



University
of Glasgow

<https://theses.gla.ac.uk/>

Theses Digitisation:

<https://www.gla.ac.uk/myglasgow/research/enlighten/theses/digitisation/>

This is a digitised version of the original print thesis.

Copyright and moral rights for this work are retained by the author

A copy can be downloaded for personal non-commercial research or study, without prior permission or charge

This work cannot be reproduced or quoted extensively from without first obtaining permission in writing from the author

The content must not be changed in any way or sold commercially in any format or medium without the formal permission of the author

When referring to this work, full bibliographic details including the author, title, awarding institution and date of the thesis must be given

Enlighten: Theses

<https://theses.gla.ac.uk/>
research-enlighten@glasgow.ac.uk

OBSERVATIONS OF THE RESISTANCE OF THE
HUMAN CERVIX TO SURGICAL DILATATION.

GEORGE STRATHIE ANTHONY.

M.B., Ch.B., M.R.C.O.G.

Degree of Doctor of Medicine
University of Glasgow.

University Department of Obstetrics and Gynaecology,
Glasgow Royal Infirmary, Glasgow.
Department of Obstetrics and Gynaecology,
Stobhill General Hospital, Glasgow.

March, 1983.

ProQuest Number: 10646085

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 10646085

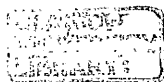
Published by ProQuest LLC (2017). Copyright of the Dissertation is held by the Author.

All rights reserved.

This work is protected against unauthorized copying under Title 17, United States Code
Microform Edition © ProQuest LLC.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

Thesis
6972
copy 2



"Dilatation of the cervix may prove hurtful,
indeed may be dangerous to life, but not
when properly performed."

G.T. Gream. March, 1865.

TABLE OF CONTENTS.

	<u>PAGE.</u>
Index of Figures.	4
Summary of Thesis.	5
Abbreviations.	10
 <u>CHAPTER 1. INTRODUCTION.</u>	 11
Circumstances of the Research Work,	12
Outline of Thesis.	13
Acknowledgements.	17
 <u>CHAPTER 2. HISTORICAL BACKGROUND OF THE THESIS.</u>	 19
History of Dilatation of the Cervix.	20
Anatomy and Physiology of the Cervix.	23
Physical Properties of the Cervix.	26
Complications of Termination of Pregnancy.	31
History of Cervical Incompetence.	44
Diagnosis of Cervical Incompetence.	51
Complications of Cervical Cerclage.	56
 <u>CHAPTER 3. DEVELOPMENT OF AN INSTRUMENT TO MEASURE THE</u> <u>FORCE REQUIRED TO PASS A DILATOR THROUGH</u> <u>THE CERVIX.</u>	 59

TABLE OF CONTENTS CONTINUED.

	<u>PAGE.</u>
<u>CHAPTER 4. ANALYSIS OF DATA OBTAINED DURING MEASUREMENT</u>	
<u>OF THE FORCE REQUIRED TO PASS A</u>	
<u>DILATOR THROUGH THE CERVIX.</u>	64
Characteristics of Force Required to Pass a Dilator Through the Cervix.	65
The Effect of Time Taken to Pass a Dilator Through the Cervix.	67
Dilatation Characteristics in Non-pregnant Patients.	69
The Effect of the Diameter of the Cervical Canal on the Force Required to Dilate the Cervix.	70
<u>CHAPTER 5. CERVICAL RESISTANCE IN NON-PREGNANT PATIENTS.</u>	73
The Effect of Parity on CRI.	75
The Influence of the Phase of the Menstrual Cycle on CRI.	76
The Effect of the Hormone Status of the Patient on CRI.	78
<u>CHAPTER 6. THE EFFECT OF EXOGENOUS HORMONES ON CERVICAL</u>	
<u>RESISTANCE IN EARLY PREGNANCY.</u>	81
The Effect of Pregnancy on CRI.	84
The Effect of Hormone Treatment on CRI.	85
The Effect of Prostaglandin E ₂ on CRI.	89
Mode of Action of Prostaglandin E ₂ .	93

TABLE OF CONTENTS CONTINUED.PAGE.

<u>CHAPTER 7.</u>	<u>CERVICAL RESISTANCE IN PATIENTS WITH A</u>	
	<u>HISTORY OF PREVIOUS SPONTANEOUS</u>	
	<u>MID-TRIMESTER ABORTIONS.</u>	97
	Patients and Methods.	98
	Previous Obstetric Performance.	99
	Past Procedures Likely to Cause Cervical Trauma.	100
	Cervical Resistance Studies.	101
	Subsequent Pregnancies.	103
<u>CHAPTER 8.</u>	<u>CONCLUSIONS.</u>	109
REFERENCES.		117

INDEX OF FIGURES.

	<u>Facing Page.</u>
Figure 2.1 Cervical Dilators from the Hippocratic Era.	21
Figure 2.2 Graduated Cervical Dilators.	23
Figure 2.3 Karman Suction Currettes.	24
Figure 3.1 Force Measuring Instrument with Dilators.	61
Figure 3.2 Diagram of the Force Measuring Instrument.	61
Figure 3.3 Devices Recorder.	62
Figure 3.4 Specimen Chart Recording from a Non-pregnant Patient.	63
Figure 4.1 The Relationship between Peak Height and Area Under the Curve.	69
Figure 4.2 The Effect of Parity on the Median Force for Each Dilator.	70
Figure 4.3 The Effect of Hormone Status on the Median Force for Each Dilator	71
Figure 5.1 The Effect of the Menstrual Cycle on CRI.	79
Figure 5.2 The Relationship between Serum Progesterone Concentration and CRI.	79
Figure 5.3 The Relationship between Serum Oestradiol Concentration and CRI.	79
Figure 7.1 The Effect of the Number of Spontaneous Mid-trimester Abortions on CRI.	103

S U M M A R Y.

This thesis describes clinical research carried out between October 1979 and January 1983. In the first year of the research the candidate was Lalor Post-Doctoral Fellow in the Glasgow University Department of Obstetrics and Gynaecology, at Glasgow Royal Infirmary. From December 1980, the candidate has been Senior Registrar in the Department of Obstetrics and Gynaecology at Stobhill General Hospital, Glasgow.

The thesis begins with a historical review of dilatation of the cervix and then considers the anatomical and physiological properties of the cervix which affect its physical properties. The ease with which the cervix can be dilated is determined by the diameter of the cervical canal prior to dilatation and by the compliance of the cervical tissue. The diameter of the cervix is influenced by the number of pregnancies which the patient has had. The compliance of cervical tissue is affected by the complex changes which take place in the collagen fibre matrix and ground substance of the cervical stroma. A review of the complications of first trimester termination of pregnancy has shown that the earlier a pregnancy is terminated, the less likely the patient is to have complications. The cervix may sustain damage during dilatation of the cervix, which may compromise her future reproductive capacity.

Attention is then turned to the problem of cervical incompetence. The history of this condition is reviewed and a discussion of the aids to diagnosis is presented. The original work described in the thesis hinges on measurements of the force applied during surgical dilatation of the cervix. These measurements were made using an instrument which was developed by the author and his associates, specifically for the purpose of the studies here presented. The factors which influence the passage of a dilator through the cervix are discussed. Measurement of the force required to dilate a cervix from 3 mm to 8 mm which was defined as the Cervical Resistance Index (CRI), takes account of many of these variable factors.

Measurement of Cervical Resistance Index was performed on a total of 590 patients in 3 groups:-

1. 200 non-pregnant patients.
2. 355 pregnant patients undergoing first trimester termination of pregnancy.
3. 35 patients with a history of previous spontaneous mid-trimester abortion.

The study of non-pregnant patients was undertaken to establish baseline values of cervical resistance. The influence of parity, hormone status contraception and the stage of the menstrual cycle on CRI is presented. Increasing

parity significantly reduces CRI. Postmenopausal women show significantly higher CRI than pre-menopausal women, while patients using Depo-Provera for contraception have significantly lower CRI than normal cycling women.

The study of pregnant patients undergoing termination of pregnancy was performed in order to evaluate the use of four hormones (oestradiol, progesterone, medroxy-progesterone acetate and prostaglandin E_2) in bringing about changes in cervical compliance. All these substances are thought to play a role in the biological control of cervical softening in late pregnancy. An increase in cervical compliance makes the cervix easier to dilate and thus reduces the likelihood of damage being sustained during dilatation. Such damage has been shown to compromise a patient's future reproductive capacity.

Prostaglandin E_2 was shown to significantly reduce the cervical resistance index in multiparous patients. In nulliparous patients, this hormone did not have the consistent effect on CRI seen in multiparous patients. Since nulliparous patients are more likely than multiparous patients to suffer damage to the cervix during dilatation, further research should concentrate on making termination of pregnancy safer for these women.

A study to measure cervical resistance index in patients with a history of spontaneous mid-trimester abortions is then described. This study was undertaken to evaluate the use of this technique in assisting in the diagnosis of cervical incompetence. The study identified patients with abnormally low CRI. The number of these patients who have subsequently conceived is small but knowledge of the CRI has allowed a more rational management and consequently improved obstetric performance.

LIST OF ABBREVIATIONS.

cm	centimetre (s)
CRI	Cervical Resistance Index
kg	Kilogramme (s)
ml	millilitre (s)
mm	millimetre (s)
16 meE ₁	16 16 - dimethyl - trans - Δ^2 PGE ₁
ng	nanogram (s)
PEG	Polyethylene Glycol
PG	prostaglandin
pg	picogram (s)

CHAPTER I.

INTRODUCTION.

This thesis describes work carried out between October, 1979 and January, 1983. In the first year of this work the candidate was Lalor Post-Doctoral Fellow in the Glasgow University Department of Obstetrics and Gynaecology at Glasgow Royal Infirmary. Subsequently as Senior Registrar in Stobhill General Hospital, Glasgow, this work has continued.

