

GENERAL STAFF MEETING  
MINNESOTA GENERAL HOSPITAL  
UNIVERSITY OF MINNESOTA

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THE NEEDS OF CANCER RESEARCH

Editorial from Amer. J.  
of Cancer, XVII, 154-157  
(Jan.) '33.

Some time ago the writer was asked by an inquisitive reporter to state categorically just what was needed to solve the cancer problem. The reply was: First and foremost, brains; second, time, and third, some money. Recently it has been said that the extraordinary advances in the theory and application of physics have shown that, if an organization could be assembled such as the Research Laboratory of the General Electric Corporation, or one of the laboratories of the great chemical industries in Germany, with two or three million dollars, the cancer problem could be solved in a few years. The only reply necessary to this admirable bit of optimism is that, if this were true, the three million dollars could be collected over night.

Let us take up first the problem of brains. Everyone thinks that genius is widely distributed, and all that is necessary to obtain results is to offer a sufficient amount of money. This statement is still being made in the face of the world-wide breakdown of civilization, of banking, and of politics! Where are the constructive brains in these fields today? There are available at present a few most competent men who, if given the power, could do much to straighten out the financial difficulties of the world, but instead the power is largely in the hands of the incompetent. And if such power were granted to the exceptional, would they invent any new method? Would they discover anything new in finance that is not already known? Has anyone found a means of preventing waste, poverty, political idiocy, racial jealousies? The cancer problem is as difficult as any one of these. Probably not in the entire world of science are there fifty men who are competent to produce first-class research in cancer. This does not mean that there are not a mass of second-rate minds who could do the hod-carrying, as Huxley phrased it, for cancer research, and pile the bricks of observation in little heaps where the master-mason could obtain his material for generalizations,

but hod-carrying never achieved anything more than piles of bricks and heaps of mortar. Before the building can even take shape, there must be the great architect with his vision, the engineer with his mathematics and knowledge of permissible stresses in steel, limits of speeds of elevators, and electrical technic. The hod-carrier often thinks himself the most important member of the organization, and never sees the planning mind behind the whole, never realizes who directs him. Of the fifty who are competent, many are not physicians, are not working in hospitals, have no idea that they are adding facts which some day may solve the cancer problem. They are working instead in zoological or chemical laboratories, discovering facts which may eventually be of use in the ultimate structure.

The cancer problem is a problem of life, of those forces which make cells grow, divide, and die. The cancer problem in its cellular aspects can be studied just as well in the chemical laboratory, or at any zoological station where marine material is available, as in the hospital -- better, in fact, because human beings with cancer cannot be experimented upon; they can only be observed and treated according to our best knowledge. Yet such observation and classification are exactly what men like Linnaeus and other collectors and classifiers of plants did before 1859, what all the breeders of domesticated animals did before that date, what the geologists did who studied the strange fossils found in the rocks. Then, suddenly, Charles Darwin saw, as in a dream, running through all this dull accumulation of facts the thread which, when followed, led to that generalization which is one of the great discoveries of human genius, which has fertilized all subsequent genetic studies, and in the hands of men like Morgan, and others too numerous to name, has clarified the mechanism of heredity until we are approaching the control of animal structure in much the same way that the German chemist was able to produce a dye of a given color on request.

Cancer is still waiting for its Darwin, and it may be long before he arrives. He will never arrive unless the facts are ready for him to shape his dream, unless the laborer does his work and provides the bricks and mortar.

What we need, then, for cancer research are men whose minds are trained in the experimental methods of zoology and chemistry, who have ideas which are capable of being attacked experimentally, who have enormous patience, and a certain amount of self-confidence which will keep them at work when everything goes wrong and experiments lead to nothing.

We need fresh technical methods of attack. The great Paul Ehrlich, who discovered salvarsan, renounced the cancer problem as insoluble with our present technical methods, and turned to the production of a drug which would attack a particular organism, and succeeded. He knew the limitations of his field--one of the striking characteristics of a genius.

Time, therefore, is necessary. The investigator never works well when driven by efficiency methods. If he were happy and effective under these conditions, he would be a banker or the head of a great manufacturing corporation, selling motors or lead pencils or diary products. But the true scientist cares more for a new discovery than for money, and this is fortunate, because he never will be paid anything commensurate with his labor. He will not care who patents what he finds. He will not care if he works for years and fails, because at least he can save someone else from travelling the same road. Nevertheless, he must have a certain shrewdness in attack. The saddest sight in the world is what may be termed the rabbit type of research, best imaged by the dog who spends hours barking at a rabbit hole and diffing frantically, while the rabbit has fled, miles away. If the dog knew more of rabbit psychology, he would give up; so the researcher must know when he is beaten.

Where the solution of the cancer problem lies, no one knows. If, therefore, studies in zoology produce no results, turn to biological chemistry; turn to serology; turn to physics. If a frontal attack

fails, try to turn the flanks. Somewhere facts will be obtained which fit into the plan which the master is ultimately to draw. How cruel to tell the investigator if he would only work a little harder, he would be paid more money; if he were only paid enough money, he would be able to make much more important discoveries! President Woolsey of Yale once said that college salaries should never be large enough to attract a man for the money alone. That danger has been successfully avoided so far in the educational world, and promises to be for a long time to come, but the fact remains that more money paid to a man will not sharpen his wits. Therefore, the point made earlier in this discussion--that at present only a moderate amount of money is needed for cancer research.

