ROLE OF VASCULAR ARCHITECTURE OF THE ENDOMETRIUM IN THE ETIOPATHOGENESIS OF DYSFUNCTIONAL UTERINE BLEEDING

by

SHEELA PURKAYASTHA,* M.D.,
PARVATI K. MALKANI,** F.R.C.O.G., F.A.C.S., F.A.M.S.
and
KAMAL BUCKSHEE,*** M.D.

Introduction

Endometrial blood vessels undergo cyclical changes throughout the menstrual cycle. This was studied by Markee (1940) and Hasner (1946). Study of vascular architecture in dysfunctional uterine bleeding is rather a new approach to the subject. Deviations from normal patterns are often noted in different types of dysfunctional uterine bleeding. That dysfunctional uterine bleeding is sometimes associated with normal endometrium showing abnormal vascular architecture has led to the concept that these abnormal blood vessels might be responsible for its etiopathogenesis.

As early as 1950, Schwarz and Sherman have studied the definite relationship between hyperplastic endometrium and hypertrophy and hyperplasia of the uterine blood vessels. Later on Faulkner (1951), Salvatore (1968) and Blaustin and Shenker (1970) found that hyperplastic endometrium was frequently associated with abnormal arterioles. High incidence of abnormal venules was also noted by Sippe (1962) in hyperplastic endometrium. Salvatore (1958) in his study of 100 cases of dysfunctional uterine bleeding found that 71% of endometria showed alterations in the arterioles.

*Medical Officer, Santoria Dishergarh, Dist. Burdawan.

**Professor of Obstetrics & Gynaecology, All India Institute of Medical Sciences, New Delhi.

***Assistant Professor of Obstetrics & Gynaecology, All India Institute of Medical Sciences. New Delhi.

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Vascular Architecture of the Endometrium during Normal Menstrual Cycle

Some changes observed in the blood vessels during the normal cyclical changes of the endometrium which were studied by Hasner (1946) in detail and can be summarised as follows:

Proliferative Phase—The arterioles are thin walled with a small calibre. The inner elastic coat is sparse. The intermediary coat consists of two or three layers of smooth muscle cells. No thrombosis or degenerative changes are noted. There are two categories of veins found; the comparatively thick walled stems and their plexus in which incipient distension occurs.

Secretory Phase—The arterioles become coiled. There is increase in the elastic fibrils in the intermediate coat.

The stroma surrounding the arteries become loose and edematous making the arteries prominent. In the late secretory phase the endothelial cells are swollen but there is no endothelial proliferation. The muscle cells have the appearance of being subject to a diffuse pre-hyalinisa-

tion. The veins are more distended and are thin walled. Such enlargements may be developed into the so-called venous 'lakes'.

Menstrual Phase—The degenerative changes in the wall reach the maximum and in the compact layer the finer structure of the arterial wall may be obliterated. The capillaries show extreme distension in the entire superficial region. Here the vascular walls show endothelial swelling and degenerative features.

Regenerative Phase—The adventitial layer becomes more well defined. Degenerative changes disappear. The endothelium is budding off new formed cell groups. Similar changes are also seen in the venous system.

Material and Method

Endometrial histology with special reference to the vascular architecture was studied in 125 cases attending the Gynaecological Out-Patient's Department of All India Institute of Medical Sciences Hospital, New Delhi. Of these, 25 women were eumenorrhic and 100 were patients with presumptive diagnosis of dysfunctional uterine bleeding.

Endometrial tissue was obtained by either endometrial biopsy or curettage, fixed in 10% formol solution and sections stained with haematoxylin and eosin.

Histopathology of the endometrium was studied according to the criteria for dating the endometrial biopsy as established by Hertig, Rock and Noyes (1950). The features of vascular architecture of the endometrium were recorded as:

I. *Spiral arterioles*
- (1) Size of the lumen
- (2) Endothelial proliferation
- (3) Muscular hypertrophy
- (4) Thrombosis

II. *Venules*
- (1) Distribution
- (2) Size of the lumen
- (3) Thickness of the wall
- (4) Thrombosis

Observations

Endometrial pattern in 100 cases of dysfunctional uterine bleeding was as follows:

Secretory endometrium	26
Proliferative endometrium	33
Adenomatous hyperplasia	25
Cystic glandular hyperplasia	12
Irregular ripening of endometrium	2
Irregular shedding of endometrium	1
Atrophic endometrium	1

No abnormality in vascular architecture was found in 25 cases of eumenorrhic women. Out of 100 cases of dysfunctional uterine bleeding, 46 had abnormal changes in the arterioles. Abnormalities in venules were observed in 45 cases. Only 25 cases showed abnormal changes both in the arterioles and venules.

