of each hospital; this includes general practitioners as well as specialists. All committees have general-practice representatives and we find that they are the more conscientious members and work hard on committees. The departments are managed by committees of at least five members representing all pertinent groups. For instance, the Obstetrical-Gynecological Committee consists of three qualified specialists, two general practitioners and usually one or more general surgeons who do gynecologic surgery.

THE DEPARTMENTAL COMMITTEES

Functions

The function of the departmental committees in our hospitals essentially is to manage the department as follows:

1. Liaison with administration, record department, nursing department, staff members, and residents. Meetings are held once monthly for joint discussions—solving problems, establishing policy, and ironing out difficulties.

2. In charge of training program. Responsible for resident training program in cooperation with the Santa Clara County Hospital from where residents are "farmed."

3. Act as Therapeutic Abortion and Sterilization Committee. Members consult with the attending physician, discuss the case, and the majority of the committee members rules on each case by vote.

4. Act as Record Review Committee. During the month all charts are reviewed by members of the Committee. All substandard poorly handled and problem cases, as well as deaths, are then discussed by the Committee as a whole. This audit is not a written document, on advice of our Malpractice Education Committee. The physician concerned is interviewed, and if the problem can be settled at this level, it is closed. If a serious problem involving negligence, grossly poor judgment, breaking of rules, and so on, cannot be settled at this level, it is referred to the next echelon for solution—that is, to the Council, Executive Committee, or Record Committee, depending on the organization plan. If discipline requiring authority is necessary, the Council or Executive Committee reviews the case and acts.

5. Acts as Consulting Committee for hospital without charge. If regulations require Consultations, the Committee members give this service. This provides assistance in any needed case.

6. Arranges and conducts departmental meetings monthly. These meetings consist of current case presentations with critical, scientific, and instructive discussion by both prearranged and interrogative plans. The idea is to serve in an educational, semidisciplinary, and even research capacity. Most departments have a rotating chairman from its committee for their meetings and this chairman is responsible for developing the program.

7. Inspects the department regularly, advising the nursing staff as to policy. The members keep complicated cases under close observation.

8. All new members are assigned to sponsors who may or may not be committee members. In any case, the committee members seek to familiarize themselves with the individual's conduct and han-
Meeting attendance, complications in record keeping, and other such difficulties should be delved into locally, in an effort to find a proper solution. All constructive data should be given to the Current Review Committee of the American Medical Association, recently appointed by the speaker of the House of Delegates to make a detailed study of the Joint Commission activities at the grass-roots level.

THE TISSUE COMMITTEE

Functions

There is no satisfactory manual describing the proper function of a Tissue Committee in a hospital. Many experiments are being conducted and I am certain that a satisfactory and beneficial result will eventually evolve. In our hospitals the Tissue Committee is made up of representatives from each departmental committee, the pathologist, and at least one general practitioner. The chairman is the representative of the Surgical Department. Their deliberations at their monthly meetings cover the following categories:

1. A study of statistics in the Pathology Laboratory. This includes the number of submitted tissues; number of apparently missed diagnoses; number and percentages of normal tissues removed; and number of deaths.

2. Discussion of all cases in which there is inconsistency in clinical, operative, and pathologic diagnoses; investigation of all cases in which normal tissues were removed; and discussion of such cases as removal of pregnant uteri, and so on.

3. Discussion and study of all deaths. One hospital has the department committees do this chore, while the other allots it to the Tissue Committee. I believe the former is preferable.

If the discussions reveal any type of improper or substandard practice, the physician should be confronted with it promptly and should be given an opportunity to explain it and correct it. No one should be protected in this manner, and all constructive data should be given to the Current Review Committee at the American Medical Association.
Hospital Departments and Tissue Committees

The physician in question is interviewed, as in the Departmental committee. Minor problems are settled at this level, while others are referred to the Council or Executive Committee for disciplinary disposal.

Relationships with Departments

A close relationship is maintained between departmental committees and the Tissue Committee. The members from the various departments bring their problem cases for detailed discussion. Many times the pathologist is called to task as well as the physician in charge of the case until a fair and proper solution is found.