There are already in this country and Europe several large institutes doing cancer research, and a number of smaller ones, which have excellent facilities for research, and in which a moderate additional income would care for all the really competent men that are available at the moment. Some of these men are now in universities scattered throughout the world. They are spending their time teaching because no money is available for research. Such a man may be given a moderate sum to enable him to divert his interests to this special field, and a small amount for supplies and assistants in order to produce that of which he is capable. When his ideas are exhausted, he can return to his teaching and the money be diverted to those with new ideas.

There are but few minds which are capable of continuous production, and the time for productive work in any man's life is short. The young man is usually the one with ideas and sufficient energy to apply them. Yet he needs the advice, instruction, and criticism of a more experienced person. At forty he may be wholly ossified mentally, as regards research. One of the greatest difficulties that the director of any research problem has is to find suitable positions for these men who have ceased to be useful in their very narrow lines of investiga-

tion, and one of the dangers of large institutions, as is well known, is loss of effectiveness which results from decline of initiative.

It is obvious that the making of individual grants of the type suggested is fraught with the danger of losing the entire investment by conferring it upon some person whose ideas are much more magnificent than his capacity to achieve them. Very often the problem, though clearly visualized, is not capable of yielding to direct experimental attack, and for this reason a certain number of negative results may be expected, so that those who wish to spend their money on cancer research must be aware of the fact that 100 per cent dividends are never seen in science. Nor is there any formula for selecting an individual who is capable of stumbling over some important fact. The only basis for allotting such funds is a careful study of the man's previous record by an expert. If he has done good work in the past, he is likely to do good work in the future. So it seems that the endowment of cancer research today should be in part at least unrestricted.

But far more important than funds, and far more difficult to find, is a constructive and resourceful mind. Any idea that the setting aside of a large sum of money, and the organization of a commercial type of laboratory, will accomplish in a few years some stupendous achievement is to confuse commercial invention with scientific research, and though great commercial laboratories have occasionally produced some splendid discoveries in pure science, it has not been the laboratory nor the money, but the brains of an individual which were responsible, and the discovery would probably have been made, no matter where that individual was working. The facilities and the leisure which have been granted to him may have enabled him to make the discovery earlier, but I know of no great single discovery in science which has been due to money alone, or cooperative work alone; rather it was due solely to the vision of the individual intelligence that produced it.

## I. ABSTRACT

### UTERINE HEMORRHAGE, CAUSE, DIAGNOSIS, TREATMENT

Abstr. Ritchie.

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"Older textbooks have little to say  
on this subject and much of their material  
is obsolete because our concept of genital  
physiology has changed in the last quarter  
of a century." (3).

Most of the causes of uterine hemorrhage  
are familiar but lately a great deal  
is being said about dysfunctional types of  
bleeding, i.e. those due to endocrine  
dysfunction. Type is characterized by  
hyperplastic endometrium,—"hyperplastic  
endometritis", "Swiss cheese endometrium",  
etc. We now know that while the uterus  
is the point of origin of menstrual flow,  
it cannot itself initiate it. We also  
know that the uterus responds to stimulation  
of the ovary whose hormones cause  
first, proliferation (hormone of graafian  
follicle) and then secretory activity  
(stimulated by corpus luteum).

A general review of all types of  
uterine hemorrhage is attempted.

#### Classification:

There are many different classifica-  
tions of uterine bleeding. Generally  
speaking, uterine bleeding can be classi-  
fied under two main heads. (4, b).

- A. Physiological bleeding (menstrua-  
tion).
- B. Pathological bleeding ((menorrhagia  
prolongation and accentuation of normal  
menstrual period) and metrorrhagia, irre-  
gular uterine bleeding which occurs between  
periods, and polymenorrhoea)).

From this point on there are  
several different classifications. Phan-  
ouf, Schmitz, Cullen divide pathological

types of bleeding, with slight varia-  
tions, into:

A. Bleeding connected with pregnancy.  
(Of all conditions this is the one most  
mistaken for other disturbance (11).  
(Probable pregnancy causes 90% of all  
uterine hemorrhage (?)--opinion of  
Fulkerson (10);

(1) Abortion and miscarriage  
(threatened, imminent or inevitable;  
complete or incomplete). (Bleeding  
from spontaneous abortion usually less  
in duration and amount than in instru-  
mental abortion) (11).

(2) Ectopic pregnancy.

(3) Hydatiform mole or cystic  
degeneration of chorionic villi. (More  
frequent in multipara. Sunde found  
5% of 240 cases became malignant. (9).  
Occurs 1 in 2400 or 3000 cases -  
Williams.

(4) Chorio-epithelioma. Sunde  
found 44% developed from hydatiform  
mole, 30% after abortions and 22% after  
labor. (9).

(5) Placenta praevia. Hemorrhage  
without pain in last trimester of preg-  
nancy usually due to one of varieties  
of placenta praevia. (4, b).