With the encouragement of Professor M.C. Macnaughton, I was fortunate to join the research group headed by Dr. Andrew Calder. This group had an established interest in cervical function in pregnancy, especially at term. The group therefore turned its attention to cervical function in non-pregnant patients and in early pregnancy. Mr. John Fisher of the Department of Clinical Physics and Bioengineering, joined the research group and we developed an instrument to measure the force required to pass surgical dilators through the human cervix.

With the development of the instrument completed, the research was directed to measuring the resistance of the cervix to dilatation in three main areas, namely, non-pregnant patients, pregnant patients undergoing first trimester termination of pregnancy and patients with a history of spontaneous mid-trimester abortion. The work was discussed at all stages within the group but I had complete freedom to initiate and direct the clinical studies.

OUTLINE OF THE THESIS.

The subject of this thesis is observations of the resistance of the human cervix to surgical dilatation. The human cervix is dilated to allow endometrial biopsy to be performed in many gynaecological conditions and also prior to suction termination of pregnancy in the first trimester. When difficulty is encountered at dilatation of the cervix, the gynaecologist worries that the cervix may be damaged with serious consequences for the patient's future reproductive life.

The studies were to assess the feasibility of quantifying the forces required to achieve dilatation of the cervix and also to study the feasibility of treatment

: increasing cervical compliance and thereby reducing
k of cervical damage. The third aim of the study
investigate patients where a diagnosis of cervical
etence was considered, with the hope that this might
; more rational selection of patients for treatment
is condition.

The present Chapter describes the circumstances in
h the research work was carried out, gives an outline
he thesis and acknowledges the help of those who
isted.

Chapter 2 presents a historical review of the
literature on dilatation of the cervix, the anatomical and
physiological properties of the cervix which affect its
surgical dilatation. The problems encountered during
dilatation of the cervix for first trimester termination
of pregnancy are reviewed. The history of cervical
incompetence and of aids to diagnosis of this condition
are also discussed.

Chapters 3 and 4 cover the development of the
instrument used in the clinical studies and discuss various
methods of interpreting the data.

The following chapters (5, 6 and 7) describe the clinical

trials performed by the author on a total of 590 patients. Chapter 5 describes a study of 200 non-pregnant patients undergoing dilatation and curettage. Particular attention is given to the effect of parity, hormone status and the stage of the menstrual cycle on the resistance of the cervix.. In Chapter 6, 355 pregnant patients have been studied prior to suction termination of pregnancy. Treatment with oestradiol, progesterone, medroxy-progesterone acetate and various doses of prostaglandin E_2 have been assessed. Chapter 7 describes 35 patients with a history of spontaneous mid-trimester abortion in an attempt to diagnose cervical incompetence. The obstetric performance of those patients who have subsequently become pregnant is discussed.

Chapter 8 presents the conclusions drawn from the clinical studies.

Data from these studies have been published in scientific journals as follows:-

In Chapter 3.

"Use of a force measuring instrument during cervical dilatation".

by J. FISHER, G.S. ANTHONY, T.J. McMANUS, J.R.T. COUTTS and A.A. CALDER.

Journal of Medical Engineering and Technology. Volume 5, July, 1981. Pages 194 - 195.

In Chapters 5 and 6.

"Forces required for surgical dilatation of the pregnant and non-pregnant human cervix"

by G.S. ANTHONY, J. FISHER, J.R.T. COUTTS and A.A.CALDER.

British Journal of Obstetrics and Gynaecology.

Volume 89, November, 1982. Pages 913 - 916.

In Chapter 6.

"The effect of exogeneous hormones on cervical resistance in early pregnant human cervix".

by G.S. ANTHONY, J. FISHER, J.R.T. COUTTS and A.A. CALDER.

This paper has been submitted to the British Journal of Obstetrics and Gynaecology.

In Chapter 7.

"Cervical Resistance in patients with previous spontaneous mid-trimester abortion".

by G.S. ANTHONY, A.A. CALDER and M.C. MACNAUGHTON.

British Journal of Obstetrics and Gynaecology.

Volume 89, December, 1982. Pages 1046 - 1049.

In compiling this thesis I have personally carried out the literature research and the composition of the text but I wish to acknowledge the invaluable assistance of a number of individuals.

ACKNOWLEDGEMENTS.

Dr. Andrew Calder made this project possible. He raised the finance and supervised the research throughout. He allowed me freedom to develop the research, maintained a keen interest and provided encouragement to write the thesis.

Drs. J.R.T. Coutts and R. Fleming provided encouragement and help with preparation of the data and performed the serum hormone estimations.

Drs. C.B. Lunan and R.C.L. Howat of Glasgow Royal Infirmary were always very willing to allow me to study their patients.

On transferring to Stobhill General Hospital, Dr.R.A.L. Low and Dr. D. McKay Hart, readily made their patients available for me to study and encouraged me to complete the thesis.

Mr. Peter Waldie of the Department of Audio-Visual Services at Stobhill Hospital has given assistance with preparation of the illustrations.

Mr. John Fisher designed, manufactured and maintained the instrument used in the studies. Throughout the project he maintained a keen interest and was an invaluable member of the research group.

The Lalor Foundation generously provided the financial support for the first year of this project.

Professor M.C. MacNaughton encouraged me to undertake this project and to write this thesis.

CHAPTER 2.

HISTORICAL BACKGROUND OF THE THESIS.

History of Dilatation of the Cervix.

Complications of Termination of Pregnancy.

Cervical Incompetence.

HISTORY OF DILATATION
OF THE CERVIX.

Dilatation of the cervix has been carried out since the time of Hippocrates (463 - 399 B.C.). In the Hippocratic era the cervix was dilated to allow fumigation of the uterus and instillation of medicaments, as many ill-defined conditions of women were attributed to disease of the uterus. The dilators were hollow and usually made of tin or lead, mounted on wooden handles (Figure 2.1). Since anaesthesia was unknown at these times the dilators were passed with the patient conscious. In A.D. 79, Vesuvius erupted and buried the city and inhabitants of Pompeii. In the excavation of this city many centuries later, vaginal speculae made of bronze and cervical dilators of tin were uncovered - the first evidence that gynaecology was practiced in these early times.

By the late nineteenth century, gynaecological techniques had progressed little but laminaria and sponges were in use for dilating the cervix. T. Galliard Thomas, Professor of Gynaecology in New York in 1873, advocated the following treatment for a 17 year old girl suffering from

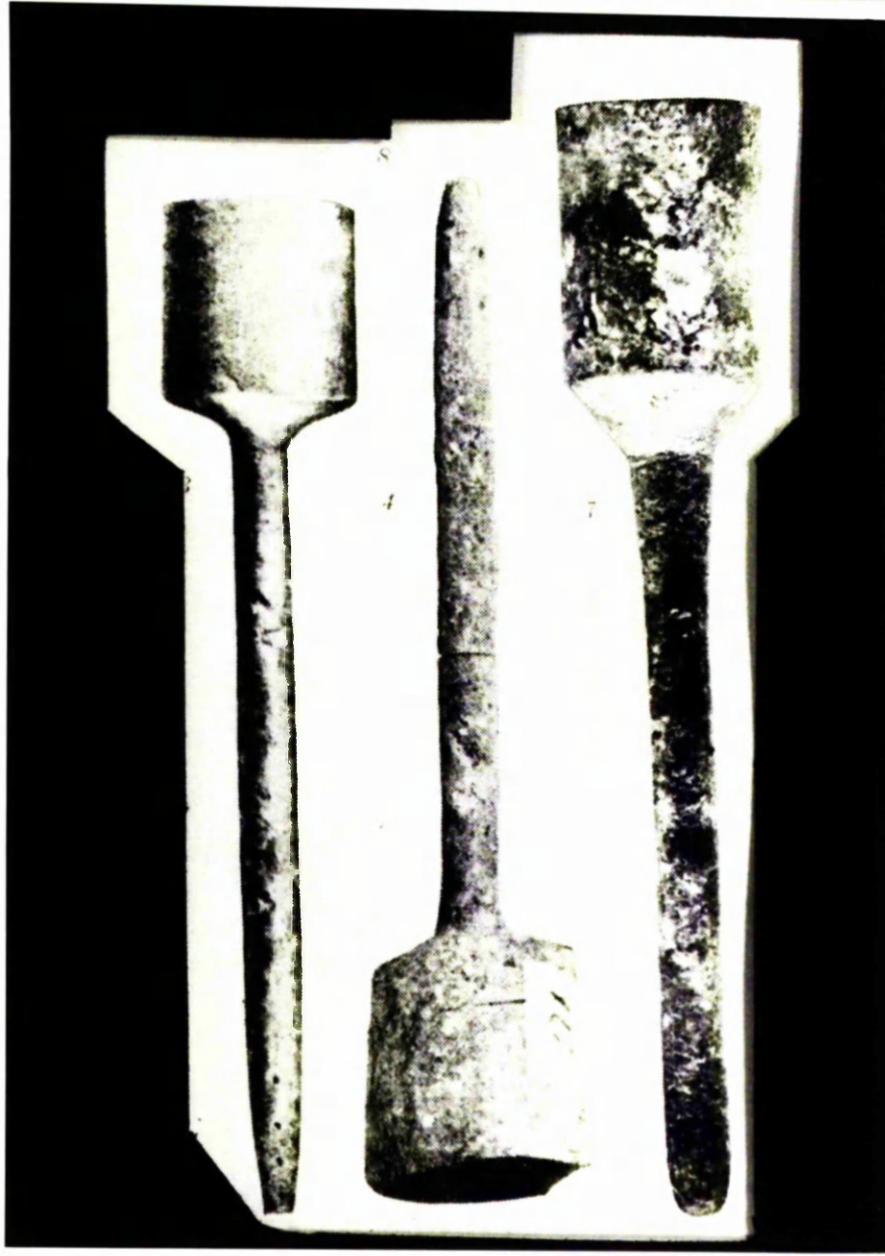


Figure 2.1 : Cervical dilators from the Hippocratic era.

dysmenorrhoea. "She should be put under an anaesthetic and a delicate sponge tent should be introduced into the uterus and left there for four days. It should then be replaced by another a little larger and the procedure repeated every four days until the uterus is completely dilated. The irritation brought on by this will cause congestion of the uterus and increase nutrition" !