Relationships between the Department of General Surgery Department and Department of Obstetrics and Gynecology have at times become strained in our experience as well as elsewhere. Time, toil, and a better understanding on the part of the members of both departments have brought about a friendly working relationship of great value. We have no objections to the title a person has when he does work in our field but we have a great interest in the training, experience, and limitations of that person. Many general surgeons and general practitioners have been trained in our field and have every right to include our branch in their broad repertoire. Likewise, many certified gynecologists have been well trained in breast surgery, urology, and even bowel conditions, and certainly should not be restricted in such areas if they demonstrate such ability.

In our hospitals, gynecologic surgery is done in the general surgery theatres. We try to do our cesarean sections in the delivery suites. The Department of General Surgery is technically in charge of the operating rooms and ancillary facilities. The committees observe their respective operative schedules daily and review the work done at frequent intervals. The members of the committee are alerted by the nursing staff when unusual, questionable, or special-risk cases are being done as well as when rules are being infracted. Courtesy, tact, and unrelenting insistence on protocol keeps almost everyone in complete accord.

Our experience shows an improving standard of practice generally in our hospitals. The percentage of normal tissue removed as determined by pathologic study averages about 0.2 per cent and has been about the same for five years. There have been more consultations in every department. The autopsy rates are rising. Mortality and morbidity rates are comparable to other areas. Our cesarean section rates are always less than 5 per cent.

We have come to realize that mishandled coronary occlusion, virus pneumonia, or marasmus in children is as important a consideration as an unnecessary or ill-advised operative procedure. The field of obstetrics and gynecology can now share its singular position in bearing the brunt of undue policing.

With medicine, pediatrics, and general surgery, consultation requirements for conditions in their fields should be as strict as for a first cesarean section or hysterectomy in obstetrics and gynecology.

We hope the Joint Commission will continue to look into our many local problems and help us solve them in a practical manner.

References

Reinier de Graaf (1641—1673)

AFTER OFFICE HOURS

Obstetric-Gynecologic Eponyms

Reinier de Graaf and the Graafian Follicles

The graafian follicle, like the fallopian tube, belongs to that select group of eponymics which, through long usage and universal acceptance, are no longer capitalized in spelling. The story of the graafian follicle comprises an exciting chapter in man’s long search for the mammalian egg, an effort that engaged his attention for two millennia. The highlights of this search have been narrated with charm and authority by George Corner in one of his delightful essays on the history of medicine.

According to the views of Aristotle, long accepted by succeeding generations, the mammalian egg was formed in the uterus as the result of activation of the menstrual blood by the male semen. This theory was seriously disputed for the first time by Galen, who thought that the female semen, like the male semen, was made in the blood vessels supplying the gonad, in which organ the semen was strained and purified. The semen elaborated by the ovary, according to Galen, was then transmitted via the tubes to the uterus, where admixture with the male semen produced a coagulum from which the embryo evolved.

The presence of vesicles in the female testes was mentioned in the sixteenth-century writings of Vesalius and his disciple, Falloppio, but these Paduan anatomists had no thought of the true function of the fluid-filled structures. Falloppio’s successor, Fabricius ab Aquapendente, described the hen’s ovary and even gave it the name ovarium, recognizing it as the organ of egg formation. But so strongly entrenched was the Aristotelian teaching that the egg was formed in the uterus that Fabricius naturally believed the ovary to be simply a part of the brood chamber. According to La Torre, Gian Matteo de Gradi of Milan, also known as Ferrari d’Agrate (died 1480), had long before applied the name ovary to the female testis and, by analogy with the hen, assumed its egg-producing function in other species.

The latter part of the seventeenth century witnessed a resurgence of the idea that the mammalian female testes, like the ovaries of birds, are the site of egg formation. Swammerdam and Van Horne, working together in Leyden in 1666, and the Danish anatomist Stensen in 1667, independently developed this theory in relation to the human and exchanged letters concerning their views. Stensen, “for friendship’s sake,” acceded to

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Swammerdam's brazen request that he and Van Horne be permitted to publish a proposed book on the subject, in preparation by Van Horne, before Stensen; but Van Horne never completed it and died in 1670, the book remaining unpublished.