(6) Premature Separation. Uter-  
ine bleeding with pain in last trimester  
of pregnancy usually due to premature  
separation. (4, b).

(7) Retained placenta. No  
further discussion of these types of  
bleeding.

B. Bleeding not connected with  
Pregnancy. (4, b).

1. Benign.

- (a) Endocrine
- (b) Hypothyroidism
- (c) Blood diseases
- (d) Vascular hypertension
- (e) Uterine adenomyomata
- (f) Polypi, cervical and  
corporeal.
- (g) Uterine malposition and

regeneration of cervix.

(h) Subinvolution of uterus

and hyperplasia of endometrium.

(i) Pelvic inflammation

(j) Benign tumors of ovaries

(k) Functional bleeding

## 2. Malignant

(a) Carcinoma of cervix

(b) Carcinoma of corpus

(c) Sarcomata

(d) Malignant tumors of ovaries

Other classifications all take in previous causes but several others are added. Hudson's (Minnesota) classification more explanatory. Limited to Gynecological Types.

## Causes of Uterine Bleeding

1. Infection of internal genitalia.
2. (a) Ectopic pregnancy  
(b) Threatened or inevitable abortion  
(c) Missed abortion
3. Tumors  
(a) Polyps - endometrial, fibroid, placental  
(b) Myomata  
(c) Carcinomata  
(d) Ovarian cysts
4. Displacements of uterus  
(a) Prolapse 3rd°  
(b) Retroversion (in the puerperium or if associated with injected genitalia).
5. Endocrine  
(a) High or low basal metabolic rate  
(b) Cystic ovaries  
(c) Anterior pituitary disturbances  
(d) Pubescent genitalia  
(e) Unclassified endocrine causes
6. Acute infections (especially if severe)
7. Chronic diseases (especially if nutrition suffers), e.g. tuberculosis, blood dyscrasias, cardiac decompensation, etc.
8. Trauma
9. Fibrosis uteri - a very rare condition.
10. Hyperplasia - seldom primary, usually secondary to displacements of uterus with or without infection or to

cystic ovaries.

## Causes:

### A. Benign:

#### 1. Endocrine bleeding or dysfunctional bleeding.

Knowledge is scanty.

Hemorrhage found in 9% of cases of endocrine dysfunction in Woman's Hospital (N.Y.C.) (10). Hemorrhage less severe and of shorter duration in spontaneous abortion than in instrumental (11). In menstrual cycle graafian follicle influences normal proliferative stage of endometrial cycle (hypertrophied, lengthened, tortuous glands), then ovulation takes place and hormone of newly formed corpus luteum transforms endometrium into secretory organ.

If for some reason ovulation does not take place, graafian follicle persists and no corpus luteum is formed. Consequently, endometrium, in absence of hormone of corpus luteum does not undergo accustomed premenstrual stage; but, under the influence of persisting graafian follicle acquires an irregular growth commonly called gland hypertrophy, gland hyperplasia, or "Swiss cheese" endometrium (8, a). Picture really represents persistence and an exaggeration of the picture seen in the so-called interval phase of endometrium.

Not so simple to explain mechanism of bleeding in endocrine dysfunction. Schroeder believes it due to small localized areas of necrosis on surface of endometrium (Also Graves). Novak - difficult to believe such punctate areas can be cause of abundant hemorrhage often seen. More likely due to some change in permeability of vessels since there is no desquamation as with normal menstruation. That endometrial lesion in itself cannot be responsible for bleeding indicated by fact that exactly same histological picture is seen in amenorrhea. Formerly would be considered heretical or paradoxical statement but has been observed by Novak et al in small number of instances (1).

Novak and associates emphasize importance of ovario-hypophyseal interaction and its dysfunction is bleeding. No doubt chiefly responsible for alternating phases of long continued amenorrhea and persistent bleeding seen in some instances.

Known fact that hypophyseal lobe undergoes marked hypertrophy during gestation (?), and to this are attributed cromegaloid changes at times seen in later pregnancy which disappear following pregnancy (?). This fact only suggestive as far as a possible role of anterior pituitary in etiology of functional bleeding is conceived.

However, observation of Smith and Angle, Zondek and Ascheim (for ref. see ref. 1), demonstrate subordination of ovary to anterior hypophysis. Hartman, Piror, Geiling (for ref. see ref. 1) conclude uterine bleeding (menstrual bleeding as well as dysfunctional endocrine bleeding) is due to active substance originating outside ovaries. They show that administration of anterior lobe hormone, in any form, to monkeys, results in bleeding whether animal be normal, sick, menorrhagic, castrated, hypophysectomized, old or young. However, (Novak) does not believe that this can be accepted as factor responsible for bleeding of normal menstruation (1).

Preceding work draws attention to one type of endocrine bleeding which involves in some way ovario-hypophyseal interaction. (For further discussion see anterior pituitary luetinizing substance in treatment).

Hypothyroidism as cause of menorrhagia probably due to perverted calcium metabolism which produce diminution in coagulability of blood (8, b).

Another type of endocrine bleeding is linked with ovarian hyperfunction and thyroid hypofunction. Meigs suggested ovary in some way compensated for an abnormally low thyroid secretion and in consequence of ovarian hypersecretion menorrhagia resulted.