Changes in the Arterioles: The abnormal features in the arterioles (46 cases) were as follows: (Figs. 1 and 2).

Narrow or obliterated lumen	47.9%
Endothelial proliferation	41.3%
Muscular hypertrophy or hyperplasia	23.8%
Dilated arterioles	21.7%
Both endothelial and muscular proliferation	12.5%

Endometrial pattern in cases showing altered arterioles (46 cases).

(A)	Non hyperplastic	22
	(a) Proliferative phase	12
	(b) Secretory phase	9
	(c) Irregular shedding	1
(B)	Hyperplastic	24

Changes in the Venules: The abnormal features of the venules (45 cases) (Fig. 3) were:

Superficial in position	100%
Abnormally dilated	100%
Extremely thin walled	100%

Endometrial pattern in cases showing abnormal venules (45 cases).

(A)	Non hyperplastic	25
	(a) Proliferative phase	11
	(b) Secretory phase	13
	(c) Irregular shedding	1
(B)	Hyperplastic	20

Concurrent Changes: Endometrial pattern showing abnormalities both in arterioles and venules (25 cases).

(A)	Non hyperplastic	10
	(a) Proliferative phase	6
	(b) Secretory phase	3
	(c) Irregular shedding	1
(B)	Hyperplastic	15

Luminal Size of Blood Vessels: Relationship between luminal size of blood vessels and endometrial histology of 100 cases of dysfunctional uterine bleeding is shown in Fig. 4.

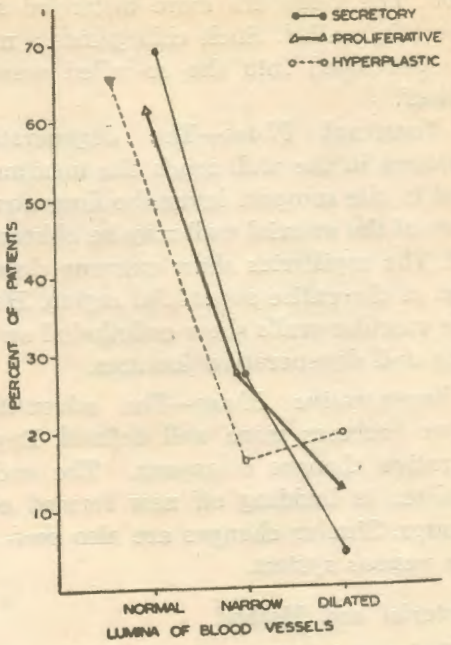

Fig. 4.
Relationship between luminal size of blood vessels and endometrial histology. (100 cases).

Discussion

Hasner (1946) studied in detail the changes in the vascular architecture of the endometrium in normal menstrual cycle.

Study of vascular changes in dysfunctional uterine bleeding is a rather new approach to the subject. Hoffman (1944) described numerous dilated, elongated, often thick walled vessels in hyperplastic endometrium and later on Schwarz and Sherman (1950) studied the definite correlation between hyperplastic endometrium and its vascular changes. Salvatore (1958) found the incidence of altered arterioles as high as 71% of cases of dysfunctional bleeding. In the present study altered arterioles were found only in 46%. Abnormal arterioles in the endometrium as observed by various investigators is shown below.