Two years later there appeared a brilliant volume by Reinier de Graaf, his third, entitled De Mulierum organis generationi inservientibus (Figs. 1 and 2), Chapter XII of which was devoted to the female testes. Here, with due credit to Van Horne, de Graaf advanced the evidence that this organ is indeed an ovary and in it he described the follicles which have ever since been associated with his name.

After describing the gross morphologic characteristics and anatomic relations of the female testes and contrasting them with the male, de Graaf proceeded to the internal structure of the organ, illustrating the chapter with drawings of the bisected ovaries of the cow, sheep, and human (Fig. 3). Of the follicles, he wrote:

The normal structures, regularly found in the membranous substance of the testicles just described, are vesicles full of liquor, nerves, and nutritive vessels, which run to the testes in al-

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Fig. 1. Frontispiece from De Mulierum organis.
Fig. 2. Title page of De Mulierum organis.
most the same way as in males... and course throughout the whole of their substance, and enter the vesicles, within whose tunics many branches end after free division, in just the same way as we have seen happening in the ovaries of fowls composed of clustered egg yolks. ...

These vesicles have been described under various names by Vesalius, Fallopius... and others, whose accounts it would be too tedious to repeat here in full. Some call these vesicles hydatids, but the celebrated Dr. Van Horne in his *Prodromum* preferred to call them ova, a term which, since it seems to me more convenient than the others, we shall in the future use, and we shall call these vesicles ova as does that distinguished man, on account of the exact similitude which they exhibit to the eggs contained in the ovaries of birds; for these, while they are still small, contain nothing but a thin liquor like albumen. That albumen is actually contained in the ova of women will be beautifully demonstrated if the ova are boiled, for the liquor contained in the ova of the testicles acquires upon cooking the same color, the same taste and consistence as the albumen contained in the eggs of birds.

It is of no importance that the ova of women are not, like those of fowls, enveloped in a hard shell, for the latter are incubated outside the body in order to hatch the chickens, but the former remain within the female body during development, and are protected as thoroughly from all external injuries by the uterus as by a shell. ...

These ova arise and are developed in the testes in exactly the same way as the eggs in the ovaries of birds, inasmuch as the blood flowing to the testes through the nutritive arteries deposits in their membranous substance materials suitable for the formation and nourishment of the ova, and the residual humors are carried back to the heart through the nutritive veins or lymphatic vessels... .

Thus, the general function of the female testicles is to generate the ova, to nourish them, and preserve them in the ovaries of birds, and we shall see how they operate in a similar manner in the ovaries of women.
and to bring them to maturity, so that they serve the same purpose in women as the ovaries of birds. Hence, they should rather be called ovaries than testes because they show no similarity, either in form or contents, with the male testes... *

De Graaf's great mistake, now obvious, but one which can scarcely fail to arouse our sympathy as a natural conclusion in a premicroscopic era, was his assumption that the entire follicle was the ovum. We can only surmise how many troubled hours he must have spent in an unsuccessful effort to reconcile this concept with his observations on early rabbit embryos. Examining the contents of the doe's genital tract at different time intervals after mating, he recovered nothing in animals killed during the first 2 days; on the third day after coitus he found only tiny spherical masses in the fallopian tubes, and only slightly larger spheres in the uterus on the following day. De Graaf had unwittingly made the first discovery of tubal ova and supplied the potential, crucial evidence that the embryo begins to develop before reaching the uterus.

Only a few weeks after the publication of de Graaf's book the irate Swammerdam, whose priority of publication had been thwarted by the procrastination of his erstwhile collaborator, Van Horne, issued a bitterly worded pamphlet impugning de Graaf's personal integrity as well as the scientific accuracy of his observations and claiming for himself the credit for discovery of the ovarian function of the female testis. Diemerbroeck, Professor of Anatomy at Utrecht, who knew both contestants, remarked that Swammerdam had "smeared the ovary, not with honey, but with the bitterest gall." Swammerdam had made his bid too late; and de Graaf was rewarded with eponymic immortality.