## 2. Ovarian cysts and tumors:

Menstrual function not greatly

disturbed by ovarian tumors but they may cause bleeding even after menopause (8, b).

Hemorrhagic cystic disease most common cause.

Simple cysts unless having twisted pedicle seldom cause bleeding.

## 3. Blood dyscrasia:

(a) Chlorosis - Virchow distinguished between menorrhagic and amenorrhagic form (latter most common).

Otten studied 448 cases of chlorosis and of 262 cases with disturbances of genital function (delayed menorrhagia, amenorrhagia, etc.) there were a few instances of menorrhagia (8, b).

(b) Hemophilia - probable that few severe menorrhagia and metrorrhagia that occur at puberty have hemophilic source (8, b).

(c) Thrombocytopenic purpura. More often found in adolescent girls. More than three times as common in women than men (8, b).

4. Vascular hypertension. Same cause as epistaxis?

5. Myomata - occur with great frequency. Many give no symptoms. Most important effect is bleeding. Rare under 25 years. Usually begin growing between 25 and 40. Become subject to treatment between 40 and 50. Bleeding more common from submucous type. Bleeding of menorrhagic type (8, b).

6. Adenomyomata - endometriosis (chocolate cysts of ovary, etc.). Great interest lately. Discussion centers around origin of endometrial tissue when found in extra-uterine areas. Found in round ligaments, Fallopian tubes, rectogenital space, alimentary canal and umbilicus as well as in uterus. Great majority appear between 30 and 50 (8, b).

## 7. Polyps.

(a) Cervical, - most common after puberty. Chief symptom is bleeding, mild in character, apt to be menorrhagic. (8, b).

(b) Mucous polyps of endometrium less common than cervical. Same symptoms.

8. Displacement of uterus. Owing to obstruction of circulation and permanent hypertrophy of endometrium common in retroverted uterus, various degrees of menorrhagia are encountered.

9. Subinvolution of the uterus. Fibrosis uteri, rare condition. Clinically, characterized by bleeding from senile uterus. Curettage shows atrophy of the endometrium. Uterus somewhat enlarged. Bleeding may be due to functional rather than anatomical disturbance. (9).

10. Hyperplastic endometrium - See #1. Corpus luteum hormone does not develop).

11. Pelvic inflammation. Menorrhagia and metrorrhagia not uncommon in acute inflammation of Fallopian tubes. More pronounced when ovaries are involved (4, b). Menorrhagia may follow period of amenorrhea, this sequence in connection with pelvic pain and a palpable mass may cause excusable diagnosis of extra-uterine pregnancy (8, b).

12. Chronic diseases (especially of nutrition suffers tuberculosis, cardiac decompensation, etc.)

## B. Malignant:

1. Carcinoma of cervix about 50% appear between 35 and 50, about 30% after 50, 20% 30. Bleeding is one of three cardinal signs (leucorrhoea, bleeding, pain). Ready bleeding on slightest manipulation suggestive. (8, b).

2. Carcinoma of corpus uteri. Bleeding and blood-stained discharge after the menopause always suggest malignant disease (but do not prove it), whereas according to Gordon, before menopause and up to age of forty-five, cancer of cervix is twenty times more probable than cancer of body of uterus; as 50 is approached probability of carcinoma of body of uterus becomes equal to that of carcinoma of the cervix (4, b). Different figures show

from 2% to 35% of uterine carcinoma are of body. Bleeding is "spotty" and usually excites attention as it occurs after the menopause. (8, b).

3. Sarcoma - a rare occurrence.

## Statistics:

Schmitz - study of 2523 consecutive gynecological cases. (Cases - 2393) - number of bleeding uteri - 791 (33%). Inflammatory lesions of tubes and ovaries furnished largest number of cases of hypermenorrhoea, i. e., bleeding due to myoma, hypoplasia, asthenia, pelvic infection and general stasis, 51% of 386 cases. Inflammatory lesions of ovaries furnish largest number of cases of endocrine bleeding - 67% (71 cases).

Kanter and Klawans - Post-menopausal bleeding - 98 consecutive cases. Carcinoma of: Cervix 52%, corpus 11%, vagina 1%, ovary 1%, vulva 2%, zona granulosa tumor 1%, senile vaginitis 3%, urethral caruncle 2%, fibromyomas 7%, erosion of cervix 3%, prolapse of uterus 5%, polyps of cervix 8%, ulcer of vagina 1%, fibrosis uteri 2%, total 100%. 11 patients had been bleeding more than one year while 53 were seen within first six months.

## Treatment:

Up to the present time curettage was and still is favorite method of treatment for bleeding, especially for hyperplastic type of endometrium. It is fully realized however that the curettage is not reaching basic cause of the trouble, but it has been our only rational method available. X-ray and radium are of particular interest and are now more widely used. Organotherapy has possibilities?

## Brief resumé of treatment:

(a) Endocrine bleeding (functional). Little of definite value for permanent cure. Curettage with full realization that condition may return is most popular (Miller).

Radium and x-ray must sometimes be used in young girls in which every other method has failed and hysterectomy would otherwise have to be resorted to. In older people if lesion is benign and there is no history of previous infection, radium is specific (Miller).