This gradual dilatation of the cervix over several weeks may have been beneficial in treating dysmenorrhoea, while avoiding cervical damage but the high incidence of pelvic infection as a result of this procedure would undoubtedly have caused as many problems as it solved.

Laminaria were gradually replaced by steel dilators, principally those named after the German Gynaecologist, Alfred Hegar (1830 - 1914). These dilators allowed a gradual dilatation of the cervix over a much shorter time than that advocated by Thomas, thus reducing the incidence of infection.

Dilatation of the cervix was performed as a cure for primary dysmenorrhoea from the nineteenth century until about ten years ago. Clinicians had observed that dysmenorrhoea was often abolished after the patient had delivered a child and they assumed that this was as a result

of the cervix being dilated during labour. In an effort to reproduce this physiological cure of dysmenorrhoea, patients were subjected to vigorous dilatation of the cervix. It was felt that dilatation of the cervix would rupture some of the muscle fibres of the cervix, thereby leaving the patient with a greater diameter of cervical canal. Primary dysmenorrhoea was thought to be due to the cervical canal obstructing the flow of the menses and thus enlargement of the canal would relieve the obstruction. Patients with primary dysmenorrhoea have been shown to have abnormally high levels of prostaglandin synthetase. Drugs which inhibit this enzyme have recently been shown to be effective in the treatment of this condition, (Anderson et al., 1978).

Dilatation of the cervix is now undertaken in order to obtain an endometrial biopsy for the diagnosis of numerous gynaecological conditions and in order to permit evacuation of the contents of a pregnant uterus.

To obtain an endometrial biopsy it is necessary to dilate the cervix to about 8 mm to allow a uterine curette to pass through the cervix. The curette is then used to scrape portions of endometrium from the uterus which can be submitted to histological examination. A typical set of dilators is seen in Figure 2.2.

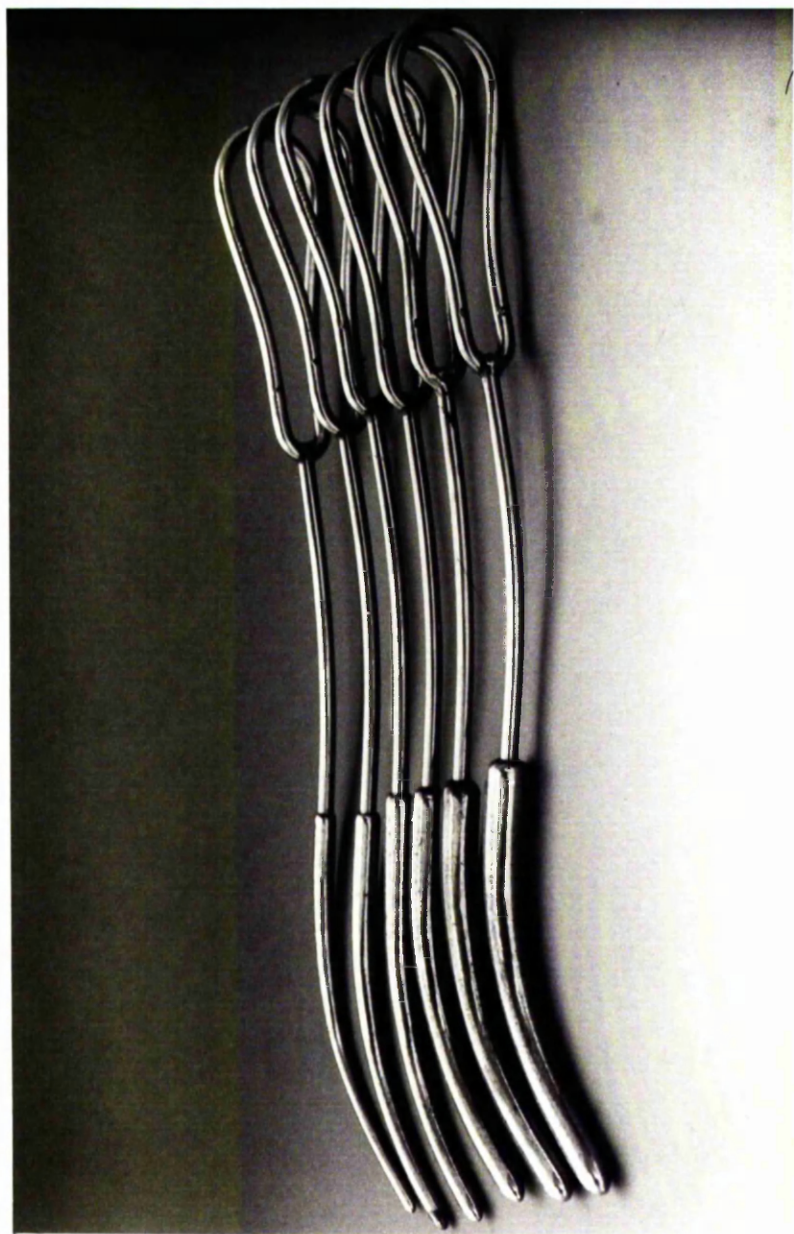


Figure 2.2 : Graduated Cervical Dilators.

In termination of pregnancy the cervix has to be dilated to allow evacuation of the conception. The diameter to which the cervix must be dilated is determined by the gestational age of the pregnancy, a rough guide being 1 mm dilatation for each week of gestation. After dilatation of the cervix the uterus is emptied with a flexible plastic suction canula of the type seen in Figure 2.3.

ANATOMY AND PHYSIOLOGY OF THE CERVIX.

The human cervix has two main roles to play between conception and delivery of the foetus. The first role it plays is that of a sphincter which holds the developing ovum safe within the uterus until late pregnancy. This role is then discarded and it has, under the influence of myometrial contractility, to dilate up to 10 cm and allow the foetus to pass safely through the birth canal. In making the change from its pregnancy role to its labour role, the cervix undergoes complex modification in structure and function; from a relatively rigid structure which resists surgical dilatation, to a soft compliant cervix which can undergo dilatation to 10 cm in the course of a few hours of labour.

A knowledge of the structure of the cervix is necessary to understand its functions. Early workers who studied the

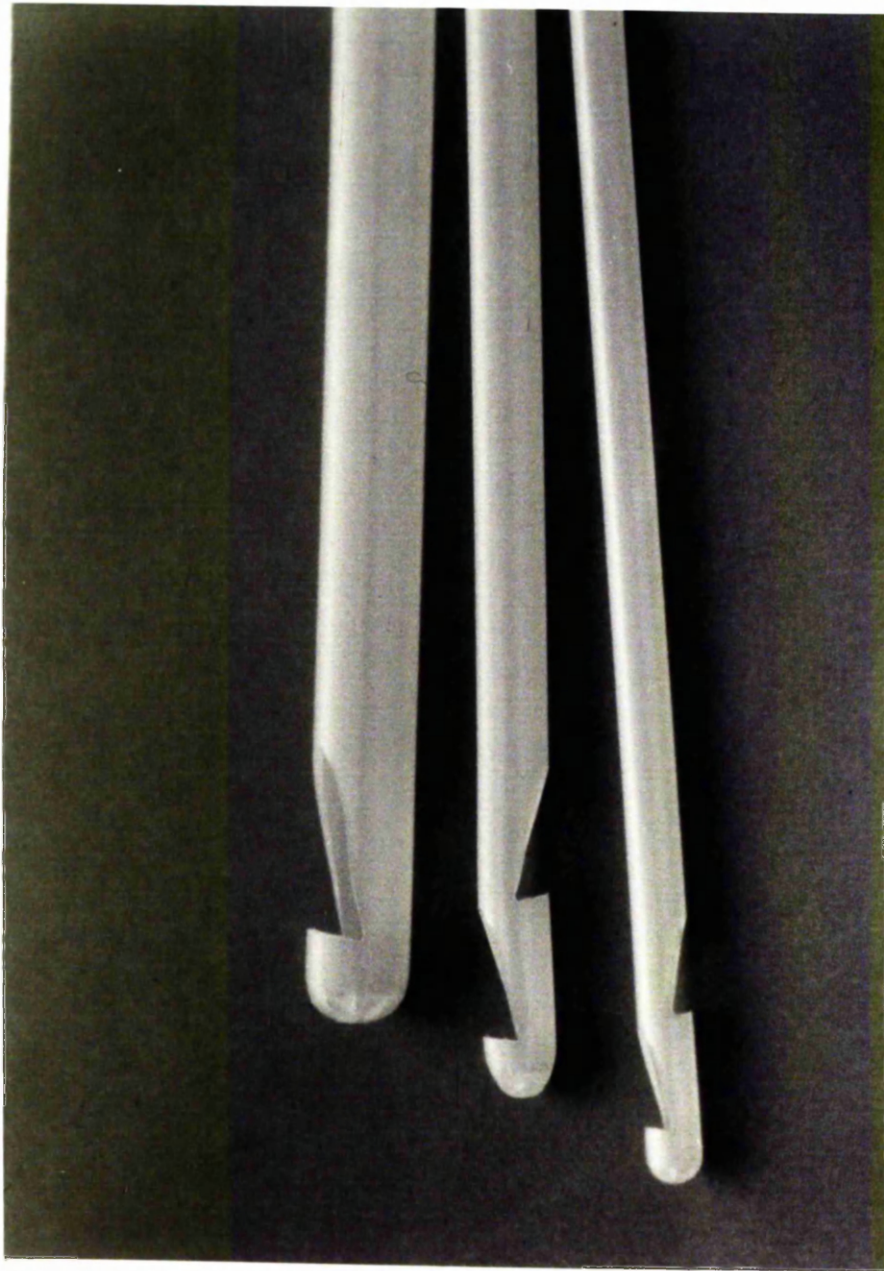


Figure 2.3 : Karman Suction Curettes.

cervix were concerned with where the corpus of the uterus ended and the cervix began. Aschoff (1905) described the isthmus of the uterus as the portion which lay between the anatomical internal os (where the cavity of the non-pregnant uterus joins the cervix) and at the lower end, the histological internal os (where the epithelium changed from an endometrial type, to an endocervical type). The isthmus is the part of the uterus which develops to form the lower segment of the uterus during late pregnancy.