More original than his thoughts concerning the ovarian follicles were de Graaf's observations on the corpus luteum, of which he gave the first detailed description, calling it the *substantia glandulosa*. He believed that each egg (follicle) was surrounded by this glandular substance which, as it ripened and moved toward the surface of the ovary, forced the egg out. His erroneous assumption that the presence of a corpus luteum implies impregnation was doubtless based on his study of rabbits, in which species ovulation normally occurs only after coital stimulation. He wrote:

These structures [corpora lutea] which, though normal, are only at certain times found in the testes of women, are globular bodies in the form of conglomerate glandulae which are composed of many particles, extending from the center to the circumference in straight rows, and are enveloped by a special membrane. We assert that these globules do not exist at all times in the testicles of females; on the contrary, they are only detected in them after coitus [being one], or more in number, according as the animal brings forth one or more foetuses from that congress. Nor are these always of the same nature in all animals, or in the same kind of animal; for in cows they exhibit a yellow color, in sheep red, in others ashen; because a few days after coitus they are composed of a thinner substance and contain in their interior a limpid liquor enclosed in a membrane, which when ejected with the membrane leaves only a small space within the body which gradually disappears, so that in the latter months of gestation they seem to be composed of a solid substance; but when the foetus is delivered these globular bodies again diminish and finally disappear.

De Graaf and his contemporary scientific world thought that the mammalian ovum and its ovarian origin had been demonstrated; yet a century and a half later, in 1821, a contest was sponsored by the Göttingen Academy of Sciences offering a prize for the discovery of its site of formation. The prize was awarded, 3 years later, to the author of a paper proving that the ovum is formed in the uterus!

Our story concludes about the first of May, 1827. Karl Ernst von Baer, studying the embryology of the dog, had departed slightly from the usual procedure of examining the embryos in sequential stages of development and was working backward instead, taking themselves expelled from the ovary, nor does it seem likely that such solid corpuscles as we find the tubal ova to be are formed by coagulation of the follicular fluid. Examining the ovaries before making any incision I saw plainly in almost every follicle a yellowish-white point. . . . Led by curiosity rather than by any thought

the next step was to learn the state of the ova in the ovary, for it is very clear that such minute eggs cannot be the graafian follicles that I had seen the ovules in the ovaries through all the layers of the graafian follicle, I opened one of the follicles and took up the minute object on the point of my knife, finding that I could see it very distinctly and that it was surrounded by mucus. When I placed it under the microscope I was utterly astonished, for I saw an ovule just as I had already seen them in the

Fig. 4. One of the anatomic drawings of the female generative organs in De Mullerum organis.
Reinier de Graaf* was born in Schoonhaven, Holland, July 30, 1641. After completing his early studies in Delft, he continued his training in France under de la Boë, then returned to Delft where he entered the private practice of medicine. When only 23 years old, and while still a student, he published his famous De natura et usu succi pancreatici, which reported his pancreatic-fistula experiments and established the digestive function of the pancreatic juice. He subsequently studied the functions of the bile by the same method. Four years later, in 1668, his De virorum organis generationi inservientibus appeared, dealing with the anatomy of the male genital organs and giving especially good descriptions of the vasa deferentia and the spermatic tubules of the testicle.

It was his De mulierum organis, however, published in 1672, which achieved for de Graaf his greatest renown. This volume contains a full and remarkably accurate account of the female reproductive organs, including certain gynecologic disorders, and is beautifully illustrated with detailed drawings (Fig. 4). In it he described the pelvic blood supply, the lymphatic system of the uterus, and the crura of the clitoris, in addition to the ovaries and their function. He also reported on prolapse, myoma, and closure of the fallopian tubes, illustrating the last condition with excellent drawings (Fig. 5), probably the first recorded of this common affliction, with the titles Oviductus extremum Testibus Naturam agglutinatum and Oviductus extremitas praeter Naturam clausa. Gonorrhea was not mentioned by de Graaf as the cause of tubal closure, but he clearly recognized the paraurethral ducts as a focus of this disease.

De Graaf had been deeply aggrieved by Swammerdam's reckless and damaging charges against him; and although de Graaf published a pamphlet in his own defense which convincingly absolved him of all taint of plagiarism or dishonor, he continued to brood over the affair. Some believe that his continuing preoccupation with this unpleasant incident was a factor in his premature death on August 17, 1673, at the age of only 32 years.

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REFERENCES