Hysterectomy is last resort.

Organotherapy - previous efforts unsuccessful. Novak et al treated 51 cases of functional bleeding with prolan B., the luetinizing hormone of anterior pituitary body. In 44 of cases, treatment was successful in stopping hemorrhage (?).

(b) Blood diseases and hypertension.  
Treat general condition.

(c) Myomata depends on size and situation. Myomectomy favored in young women. After menopause opinion is divided as to use of radium or surgery. (4, a).

(d) Adenomyomata - hysterectomy, radiation (for small ones). (4, a).

(e) Polyp - surgical removal.

(f) Uterine displacement - correction.

(g) Fibrosis uteri. Use of ergot, pituitary extract, calcium lactate in doses of 60 grains a day for one week. Curettage proceeded by use of these drugs is useful. Radium therapy is useful. (4, b).

(h) Hyperplastic endometrium - See #1. (Curettage, x-ray, radium, organotherapy, etc.).

(i) Malignant disease.

(1) Cervix- all agree that in advanced cases radium and x-ray offer only hope. In early cases, opinions differ on surgical or radiation therapy. (8, b).

(2) Uterus - In contradistinction to carcinoma of cervix, a pan-hysterectomy is advocated in operable cases, otherwise radiation. (8, b).

(3) Sarcoma - panhysterectomy.

### Radium Therapy in uterine hemorrhage of benign origin (8a)

(1) Radium employed in properly selected cases valuable.

(2) Finds its greatest field of usefulness in women near or at menopause, having severe hemorrhages from uteri showing no gross macroscopic lesions as hypertrophy and hyperplasia of the endometrium.

(3) It should be used cautiously to avoid hysterectomy in the hemorrhages of adolescence and only after medical endocrinal and hemostatic treatments have failed. Here it should be used in minute doses.

(4) It is of value in treating small fibromyomas of the interstitial type especially in women nearing the menopause (subserous fibroids, if pedunculated are but little affected by radium).

(5) A single application giving an appropriate dose is sufficient to bring on a permanent amenorrhea.

### II. ABSTRACT:

#### THE THERAPEUTIC AND DIAGNOSTIC VALUE OF CURETTAGE IN SO-CALLED FUNCTIONAL UTERINE BLEEDING.

Geist, S.H. and Glassman, O.  
A.J. of Obst. & Gynec. 23:  
14-24, (Jan.) '32.

Abstr. Ritchie.

What is purpose of curettage and what value has it? That it is important and often necessary is unquestioned. Value as a diagnostic measure well-established fact. Necessity for its use in all cases before introduction of radium, or utilization of x-ray therapy is too well accepted to admit of discussion, but does it in addition hold out a hope of cure, and if so, in what type of case?

Novak mentions fact that cases of uterine hyperplasia and associated bleeding were not usually cured by curettage. Hintze had 24 cases of benign uterine bleeding, 20 of a serious type and 4 atypical cases. In follow-up, which lasted from four months to three years, had 6 cures in mild cases following first curettage; and 6 cures following second curettage from one and one-half to two years after the primary one. In severe cases hysterectomy or radiation alone gave good results.

Fuss, in 17 cases of the mild type, 13 patients were cured. In 14 cases of the moderate grade, 2 patients were cured, and of the 19 cases of the severe grade, none were cured.

Graves, Eden and Lockyer all mention use of curette as means of alleviating the bleeding associated with hyperplasia, but none of them believe it is curative.

Authors' study consisted of 142 cases. Attempted to determine if curettage alone was curative measure and to what extent it could be relied upon. Also endeavored to define a pattern from histologic study of mucosal shreds which would permit them to prognosticate in what type of cases a satisfactory, permanent result from curetting might be expected, and in what type other procedures were advisable.

Seventy-three cases were classified as cured by curetting, 69 as improved or unimproved.

#### Results:

##### (1) Age as prognostic factor.

Although the greatest number of cures was obtained between the ages of 40 and 45, a proportion of failures was greatest between the ages of 45 and 50. Too little difference in the 2 groups to enable us to utilize the age of patient as of prognostic importance.

(2) Marital status. No definite decision can be made from the marital status that would be of prognostic significance.

(3) Symptoms. Proportion of cured cases was strikingly similar to

those that were unimproved, or slightly improved, irrespective of whether the complaint was metrorrhagia, menorrhagia or polymenorrhea.

(4) Histological study. Curetted material gave more satisfactory data on which to base prognosis. 1. In those cases in which glands were not increased in number, cures most frequently obtained. 2. In those cases in which disturbance of glands either showed an increased number of glands, cystic or otherwise, in both superficial and basal layers with no definite arrangement, cures were definitely less frequent than where the disturbance of the increased or dilated glands was limited to the basal layer. 4. Those cases which presented cystic glands in large numbers were least amenable to treatment by curetting. 5. The character of the stroma did not seem to enable them to prognosticate the therapeutic result from curettage. 6. The surface of the mucosa was also studied and it was noted that in those instances where the surface was reported as polypoid, the proportion of cures was greatest.

#### Results:

9 patients cured with moderate or marked cystic glands. 6 were near menopause, 1 subsequently operated on for fibroids, 1 showed small adenoma in mucosa, 1 cured after 4 curettings.