There followed much discussion on the function of the isthmus and it was not until Danforth (1947) studied the cervix that it came to be regarded as part of the uterus rather than the cervix, because its structural elements are similar to those of the corpus of the uterus.

Danforth also drew attention to the marked difference in structure between the cervix which is predominantly fibrous connective tissue and the rest of the uterus which is mainly muscular. Danforth studied not only the change in the epithelial type but also found a marked transition in the composition of the stroma at the level of Aschoff's histological internal os, between the muscular uterus and the fibrous cervix. This area he called the fibromuscular junction.

Composition of the Cervical Stroma.

The composition of the cervical stroma can be considered under two headings, formed elements and ground substance. The formed elements consist mainly of collagen fibres, a small amount of elastic and about ten per cent smooth muscle fibres. Danforth (1954) felt that the amount and distribution of the smooth muscle made it unlikely that it could contribute to the sphincteric action of the cervix in early pregnancy. Ground substance consists of glycosaminoglycans in proteoglycan complexes which incorporate varying amounts of water in the tissue. The varying amounts of water in the tissues, together with changes in the type of collagen, are probably responsible for the changes in the cervical compliance which are seen during pregnancy.

Harkness and Harkness (1959) have shown in rats that in pregnancy the collagen fibres of the cervix undergo hypertrophy and as a result of these changes the circumference to which the cervix could be stretched increased three to four times that of the non-pregnant cervix. These authors also noted that the extensibility of the pregnant rat cervix increased eleven-fold over the non-pregnant values. The rat cervix undergoes a process of "softening", prior to labour, similar to that seen in the human cervix. It is difficult to obtain human pregnant cervix for study but it is probable that similar changes are present in the

physical properties of the human cervix.

Danforth (1960) showed histological changes in the collagen fibre matrix of the human cervix after labour. At the end of labour the collagen fibres are reduced in size and highly branched, while there is also a dissociation of the component fibrils. Von Maillot, Stuhlsatz and Gentsch (1981) suggest that there is an initial stretching of the collagen fibres and then they slip over each other. To allow slipping of the fibres, the proteinaceous links between the fibrils have to be broken down by enzymes. Collagen accounts for about 50 per cent of the dry weight of the cervix, (Danforth 1960) and it is probable that "softening" of the cervix involves changes in the framework of the collagen fibres. The changes in the collagen matrix are probably influenced by at least four hormones; oestrogen, progesterone, prostaglandin and relaxin but the precise mechanism of these changes is still not completely understood, (Calder 1980).

PHYSICAL PROPERTIES OF THE CERVIX.

The cervix acts as a visco-elastic tissue (Black 1975). It can be considered as a tissue with an elastic component which like a spring, will recoil when stretched. If it had only elastic properties, then it would always quickly

return to its original shape and diameter after stretching. This property is independent of the time taken to stretch the tissue.

The viscous element of cervical tissue can be considered like a shock absorber. When a shock absorber is compressed, fluid is displaced and then gradually returns to its original position, while retaining a "memory" of the fact that it has been compressed. This component of the physical property of cervical tissue is dependant on the rate of dilatation. Thus, the time taken to compress the tissue will affect the amount of force required to achieve compression. It is this viscous property of the cervix which makes it necessary to dilate the cervix a little at a time. If the cervix were truly elastic, then one could dilate the cervix in one step to the required diameter. In clinical practice a slow rate of dilatation is achieved by using a series of dilators which increase in diameter by 1 mm and by taking about two seconds for each dilatation. To dilate the cervix in one step to the required diameter, taking the same time for dilatation, would require a large amount of force because of the viscous element of the tissue. When excessive forces are applied to a tissue there is always the possibility that the tissue will sustain damage.

Black et al. (1975b) in an in vitro study of human cervix, using a force measuring device, found that after passing the same dilator through a cervix fourteen times at five second intervals, the force required to dilate the cervix on the last occasion had reduced to about fifty per cent of that required in the first passage of the dilator.

The difference between the first and second passage of the dilator was about three to five per cent of the force required on the first passage. By the last dilatation much smaller reductions in force were being found. This finding of gradual reduction in the force required to pass the dilator on each successive occasion, shows that the viscous element is present and the cervix is retaining a "memory" of the fact that it has been dilated. The reduction in the force required to pass the dilator on each successive occasion is small. In clinical practice one usually passes the dilator once and it is the first passage of a dilator which meets the greatest resistance. Black's study also showed the typical pattern of increasing force being required to pass dilators of increasing diameter. Despite the gradual reduction in the force required to pass a dilator on successive occasions, the next size of dilator required a larger force than that used on the first passage of the smaller dilator. If it were possible to perform multiple

insertions of a dilator at five second intervals and then change the dilator for the next size in this time before the viscous element has recovered, this might lead to a reduction in the force required for the passage of the next dilator size. The time interval between different dilator sizes is as important as the time between repeated dilatations with the same size of dilator. The technique of multiple insertions of a dilator does not have any beneficial effect in clinical practice.

Forces Involved in Dilatation of the Cervix.

In order to surgically dilate the cervix two forces need to be overcome, friction and compressibility of the cervix. Friction is present between the taper of the dilator and the cervical canal, only while the dilator is moving through the canal. Friction probably accounts for a fairly small proportion of the total force required to pass a dilator through the cervical canal, since there is no appreciable reduction in the amount of force needed to pass the dilator, when the forward movement of the dilator is stopped. Once the dilator has stopped moving, it continues to compress the cervical canal and prevents it returning to its original diameter. Cervical mucus will also lubricate the dilator and so reduce friction between the dilator and the cervical canal.

The compressibility of the cervix depends on the diameter of the cervical canal and on the compliance of the cervical tissue. The diameter of the cervical canal is affected by the number of previous pregnancies which the patient has had, Halliday, Jacobs and Heyns (1958) and Johnstone et al. (1974).

In order to measure the ease with which a cervix may be dilated, one can measure the axial force exerted on the tapered dilator. Dilatation takes place over the tapered portion of the dilator and this in turn exerts a circumferential force on the cervical canal. It is possible to directly measure the circumferential force on the cervical canal. To do this, it is necessary to design a dilator which expands radially. Measurement of the force required to open the jaws of such a dilator gives the circumferential force exerted on the cervical canal. This type of dilator is very complex and only one small study has been reported with this type of instrument (Bentov and Stubblefield 1980).

In clinical practice, a dilator is pushed through the cervix and the procedure repeated with increasing diameters of dilator. It is relatively simple to design an apparatus which will measure the force transmitted from the operator's hand to a dilator and as this involves fewer moving parts, the likelihood of mechanical failure is reduced. We

therefore decided to develop this type of instrument.

COMPLICATIONS OF TERMINATION OF PREGNANCY.

Complications of first trimester termination of pregnancy may be considered in two categories, namely, those occurring at the time of the procedure and secondly, late sequelae of the procedure which may affect future reproductive life. In considering complications at the time of termination of pregnancy, the method of termination is important. The method of termination is dependant on the gestational age of the pregnancy. In Glasgow, dilatation of the cervix followed by suction curettage is used to terminate pregnancies up to twelve weeks gestation. Thereafter extra-amniotic infusion of prostaglandin E_2 is used to terminate the pregnancy. In America and parts of Eastern Europe, suction curettage is often carried out up to sixteen weeks of gestation.

Laminaria absorb fluid which then produces an increase in the diameter of the laminaria. They have been used in America to produce dilatation of the cervix prior to termination. These devices have never been popular in the United Kingdom but they are effective in producing a gradual dilatation of the cervix.

Cervical Damage.

Hulka and Higgins (1961) investigated the effect of dilatation of the cervix in the non-pregnant state. One hundred and fifty-four patients who were about to undergo total hysterectomy were subjected to dilatation of the cervix, immediately prior to removal of the uterus. The cervix was dilated with Hegar dilators up to 12 mm and following removal of the uterus, the cervix and uterus were opened longitudinally. Thirty-nine per cent of patients had sustained tears of the internal os to a depth of 2 mm and a further twenty-two per cent had tears of over 5 mm in depth. The tears in the internal os had a characteristic pattern of a longitudinal tear, beginning in the cervical canal deepest at the level of the internal os and tapering off in the isthmic portion of the uterus. An important feature of this study was that these tears were not visible at the time of the procedure and did not give rise to undue haemorrhage.

Hulka et al. (1974) in a study of the force required to dilate the cervix at termination of pregnancy, drew attention to the greatly increased force required to dilate the cervix beyond 11 mm particularly in nulliparous patients. Dilatation beyond this diameter often produced a sudden fall in the force required to dilate the cervix and Hulka postulates that this was due to the occurrence of the tears seen in his non-pregnant study. The occurrence of these tears may explain

the sudden "give" encountered during cervical dilatation. Fitzpatrick and Dobson (1979) in studies of sheep cervix, subjected portions of the cervix to stretching and found that the cervix initially was able to withstand fairly high tension, until the epithelium of the canal ruptured and following this rupture the cervical tissue continued to stretch but at a much lower tension, until complete rupture of the tissue occurred . These findings in sheep cervix have been confirmed by our research group. The occurrence of these epithelial tears, while not giving rise to undue haemorrhage, probably often remain undiagnosed, as they are not visible and may account for the failure of the cervix to act as a sphincter in subsequent pregnancies.