	DYSFUNCTIONAL BLEEDING		EUMENORRHIC WOMEN
	Hyperplastic (%)	Non-hyperplastic (%)	Secretory phase
Salvatore (1958)	80.3	31.5	—
Blaustein (1970)	66.6	—	Nil
Present study	52.2	47.8	Nil

In the present study abnormal arterioles were seen with almost equal frequency in hyperplastic and non-hyperplastic endometria, though Salvatore (1958) and Blaustein (1970) recorded higher frequency of abnormal arterioles with hyperplastic endometrium. It is evident that with non-hyperplastic endometrium also there can be alteration in the vascular pattern in dysfunctional uterine bleeding and these alterations may be responsible for menorrhagia and hypermenorrhoea. The abnormalities in the blood vessels, viz endothelial proliferation, hyperplasia or hypertrophy of the muscular coat, increased diameter of the lumen or its obliteration may be responsible for menstrual abnormalities, possibly due to;

(a) Inability of arterioles to contract and control the bleeding during menstruation.

(b) Narrowing or obliteration of the lumen resulting in stagnation of circulation leading to anoxia and subsequently bleeding.

(c) Arterioles with thick walls probably detach themselves more slowly, producing irregular shedding and prolonging menstrual bleeding.

Hoffman (1944) described markedly dilated veins beneath the surface epithelium of hyperplastic endometrium. Sippe (1962) found these typical sinuses in 77% of cases of hyperplastic endometrium. No relation could be established between the number and size of these sinuses and the intensity of the hyperplastic process. This was in agreement with both Novak (1947) and Ogilvie (1947). No such venules were seen in normal endometrium without any uterine pathology, viz. fibroid, polyps, thickened endometrium, etc. He believes that some mechanical irritation due to polyp, submucous fibroid or thickened endometrium is responsible for its formation.

Speert (1949) noted the presence of these abnormal, superficial, dilated, thin walled veins in endometria of postmenopausal women who showed cystically dilated glands. He considered that haemorrhage results from tearing of the thin walled sinuses. Similar findings were also noted by Davies and Williams (1953) and McBridge (1954) in postmenopausal endometria.

In the present study abnormal venous sinuses were found in 45% of cases. Hyperplastic endometrium showed abnormality in 54% of cases, whereas in non-hyperplastic endometrium abnormal venules were found in 40% of cases. Though the abnormal arterioles were found in 46% and abnormalities in the venules were noted in 45% cases, concurrent changes in the arterioles and venules were recorded only in 25% of cases. These abnormalities were observed in 40% of hyperplastic endometria and 16% of non-hyperplastic endometria.

Summary and conclusions

Histopathological study of 100 cases of dysfunctional uterine bleeding was done with special reference to the vascular architecture. In 46% of cases abnormalities in the arterioles were noted, whereas pathological venules were recorded in 45%. Only 25% of cases showed the concurrent changes in the arterioles and venules.

Abnormal vascular architecture was noted in some form or the other in 61% of cases of dysfunctional uterine bleeding. Though the overall frequency of abnormal blood vessels was higher in hyperplastic endometrium, but abnormal arterioles were almost equally prevalent in hyperplastic and non-hyperplastic en-

TABLE I
Endometrial Histology

Age Group	No.	Hyperplastic Endometrium	Nonhyperplastic Endometrium
Group A	7	1 (14.3%)	6 (85.7%)
Group B	54	20 (37%)	34 (63%)
Group C	39	16 (41%)	23 (59%)
Total:	100	37 (37%)	63 (63%)

TABLE II
Recurrence of bleeding after initial curettage

Age Group	No.	Recurrence (within one year) No.	No recurrence (within one year) No.
Group A	7	6 (86%)	1
Group B	54	30 (55%)	24
Group C	39	34 (87%)	1
Total:	100	70	26

TABLE III
Relationship of recurrence of bleeding to initial histology

	Hyperplastic Endometrium (37 cases)	Non hyperplastic endometrium (63 cases)
Recurrence	31 (83%)	39 (62%)
No recurrence	3 (17%)	23 (38%)

TABLE IV
Apparent cure

Therapy	No. of patients	Apparent cure upto 1 year
Surgical curettage	*100	26
Curettage supplemented with hormone	45	37

*31 patients had Hysterectomy done
6 patients were lost for follow up.

TABLE V
Resumption of ovulation

Therapy	Initial nonsecretory endometrium	Post treatment secretory endometrium	Pregnancy
Curettage	9	4	1
Curettage supplemented with hormones	25	17	3
Total	34	21	4

dometria. Thus, it may be concluded that abnormal vascular architecture is possibly a contributory factor in the causation of dysfunctional uterine bleeding.

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See Figs. on Art Paper XV