24 cases cured with few cystic glands. 5 resembled subinvolution following pregnancy. 3 showed inflammation of endometrium. 2 were near menopause. 3 associated with polyps. 2 had adenomatous uterine polyps. 6 had no unusual findings.

41 cases cured with normal or atrophic mucosa.

52 cases unimproved. 9 had very few cystic glands. 19 showed cystic glands. 2 associated with fibroids. 2 were puberty bleeding. 2 were subinvolution. 2 had polyps. 1 was hydrosalpinx. 1 was inflammatory, and 1 showed a few cystic glands in basal layer.

The distribution of the gland content showed irregular distribution in 7% of cured cases and 29% in unimproved cases. In 3% of cases where increased content was limited to basals, there were symptomatic cures, while 9% of cases with basal limitation were unimproved.

In cases showing few cystic glands in the mucosa, 24% were cured, 16% were not cured. In cases showing marked increase in cystic glands, 15% were cured, while 47% were not cured. 61% of cases with no cystic glands were cured, while 37% of cases with no cystic glands were unimproved.

### Conclusions:

It is evident that neither from the type of bleeding, the duration of the symptoms nor the histologic data, can definite prognosis be made as to possibility of cure. It would seem, however, that in those cases with marked increase in gland content of cystic type with irregular distribution, the possibility of cure by means of curettage is unlikely.

Curettage then may be of curative value in inflammatory cases, those with polyps or polypoid endometrium with scanty or normal gland content, or in those cases where a subinvolution subsequent to a previously overlooked gravidity, presents the clinical picture of a functional metrorrhagia. All cases (except the puberty cases) should be curetted and observed, as a first procedure, and if necessary, with a recurrence of symptoms, recuretted before more drastic steps are taken.

### III. ABSTRACT:

#### THE PLACE OF THE UTERINE CURETTE

Evers, H. H.

Abstr. Ritchie.

States Berkeley once suggested addition to a woman's litany of the words, "From the obstetric forceps, and the uterine curette, Good Lord deliver us". Instrument was introduced by Marion Sims, and, <sup>as</sup> with any new method of treatment, it has passed through the usual phases (3). First it cured everything, then it cured

nothing-- and finally we feel that with the clearer conception and comprehension of pelvic pathology "a more rational attitude towards the curette seems now to be manifest."

States Fothergill clearly indicated various conditions for which the curette is useless:

(1) Leucorrhoea - as discharge in 99% of cases comes from the cervix and vagina.

(2) Congestive dysmenorrhoea.

(3) Dull aching pains in sides due to varicocele.

(4) Menorrhagia following illness or shock.

(5) "One-child sterility," menorrhagia or dysmenorrhoea in a patient who has a tubo-ovarian swelling.

Rawls made critical review of 6219 curettings done in Women's Hospital, New York, in a period of 11 years. He concludes that 96% of gynecological cases show no endometrial change and that curettage is of doubtful value in the remaining 4%. Busse found only 10% of cures in 505 cases of curettage for uterine hemorrhage; Schickele and Keller reported only 38 out of 111, i.e. about 35%.

Discussion divided into two groups:

Menorrhagia. (1) Irregular hemorrhage is always more serious than excessive regular hemorrhage. (2) In regular hemorrhage, always eliminate the general causes before proceeding to local treatment. (3) Irregular hemorrhage is always due to a local cause.

Important clinical considerations: (1) Age of patient. (2) Has intercourse ever occurred. (3) Has she been pregnant. (4) Was the hemorrhage or hemorrhages preceded by amenorrhoea of however short duration.

A. Endocrine Disorders.

Not enthusiastic about use of radium but favors use of curette.

B. Focal Sepsis.

The chief point to bear in mind about these cases is the futility of curettage. There is no disease of the endometrium and the curettage at best gives only a very transient relief, and, indeed, may be injurious.

C. Gonorrhoeal Infection.

Futility of curettage is mentioned. Is obviously essential to treat the cause.

D. Intramural Fibroids.

Small important group of cases appearing after 25 or 30. Curettage will arrest or relieve the leading symptoms, eliminate the possibility of malignant disease and save the patient an abdominal operation. Where the fibroid is complicated or submucous or sufficiently large to cause a material increase in the amount of menstruating endometrium, curetting will give little or no relief.

E. Subinvolution. (Fibrosis Uteri)

Curettage is generally tried but often gives only a temporary relief or may actually make the hemorrhage worse. Advocates radium.

Metrorrhagia.A. Retained placenta.

The curette probably finds its greatest use in the removal of products of conception.

B. Hydatiform Mole.

In all cases of hydatiform mole, however, whether spontaneously extruded or deliberately removed, I think it wise to follow digital exploration by a blunt curettage.

C. Septic Incomplete Abortion.

Advisable to remove the infected retained material as soon as possible. This, however, should be done as gently as possible with the finger and on no account should the curette be used.

D. Carcinoma of Cervix.

In carcinoma of the cervix, it is wise not to scrape the growth too much.

E. Carcinoma of Uterus.

Curettage for diagnosis.