The cervix may sustain a second type of injury when the volsellum tears off the anterior lip of the cervix during dilatation. This type of injury may not damage the patency of the internal os but often gives rise to haemorrhage and is therefore easily spotted at operation. This injury is easily treated at the time of operation with a few sutures which restore the cervix to its normal configuration and also achieve haemostasis. Cadesky, Rivinsky and Lyons (1981) describe this injury occurring in two out of twenty-nine patients (6.9%), undergoing termination of pregnancy up to sixteen weeks gestation, by dilatation and evacuation. He states that this injury is not due to dilatation of the cervix

but as the volsellum provides counter traction during dilatation, it must represent the use of excessive force in dilatation. In the patients studied in Chapter 7, this type of injury was seen in two patients in a series of three hundred and fifty-five patients (0.5%) when dilatation of the cervix was reserved for pregnancies below twelve weeks gestation.

Incidence of Cervical Laceration.

Harman, Fish and Tyson (1981) in a study of 810 patients undergoing first trimester termination of pregnancy in Manitoba, Canada, had an incidence of 3.09 per cent cervical lacerations. Their patients were limited to ten weeks gestation for primigravidae and eleven weeks for multigravidae. Atienza, Burkman and King (1980) in a series of 1,602 suction terminations, found the incidence of cervical lacerations to be 1.37 per cent. It is interesting that the rate was 2.7 per cent in nulliparous and 0.23 per cent in multiparous patients and 46.19 per cent of their patients were nulliparous.

Stallworthy, Moolgaoker and Walsh (1971) showed the incidence of cervical laceration to be 3.9 per cent in primigravidae but surprisingly the rate in multiparous patients was 3.3 per cent. Suction termination was used up to fourteen weeks gestation in this study.

Johnstone et al. (1976) showed that in cases where the cervix had been dilated beyond 12 mm to permit suction curettage, the diameter of the internal os was significantly higher than in those cases in which dilatation was restricted to 12 mm. These studies were performed six weeks after suction termination and confirmed the view that cervical trauma is more likely when excessive dilatation of the cervix is used. Excessive dilatation of the cervix can be avoided by restricting suction termination to pregnancies of less than twelve weeks.

Atienza, Burkman and King (1980) showed a ten-fold increase in the incidence of cervical trauma in nulliparous women, compared to multiparous women and it is to the nulliparous women that our attention should be focussed in attempts to increase cervical compliance and thereby reduce the incidence of cervical damage.

Uterine Perforation.

The uterus may be perforated at two sites, the fundus of the uterus and the cervix. These injuries arise from different types of accident. Perforation of the fundus can occur when a sudden "give" is encountered during dilatation of the cervix. The unexpected "give" reduces control of the dilator which may then pass through the fundus.

Following dilatation of the cervix, the fundus may be perforated if instruments are inserted into the uterus to remove the products of conception. With the introduction of the Karman Catheter and other flexible plastic suction curettes, the need for instrumentation should now be rare.

Harman, Fish and Tyson (1981) found the incidence of uterine perforations to be 0.74 per cent in their study using rigid plastic suction curettes, followed by sharp curettage. Atienza, Burkman and King (1980) using flexible suction curettes, found the rate of perforation to be 0.1 per cent. They also report two cases (0.05%) where the uterus was perforated at the level of the cervix. They ascribe this injury to the creation of a false passage during dilatation of the cervix, when the direction of the cervical canal had not been appreciated. Vaginal examination and sounding of the cervical canal prior to dilatation of the cervix, should diagnose malpositions of the uterus.

Haemorrhage.

Blood loss at the time of operation, using the techniques already described, should be very low. Hulka et al.(1974)

measured blood loss in 70 suction terminations and found it to be consistently below 50 mls. Harman, Fish and Tyson (1981) report 9 cases of haemorrhage in 810 suction termination, with 3 patients requiring transfusion. In the cases presented in Chapter 6, only 1 case out of 355 patients (0.28%) required blood transfusion. In this series excessive blood loss only occurred when the assessment of gestation had been underestimated at the initial clinical examination and suction termination was performed after twelve weeks gestation.

Anaesthesia.

In North America, the standard anaesthetic for suction termination is local anaesthetic in the form of a paracervical block, while in the United Kingdom, most patients have suction termination carried out under general anaesthesia. Harman, Fish and Tyson (1981) had anaesthetic problems in 2.35 per cent of patients undergoing suction termination with a general anaesthetic. None of the anaesthetic problems were serious and there were no anaesthetic deaths.

Peterson et al. (1981) calculated the comparative risks of death from anaesthesia in induced abortion before twelve

weeks gestation. He compared statistics for local and general anaesthesia after excluding pre-existing disease. He found the rates to be 0.37 per 100,000 abortions under general anaesthesia and 0.15 per 100,000 abortions under local anaesthesia.

With the use of local anaesthesia for suction termination, the risk of anaesthetic problems are reduced, with the added benefit of shorter in-patient stay in hospital.

Retained Products.

Post-operative complications centre round the problem of products of conception remaining in the uterus. Retained products prevent complete retraction of the uterine muscle and therefore can give rise to increased haemorrhage. The other main problem of retained products is that they provide an ideal culture medium for bacteria and so can give rise to pelvic infection which may ultimately, if untreated, cause tubal damage or septicaemia. Beric, Kupresanin and Hulka (1972) found retained products in 12.4 per cent of cases at six weeks and 100 per cent of cases at twelve weeks, although all the terminations in this series were performed with 6 mm suction curettes. Harman, Fish and Tyson (1981) found retained products to be a problem in

2.5 per cent of cases. The larger size suction curettes provide a greater area of the aspiration openings which are more appropriate in dealing with the increasing size of foetal parts that are encountered with increasing gestational age. Correct selection of suction curette for each case will minimise the incidence of complications arising from retained products of conception.

Amniotic Fluid Embolism.

This rare and often fatal condition has been described as a complication of termination of pregnancy in the United States. Between 1972 and 1978, fifteen cases of amniotic fluid embolism were reported, while approximately one million pregnancies were terminated annually. The incidence of this complication is thus very low but it does account for twelve per cent of deaths associated with legally induced abortion, (Guidotti, Grimes and Cates 1981). This complication was predominantly associated with mid-trimester abortions, performed using hypertonic solutions of urea and saline. There was a sixty per cent incidence of disseminated intravascular coagulation associated with these deaths. The incidence of amniotic fluid embolism rose from nil at twelve weeks gestation to 7.2 deaths per 100,000 abortions at twenty-one weeks (Guidotti, Grimes and Cates, 1981). One case has been recorded when suction termination

of pregnancy was performed at sixteen weeks Cates et al., (1981). Amniotic fluid embolism occurred during the suction termination and the patient died from a ruptured liver, sustained during the resuscitation procedure.

This complication can be avoided by performing termination of pregnancy as early as possible in the pregnancy. This is best achieved by minimising the delay between the referral from the general practitioner and the patient having the procedure performed. Harman, Fish and Tyson (1980) reported that thirty per cent of their patients actually presented in the first trimester of pregnancy but did not undergo termination until mid-trimester.

The average delay between consultation and admission for operation in the first trimester was 11.8 days. This is obviously unacceptable in the provision of abortion services.

The main conclusion to be drawn from this study of immediate complications of first trimester termination of pregnancy, is that the earlier the procedure is done in a pregnancy, the less likelihood there is of complications arising.

The Effect of Termination of Pregnancy
on Subsequent Pregnancies.

With the increasing numbers of patients undergoing termination of pregnancy much attention has been focussed on the performance of these patients in future pregnancies. Macnaughton (1961) has shown that patients who start their reproductive life with a spontaneous abortion, have an increased incidence of threatened abortion, prematurity and perinatal loss in their second pregnancy. Keirse et al. (1978) showed that the increased incidence of premature delivery in those patients with a previous spontaneous abortion was related mainly to those pregnancies which ended in the second trimester and not in the first trimester. The incidence of pre-term labour was also related to the number of previous spontaneous mid-trimester abortions.

Wright, Campbell and Beazley (1972) found a ten-fold increase in the incidence of spontaneous mid-trimester abortion in patients who had previously had a first trimester termination of pregnancy, compared to those with no previous termination. Seventy-nine per cent of the patients in this study had undergone termination in private clinics and many of them were before the current Abortion Act was

introduced, so that accurate details of the gestation at which the procedures were performed, were not available.

Richardson and Dixon (1976) in a study of 211 patients who had undergone vaginal termination of pregnancy, found a foetal loss rate of 17.5 per cent compared with 7.5 per cent in a group of similar parity who had had a spontaneous abortion. Unfortunately this study did not compare these patients with a matched group of normal pregnant patients. In this study 4.3 per cent of the pregnancies after legal abortion ended in first trimester abortion, 8.5 per cent in mid-trimester abortion and 13.7 per cent in pre-term delivery. It is interesting that 11 patients in this study were known to have suffered cervical laceration and these patients had a foetal loss rate of 45.5 per cent, only 1 pregnancy went beyond 36 weeks gestation. No details of the gestation at which the pregnancy was terminated were available.

Liu, Melville and Martin (1972) showed a similar pattern of increased rates of mid-trimester abortion following first trimester termination of pregnancy. Subsequently 4.4 per cent of pregnancies ended in spontaneous mid-trimester abortion, compared with 0.5 per cent in patients whose previous pregnancy ended in spontaneous first trimester abortion.

The working party on sequelae of abortion (WHO 1979) also found significantly higher rates of mid-trimester abortion and premature delivery following first trimester termination of pregnancy.

Placenta Praevia.

Barrett, Boehm and Killam (1981) have drawn attention to the increased rate of placenta praevia after first trimester termination of pregnancy. In their study they compare the rate of placenta praevia in deliveries in Tennessee between 1972 and 1974, (prior to liberalisation of the Abortion Law) with the rate between 1978 and 1980. The incidence of placenta praevia in 1972 to 1974 was 1 in 318 pregnancies, while the incidence of induced abortion was 0.6 per cent. No case of placenta praevia was seen in patients who previously had undergone induced abortion. Between 1979 and 1980 the incidence of placenta praevia was 1 in 109 deliveries and the incidence of induced abortion was 10.1 per cent. The incidence of placenta praevia in patients who had undergone termination of pregnancy was 4.6 per cent. This higher incidence of placenta praevia after first trimester termination is worrying but to date these figures have not been confirmed in the United Kingdom.

These retrospective studies all show to varying degrees, an increased risk of spontaneous mid-trimester abortion and

premature delivery following first trimester termination of pregnancy. The precise risk is hard to define and what is required is a large prospective study of patients after termination of pregnancy. There are obvious difficulties in such a study. Population shift, patients changing name and of course the problem outlined by Richardson and Dixon (1976), of patients not informing the obstetric staff of previous terminations. The patient's general practitioner may also fail to notify the obstetric staff, or may not in fact be aware that the patient has had a termination of pregnancy.

CERVICAL INCOMPETENCE.

The concept of incompetence of the cervix to act as a sphincter to retain a conception was first raised in 1865 by Gream. In a letter to the Lancet, he commented on a technique described by J. Marion Sims, the father of American Gynaecology. Sims advocated dividing the cervix from the external os to the internal os with a scalpel, as a treatment for sterility and dysmenorrhoea. The technique seemed to be successful in treating dysmenorrhoea, although complications of the operation included profound haemorrhage, pelvic abscess and even death.

Gream drew attention to a problem which arose if the patient did become pregnant after this operation. He noted that in many cases at about 16 weeks gestation, the cervix was already more than a finger dilated, similar to the state of late pregnancy and gradually the membranes herniated through this prematurely dilated cervix. Abortion inevitably followed this finding. Gream rightly attributed the abortion to the previous surgery and the technique soon fell by the wayside. Sims is now remembered for the introduction of his vaginal speculum rather than this disastrous operation that he advocated.

Gream's theory of the inability of the cervix to act as a sphincter to contain a conception seems to have been forgotten and it was not until the French authors Palmer and Lacomme (1948) in a paper entitled "La béance de l'orifice interne cause d'avortements à répétition", again drew attention to the fact that when the cervix was dilated in early pregnancy, abortion invariably resulted and these patients were likely to suffer recurrent mid-trimester abortion.

At this time the main cause of this condition was high amputation of the cervix at pelvic floor repair. Lash and Lash (1950) gave the now accepted classical description of abortion due to cervical incompetence, when one found

repeated mid-trimester abortion. The abortion was characterised by rupture of the membranes, followed by relatively painless extrusion of the conception. They also emphasised the finding of the dilated cervix in the absence of perceptable uterine activity.

Evolution of Therapy.

Lash and Lash (1950) described a characteristic finding of a thinned portion of the cervix anteriorly at the time of the abortion. They pointed out that obstetric and gynaecological trauma may be responsible for causing this defect.

It was thus hardly surprising that three years later, Lash (1953) described an operation to correct this defect in the cervix. In the non-pregnant state the bladder was pushed up off the cervix and a diamond of cervical tissue was then excised. The cervix was reconstituted with sutures, thereby reducing the lumen of the cervical canal.

Palmer and Lacomme (1948) would also seem to have thought of this type of defect in the cervix and in the case they reported, performed an operation on the cervix in which two catgut sutures were inserted into the anterior wall of the

cervical canal, to reinforce it and reduce the lumen. Following this procedure, the patient was successfully delivered of a live child.

In 1961 Lash outlined the problems encountered by his type of repair and it is not surprising that haemorrhage, infection and rupture of the uterus figure in the complications of this procedure.

The late Professor V.N. Shirodkar disagreed with the hypothesis of Lash and Lash, that the defect lay solely in the anterior part of the cervix and felt that it was much more likely that there was an intrinsic weakness in the cervix which allowed it to passively dilate. Shirodkar (1951), described a method of treating cervical incompetence by encirclement, using three strands of chromic catgut to form a purse-string round the internal os. The technique involved incising the anterior vaginal wall over the cervix, pushing up the bladder and then inserting the suture at the level of the internal os, underneath the vaginal skin. By 1955, Shirodkar had found that catgut was inadequate as it was soluble and repeat cerclage was often necessary. In the same year he described the technique of using fascia lata to make the purse-string and this did not dissolve. With this type of suture he described the successful treatment of ⁶thirty cases who had previously had between four and eleven

spontaneous mid-trimester abortions.

At the same time as Shirodkar was developing his technique in Bombay, McDonald in Australia was also looking at methods of treating cervical incompetence. In 1951 while working in England he had treated one case of cervical incompetence with a purse-string suture of chromic catgut, inserted through the vaginal cervix with a knot tied in the vagina. This technique had the advantage that it caused less disturbance at the cervix and the suture could be cut later in the pregnancy, prior to labour. Like Shirodkar's catgut suture it had the disadvantage of being soluble and he found it was often necessary to repeat the procedure some time later in the pregnancy. His first case in 1951, required three sutures in all at two weekly intervals but the patient was delivered of a live child of 6 lbs 4 ozs, having previously had four mid-trimester losses. Back in Australia, McDonald continued his work and began using a suture of No. 4 mersilk, inserted through the exocervix with five or six bites being taken. Particular attention was given to ensure that a deep bite was taken in the posterior lip of the cervix.

McDonald (1957) published the results of his first seventy cases with 43 per cent foetal survival. It is of interest that in all of these cases, the cervix was already dilated. The common clinical presentation of these patients

was with vaginal discharge, lower abdominal discomfort and a lump in the vagina which on inspection proved to be the bag of forewaters protruding beyond the internal os.

Aetiology of Cervical Incompetence.

There has been general agreement that cervical incompetence is usually an acquired condition. The condition arises following trauma to the cervix at gynaecological procedures and in obstetrics at the delivery of the foetus.

The types of gynaecological procedure which are likely to result in trauma to the cervix have changed in the time since Palmer and Lacomme first suggested the condition in 1948. The change in aetiological factors merely represents the changes in gynaecological practice that have occurred since then. Palmer and Lacomme (1948), Fisher (1957) and Shirodkar (1955), mention high amputation of the cervix at pelvic floor repair as being one of the main causes of cervical incompetence. McDonald (1957) found this to be a cause in three of his seventy patients. Of the previous gynaecological procedures which the patients had undergone, thirty had had dilatation and curettage, a further five patients had undergone wide dilatation of the cervix for dysmenorrhoea and two had undergone cauterisation of the cervix. It is interesting that of the five patients who

had been subjected to dilatation of the cervix for dysmenorrhoea, eighteen pregnancies produced only one live child, which subsequently died of prematurity. It is indeed fortuitous that dilatation of the cervix is gradually losing favour in the treatment of dysmenorrhoea. These figures suggest it is too dangerous a procedure to carry out for this condition when the success of this procedure has not been established.

McDonald (1980) found that out of 269 cases of cervical incompetence, amputation of the cervix had fallen to 3 per cent. There was a history of conisation of the cervix in 7.8 per cent and dilatation of the cervix in 68.8 per cent. By this time he had also seen 23 patients who had developed cervical incompetence as a result of treatment for dysmenorrhoea in their youth. Of the large number of patients who had previously had dilatation of the cervix, the incidence of the procedure being carried out to enable termination of pregnancy to be performed, was rising.

Cole (1982) studied all patients who received a cervical suture in Scotland between June, 1976 and May, 1977. Three hundred and eight patients received a suture and of these, forty patients had previously undergone a termination of pregnancy.

Between 1970 and 1979 the number of patients undergoing suction termination of pregnancy in Scotland, rose from 5,254 to 7,754 (Scottish Health Statistics 1979). The greatest increase was seen in single women under twenty years of age, with the rate rising from 4.9 per 1,000 women in 1970 to 9.7 per 1,000 women in 1979. With increasing frequency of abortion, it may be that there will be a similar rise in the incidence of cervical incompetence, (Kuhn and Pepperall 1977).

Diagnosis of Cervical Incompetence.

A history of recurrent mid-trimester abortion in which premature rupture of the membranes, painless dilatation of the cervix and expulsion of the products of conception, is highly suggestive of cervical incompetence. There has been a gradual change in the policy of advocating surgical treatment for cervical incompetence. When McDonald and Shirodkar first described their sutures, operation was carried out during pregnancy, after dilatation of the cervix had occurred and often when the membranes had herniated through the cervix. Current practice is to insert the suture at a much earlier stage of the pregnancy (McDonald 1963) in the hope that the suture will prevent the cervix dilating and the membranes herniating through the cervix. Once the membranes rupture, the chances of saving the pregnancy are very poor (Cushner 1963).

The trend towards earlier insertion of the suture has been associated with a rise in the foetal survival rate from 43 per cent (McDonald 1957) to 86.5 per cent (McDonald 1980).

The criteria for selection of cases for cervical cerclage varies in the numerous reported series. There is a paradox, in that if selection of cases is not accurate, then cases who do not have cervical incompetence will improve the results of the procedure.

There is still considerable doubt as to the efficiency of cervical cerclage in the treatment of cervical incompetence. Patients with repeated spontaneous mid-trimester abortions are usually keen that "something is done" to help achieve a successful pregnancy. The obstetrician has a dilemma, whether to do something of unproven value - insert a suture, or do nothing. Pressure from the patient often pushes the balance towards insertion of a suture. The current randomised trial of cervical cerclage being run by the Medical Research Council and Royal College of Obstetricians and Gynaecologists underlines this uncertainty and will hopefully shed light on the value of this procedure.

With the move towards earlier treatment in pregnancy, there has been an interest in developing diagnostic tests

help reach the diagnosis of cervical incompetence.

se diagnostic tests can be considered in two groups:-

1. In early pregnancy before the development of cervical incompetence.
2. Between pregnancies.

Tests in early pregnancy before cervical incompetence is clinically obvious, depend on showing a degree of dilatation of the cervix. Palmer, (1950) states that in cases where the cervix would admit an 8 mm dilator, cervical incompetence invariably occurred in that pregnancy. This diagnostic aid has stood the test of time and is still used in many centres when coming to a decision as to whether to perform a cervical cerclage procedure. The test is now usually done about fourteen weeks gestation (McDonald 1963).