Conclusions:

1. In young virgins, curettage is useless.
2. During the active child-bearing period, curettage is therapeutic.
3. In the region of, and after, the menopause, curettage is diagnostic.

Impressions:

1. Uterine bleeding may be classified as that associated with pregnancy or not - functional or pathological.
2. Types - metrorrhagia, menorrhagia, polymenorrhoea.
3. Associated disturbance elsewhere in body is striking feature of many of our cases.
4. A good pelvic examination is first essential in proper handling of case.
5. Dysfunctional or endocrinal bleeding is of special interest as it is type in which an attempt is made to explain it on the basis of the "newer physiology".
6. Blood dyscrasias should always be kept in mind as possibility.
7. Curette is used for diagnosis, treatment and in some, prognosis.
8. Pelvic examination, general study including laboratory aids is first step in diagnosis.
9. In most (certain exceptions) curettage is next with repeat scraping if necessary.
10. Radiation, or other means, in hysterectomy may be last resort.

IV. CASE REPORTENDOMETRIAL HYPERPLASIA

(Example of uncomplicated type? which is uncommon in our experience).

Case is white female, 25 years old, admitted to Minnesota General Hospital 10-21-31 discharged 11-7-31 (17 days); readmitted 5-30-32 and discharged 6-20-32 (21 days). Total stay 38 days.

#### Onset

1929 - Onset of Menorrhagia. Menarche at 13 years, always regular. Began excessive flow at each period, also dysmenorrhea. Period every 21 days, flow 4 to 6 days. Used up to 30 napkins during each period. Physical examination revealed Hb. 41%. Condition same up to admission.

#### Admitted to University Hospitals

10-21-31 - Past History: Frequent headaches and weakness during last year. Physical examination: Pallor. Head - negative. Throat - enlarged tonsils. Lungs - clear. Heart - normal, blood pressure 140/86, pulse 72. Abdomen - negative. Pelvic - external normal; cervix normal; corpus slightly ante-flexed, somewhat nodular on left border posteriorly. Laboratory: Hb. 70%. Urine - negative.

#### Curettage

10-22-31 - Moderate amount of curettings (last menstrual period 10 days previously). Microscopic - Some increase in number of glands, not much increase in stroma, glands moderately cystic.

#### Discharged

11-7-31 - Discharged after tonsillectomy.

#### Interval history:

First period following discharge, patient used 15 pads. Dysmenorrhea present. Last menstrual period one week before second admission. Duration 6 days. 8 pads used first day. Stated bleeding has been more but pain less.

#### Readmitted

5-30-32 - Laboratory: Hb. 77%.

#### Dilation and curettage

6-2-32 - Albert Smith pessary inserted. Microscopic examination - slight hypertrophy of glands with moderate cystic glands. Glands increased in number. Diagnosis: Endometrial hyperplasia.

6-3-32 - Suspension. No gross myomata found.

#### Discharged - Out-Patient Dept.

6-20-32 - Discharged from hospital.

7-21-32 - C.P.D. Last menstrual period one week before. Used 17 pads during 4 days. Passed few clots. Pelvic examination - negative except for some enlargement of the uterus.

8-22-32 - Corpus well anterior, bleeding less.

12-5-32 - Reports definitely decreased flow. Is she well?

#### V. ANNOUNCEMENTS:

##### 1. Thank You.

Pediatric nurses wish to thank staff for generous purchase of candy at last week's candy sale. A considerable sum was realized which will be devoted to additions to their library.

##### 2. Seminar - Preventive Medicine and Public Health.

4:30 P.M. - Staff Room - Students' Health Service.

Feb. 10 - Meet in Room 15, Auditorium, Medical Science Building, where Dr. Riley will show the film - FISH TAPEWORM IN MAN.

Feb. 17 - Dr. deBerry - Some Case Reports.

Feb. 24 - Mr. C. A. Dahl - A Study in Air Analysis in Relation to the Hay Fever Pollen in Minneapolis.

Mar. 3 - Dr. Riley - Observations on the Situation in China during the past year.

March 10 - Miss Butzerin - Topic to be announced.

March 17 - Dr. Roise - Interpretations of some Common Symptoms related to the Ear, Nose and Throat.

H. S. Diehl, M.D., Director.

### 3. Meeting:

Date: February 2, 1933  
Place: Interne's Lounge, 6th Floor, West Building.  
Time: 12:13 to 1:38 P.M.  
Program: Cause and Treatment of Burns.  
Present: 99

#### Discussion:

Irvine McQuarrie  
 Carl Waldron  
 C. H. Mead  
 H. G. Scott  
 N. L. Leven  
 A. E. Hansen  
 W. T. Peyton

#### Theme:

I. McQ.: About baby who had good tannic acid result and then died suddenly. Afraid it was too much codein (difficult to prove). One should be very careful in giving big doses to babies as they are different from adults. Chloral hydrate or morphine in small doses would be better. I had an opportunity to see a great many burns with Davidson. Tannic acid treatment is striking. Give at once 1/4 grain morphine to adults; children smaller doses; then tannic acid is sprayed every 15 minutes. Removal of blisters quite worth while. Open up early, removing gently unless there is too much shock. Spread on until brown, stop then because it gets blacker from then on.

About 5 to 7% solution is used. Pituitrin or pitressin also effective. We use them because they tend to combat shock and at the same time aid water metabolism, but don't keep them up too long. The thing that impressed me so forcibly in Detroit was absence of scars when infected necrotic tissue was lifted and beautiful skin is found underneath. Tannic acid used after primary pain is treated with morphine. These people rarely have pain later except when wounds are dressed. Delayed death in our case showed bleeding everywhere. Must have had some change in blood which allowed it to ooze everywhere which might have been

checked by more transfusions.

C. W.: - I had opportunity to see quite a few of the cases of Blair and Brown in St. Louis. They seemed to be very keen about the use of salt solution bath, salt solution packs and getting the children up and about the wards, using legs or arms that were burned. As soon as granulations are fairly healthy they aim to prevent scar contracture and deformity by grafting. Perhaps from article you get the idea that they are opposed to tannic acid treatment. That isn't their viewpoint.

Selected group of cases, particularly those involving arms and legs get out much sooner by other treatment. I don't know whether they have been able to classify the degree of burn where they should use tannic treatment or substitute salt solution. Now and then dichloramine-T used. Early repair shortens length of time of treatment, preserves function, and gets child or adult back to activity much sooner. I would like to have the opportunity of trying out some of their principles on the cases that come here, i.e., early grafting.

Use suction apparatus that holds skin graft. Here we usually depend upon 2 or 3 assistants. We have to use either arm or leg and bring the skin on tension by one hand under limb. They cut huge grafts from abdominal wall by suction apparatus. We know that a split graft has a better chance of take than a full thickness. By use of suction apparatus can start on chest and go down almost to symphysis. That has changed usefulness of skin grafting because under the older methods of skin grafting we couldn't get them uniformly thick.

One interesting case is on West 4, where we restored her burned hand by removing scar tissue and burying it in pocket of skin. Grafting burns is interesting field. We know that as an aftermath of uterine tumors severe keratosis with beginning malignancy often develops just above the symphysis pubis and they have to be grafted.

**Movable area.** Usually get big graft and bury it by sewing it around.

In my experience lots of failures due to not keeping graft quiet. Use manometer to test tension (Smith). For success pull skin up to its previous state of elasticity or tension, use pressure of approximately 20 m.m. Hg. Forehead grafts almost always take. Practically always take in mouth, although working in aseptic field yet you can put a skin graft in the mouth on a dental mould and get good takes.

C.H.M.: - I do not wish to precipitate a plastic surgery argument, but I wish to call attention to the use of implant graft advocated here by Dr. O. H. Wangenstein. We used some on a patient on P-5, who had second degree burn, extending from iliac crest over both lower extremities to malleoli, involving posterior and lateral aspects of both extremities. Total areas removed were very small because of frailness of patient and small amounts of normal skin available.

Probably three areas of skin removed, less than the size of a dollar, cut into small bits, and implanted into the granulation tissues, resulted in complete epithelization of burned areas. I was informed by a plastic surgeon that implant grafts did not produce skin, and were very unsatisfactory (unsuccessful). This case and others which I have treated in the same fashion have resulted in excellent epithelization with a minimal amount of skin implant.

Furthermore, I wish to call attention to the importance of palpation of the tissues in fresh burns for crepitation as an indication of development of gas bacillus infection. I had the honor at Minneapolis General Hospital of being accused of precipitating an epidemic of gas bacillus infections because by carefully following burned cases with Dr. R. I. Stewart. We picked up many cases of gas gangrene following burns. Important feature is daily palpation of tissues - not observation - as temperature and pulse are high due to burn and consequently no general reaction to indicate presence of gas gangrene. As a result of careful observation of these cases we had the

surgical pleasure of doing many amputations.

H. G. S.: - Similarity between effects of strangulation obstruction and burns is striking. We have not been able to demonstrate toxic factor in obstructed dogs. We believe that changes in blood volume are more important. It seems better to ascribe primary shock to loss of blood volume (escape from vessels or redistribution) and to give whole blood transfusion at once in cases. Cases of delayed shock may be due to plasma loss in the burned area. Would it be better to try delayed tannic acid treatment in all cases in which shock was present? Local effect of tannic acid on the burned area might produce further shock through changes in local blood vessels.

N. L. L.: - Seeger of Milwaukee discussed the question of tanning with a leather manufacturer. He told him that they had a great deal of difficulty in tanning different batches of leathers because of variation in the acidity of the tannic acid. By using tannic acid of Ph. 7.4 they got better results in their burned patients. I wish to recommend pinch grafts which in my experience have been even more successful than implant grafts.

A.E.H.: - Cysteine is found in large amounts in the hair and epidermis. We thought of possibility of hurrying skin growth by putting this substance on involved area. In a little girl we have upstairs at present time we thought burned area taking cysteine from body might be responsible for loss of her hair. The dermatologist suggested the possibility of ring worm as the cause of condition. We tried cysteine for its effect on regeneration of epithelium but it did not do any more good than the control treatment.

W.T.F.: - Called attention to new type of electric heating pad now used in this hospital instead of hot water bottle. Instructions must be carefully followed to avoid burning especially in unconscious patients.