More recently, attempts have been made to measure the dilatation of the cervical canal using ultrasound. This is a specialised technique which requires considerable training and expertise in ultrasound. It does have the advantage that it can exclude other causes of mid-trimester abortion, such as foetal abnormality and uterine abnormalities, (Sarti et al 1979). As the technique is non-invasive, it is possible to perform the test serially, throughout pregnancy without risk to the foetus. Brook et al. (1981) performed

ultrasound measurements on twenty-four women in whom it was planned to perform cervical cerclage because of the past obstetric history and compared these patients with a control group of nineteen women who had normal obstetric histories.

The mean width of the internal os in the cerclage group was 2.57 ± 0.36 cm, compared with 1.67 ± 0.23 cm. It is also of note that following insertion of the suture, the width of the internal os was not affected. These mean diameters seem unduly large, but Brook et al.(1981) commented that these are the widths measured by ultrasound and cannot be compared with the width measured by Hegar dilators. The finding that the diameter of the internal os is not reduced by cerclage, suggests that the suture is preventing further dilatation of the cervix and therefore the earlier in pregnancy the suture is placed, the greater the chance of success, which is in keeping with McDonald's (1963) experience.

Methods of Diagnosis Between Pregnancies.

Hysterography has been used as a test to diagnose cervical incompetence since 1950. The technique involves instillation of radio-opaque dye into the uterine cavity via a cannula and then taking x-rays of the uterus. This technique allows visualisation of the shape of the isthmic

portion of the uterus and also of the dilatation of the cervical canal. Rubovitz, Cooperman and Lash (1953) and Youseff (1958) found that more information about the shape of the isthmic portion of the uterus could be obtained by modifying the technique and inflating a balloon in the uterine cavity with radio-opaque dye. Gradual reduction of the volume of dye and traction on the cannula holding the balloon, made it possible to see cases of conical dilatation of the isthmic portion, as well as dilatation of the cervical canal. They felt that these findings indicated cervical incompetence.

The disadvantage of these techniques were that they require considerable exposure to x-rays and it is not possible to obtain accurate measurements of the dilatation of the cervical canal and isthmus of the uterus. Mann (1961) modified the balloon technique and had a two-stage filling balloon which initially filled the cavity of the uterus and then expanded in the cervical canal and isthmic portion of the uterus. With this technique he was able to measure the diameter of the internal os and cervical canal. This technique does allow measurement of the cervical canal but still however requires a considerable radiological expertise to enable interpretation of the data.

In Chapter 7 data from a study of cervical resistance in patients with a history of spontaneous mid-trimester abortion, will be presented in order to evaluate the use of this technique in diagnosing cervical incompetence.

Complications of Cervical Cerclage.

Cervical cerclage should only be undertaken when a diagnosis of cervical incompetence is certain, as the procedure has several complications, including maternal death, (Dunn, Robinson and Steer, 1959). Other serious complications include Vesico-vaginal fistula (Bates and Copley, 1977) which was particularly associated with Shirodkar type suture of mersilene tape. Uterine rupture has been reported by Thurston (1963) when a suture was not removed at the onset of labour. The suture may also cut out of the cervix during labour if it is not removed, causing considerable cervical damage. It is thus important that the patient is aware of the suture and that the ante-natal case sheet clearly records the presence of a suture.

The other main complication of cervical cerclage is infection and in particular chorioamnionitis. This condition which is often followed by premature labour is seen in increasing rates in patients with premature rupture of the membranes and in patient who have a cervical stitch

in situ, (Creatsos et al. 1980). Charles and Edwards (1981) found that the incidence of chorioamnionitis increased from fourteen per cent when the suture was inserted before nineteen weeks, to thirty-nine per cent when the suture was placed after nineteen weeks of pregnancy. This increased rate is attributed to greater dilatation of the cervix at the time of insertion of the suture. Brook et al. (1981) showed, using ultrasonography, that the diameter of the cervical canal was not reduced with the insertion of a cervical suture. Cervical cerclage would therefore seem to prevent further dilatation of the cervix and the earlier the suture is placed, the less likely the cervix is to be dilated.

A further complication of insertion of a cervical suture is the effect on the myometrium. Lipshitz (1975) reported that myometrial stimulation was a side effect of cervical cerclage and Bibby et al. (1979) showed that a significant rise in 13, 14 -dihydro 15 keto prostaglandin F (PGFM) , occurred during the insertion of a cervical suture. PGFM is a major circulating metabolite of Prostaglandin F_2 which is a potent myometrial stimulant and this presumably accounts for this undesirable side effect of cervical cerclage.

Cervical dystocia is reported as a complication of cerclage. The cervix may fail to dilate in labour, as a

result of an intense reaction of fibrosis to the suture material. Kuhn and Pepperall (1977) found cervical dystocia in 5.4 per cent of cases, with the majority of patients having had a Shirodkar type suture. Robboy (1973) reported cases of cervical dystocia which did not require caesarean section but resulted in severe cervical laceration. This complication if not diagnosed may lead to further damage to an already incompetent cervix and place the patient at risk of uterine rupture. Early recourse to caesarean section will overcome this complication.

This review of cervical incompetence shows that cervical cerclage has major side effects which may further compromise the patients reproductive capacity. These side effects make it essential that good case selection is employed before undertaking a cerclage procedure. Cervical cerclage is not without side effects and should only be used in cases of proven cervical incompetence.

CHAPTER 3.

DEVELOPMENT OF AN INSTRUMENT TO MEASURE THE
FORCE REQUIRED TO PASS A DILATOR
THROUGH THE CERVIX.

DESIGN OF FORCE MEASURING INSTRUMENT.

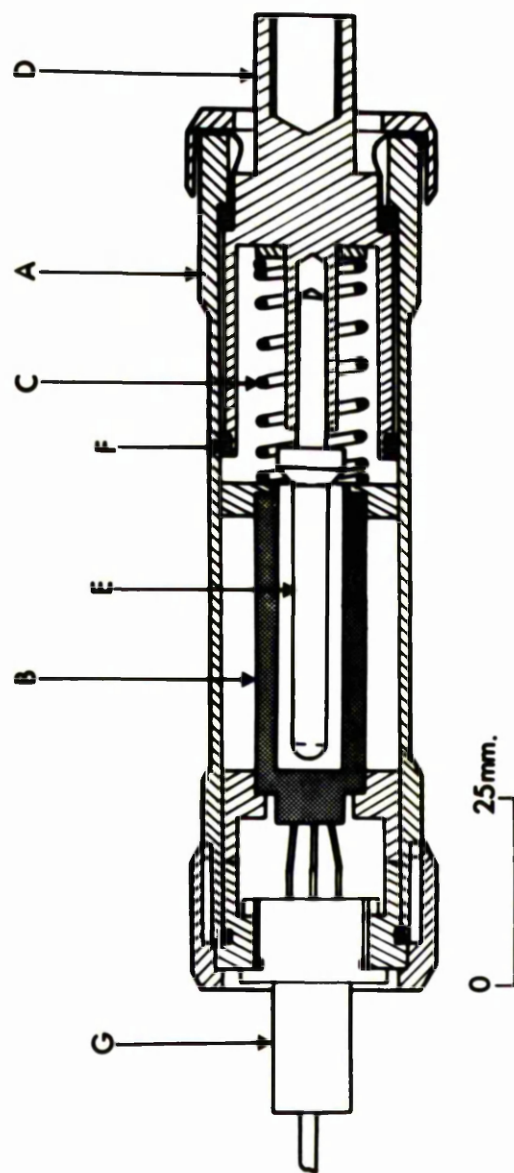
A specially designed instrument has been constructed in the Department of Clinical Physics and Bioengineering of the West of Scotland Health Boards, in Glasgow, by Mr. John Fisher.

The instrument consists of a set of graduated dilators (Figure 3.1) from 3 mm to 10 mm. The dilators are manufactured with the diameter increasing by 1 mm per dilator. The tip of this dilator is tapered at an angle of eight degrees to the axis over the last centimetre and the diameter of the dilator increases by one millimetre over this taper. Dilatation of the cervical canal takes place over the tapered portion of the dilator. Hulka et al. (1974) have shown that tapered dilators require less force to dilate the cervix than the conventional Hegar dilator which has a slightly rounded end. The dilators are manufactured from stainless steel and are sterilised by immersion in Gluteraldehyde (Cidex).

The dilators screw into the force sensing handle which is seen in Figure 3.2. A cylindrical stainless steel casing (A), contains a linear displacement transducer (B); a compression spring (C) and a stainless steel piston (D).



Figure 3.1 : Force measuring instrument with dilators.



- | | |
|----------------------------------|----------------------------------|
| A—casing | E—transducer sensor |
| B—linear displacement transducer | F—polytetrafluoroethylene bushes |
| C—compression spring | G—connector |
| D—piston | |

FIGURE 3.2 — DIAGRAM OF THE FORCE MEASURING INSTRUMENT

The transducer sensor (E) is attached to the inner end of the piston and the dilators are in turn screwed into the outer end. The piston assembly is free to slide on polytetrafluoroethylene bushes.

An axial force on the dilator displaces the piston against the spring and the displacement is monitored by the transducer. The spring gives a displacement of one millimetre for a five kilogram force. This small displacement ensures precise control of the dilators. The input and output signal from the transducer are passed through a sealed connector (G) at the rear of the instrument. The output signal is processed by Phillips Displacement Converter PR 871 - giving an output of 0.1 volt D.C. for a 0.45 kilogram force. This is displayed on a Devices MX 212 - 2 channel recorder (Figure 3.3)

Use of the Instrument.

All patients were studied under general anaesthesia. The patient was placed in the lithotomy position and the vulva and vagina cleansed and draped in the usual fashion for minor gynaecological surgery. The cervix was grasped with Volsellum forceps to steady it during the procedure. With the operator gowned and gloved, the force sensing handle was held in a sterile towel and the smallest dilator

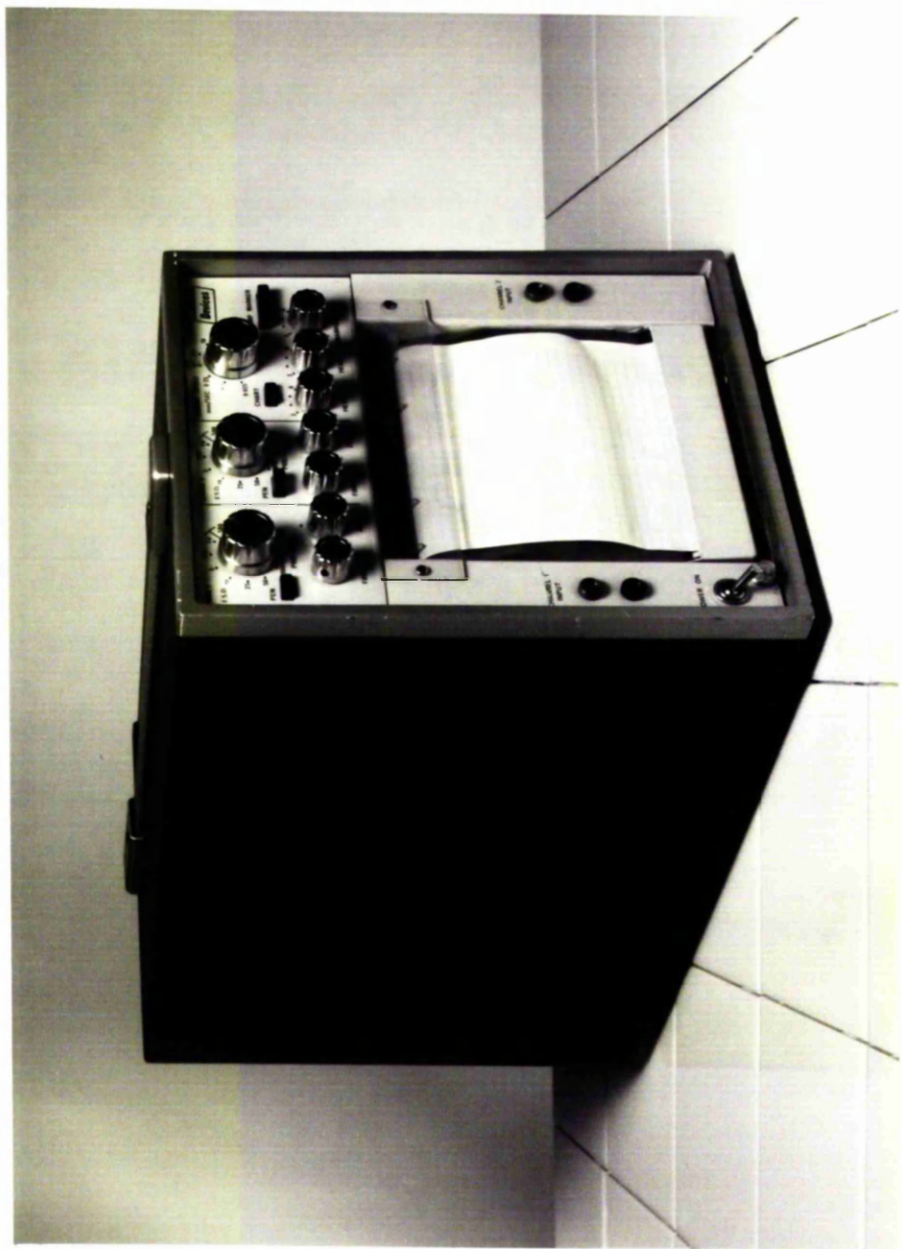


Figure 3.3 : Devices recorder.

screwed into the handle. The dilator was then passed through the cervix by applying steady pressure via the handle. In view of the time dependence of the viscous element of cervical tissue, it was endeavoured to make the time taken to pass the dilator standard, by having all estimations performed by the author.

It is not practical to ensure that every passage of a dilator lasts exactly the same time but the effect of time on dilatation will be discussed in Chapter 4. Once the dilator had passed through the cervix it was unscrewed and the procedure repeated with each dilator in turn.

Each dilator which met resistance produced a deflection on the graph paper of the Devices recorder. A permanent record (Figure 3.4) of each patient was kept and the record analysed at completion of the operation. The height of each peak on the graph was measured, a deflection of 0.5 cm representing a force of one kilogram. The force required to dilate the cervix from 3 mm to 8 mm was calculated. This force we defined as the Cervical Resistance Index (CRI).

Once the operator is familiar with the instrument it is as easy to use as a conventional set of cervical dilators. The force sensing handle is simple, portable and at a cost of £300., relatively cheap. The instrument has only one

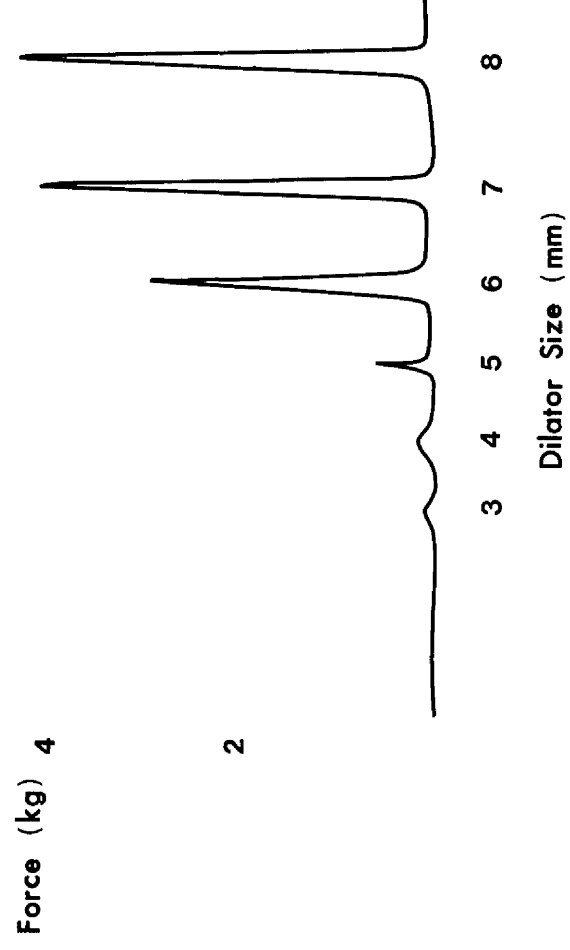


FIGURE 3.4 — SPECIMEN CHART RECORDING FROM A NON-PREGNANT PATIENT

moving part, the piston, whose movement of the transducer sensor in the transducer, alters the electromagnetic field which is then measured. Calibration of the instrument can alter if the tension in the compression spring alters, if changes occur in the electronics of the displacement convertor or, if the recorder calibration alters. In the three years that the instrument has been in use, its calibration has been regularly checked and it has not altered. It has thus proved to be a very reliable instrument.

CHAPTER 4.

ANALYSIS OF DATA OBTAINED DURING MEASUREMENT
OF THE FORCE REQUIRED TO PASS A DILATOR
THROUGH THE CERVIX.

CHARACTERISTICS OF FORCES REQUIRED
TO PASS A DILATOR THROUGH THE CERVIX.

Using the instrument described in Chapter 3, a record of the force required to pass a series of dilators through the cervix was obtained (Figure 3.4). From this record it was apparent that, in general, increasing diameters of dilators require increasing forces to pass through the cervix. This pattern has been seen in three groups of patients studied, namely - non-pregnant patients pregnant patients and patients with a history of previous spontaneous mid-trimester abortion. This finding was also observed by Hulka et al. (1974); Black et al. (1975); Liu et al. (1975) and Atienza, Burkman and King (1980). In a few cases this pattern was not observed when there was a fall in the force required to pass the dilator, after a few dilators had shown the more usual increasing force pattern.

This finding probably indicated the occurrence of a cervical tear at the level of the internal os, similar to those described by Hulka and Higgins (1961). Hulka et al. (1974) also found this type of pattern when dilatation exceeded 12 mm.

From the specimen recording (Figure 3.4) it can also

be seen that passage of a dilator produced a quick rise in the force applied to the dilator, followed by an even quicker reduction in the force, once the taper of the dilator had passed through the internal os. The average time taken to pass a dilator through the cervix was about two seconds. The time between passage of different sized dilators was kept to a minimum. The author performed all dilatations in order to standardise the technique of passing the dilator and in the hope that the time taken for this would be uniform. Three experienced Consultant Gynaecologists have also used the instrument to check whether the author's technique of passing a dilator through the cervix was comparable with their usual technique. No significant difference in the time taken to pass the dilators through the cervix was noted in this study.

Liu et al. (1975) and Black et al. (1975b) using hysterectomy specimens of uterus and cervix, claim to have standardised the time taken to pass a dilator through the cervix to five seconds but this was during an in vitro study. In vivo, it is not possible to know in advance how long it will take to overcome the cervical resistance.

The Effect of Time Taken to Pass a Dilator Through the Cervix.

Black et al. (1975) have drawn attention to the visco-elastic properties of cervical tissue and in particular that the viscous element of the cervix is time dependant. Hulka et al. (1974) and Atienza Burkman and King (1980) in their studies on forces required for surgical dilatation, expressed the results as forcetime integers. This figure was derived from computing the force required to pass the dilator and the time which was taken for passage of the dilator through the cervix. The technique used by the author was to measure the height of each peak achieved when resistance was encountered to dilatation and then by summation the total force required to dilate a cervix from 3 mm to 8 mm was calculated (CRI).

In order to establish the relationship between estimations based on peak height and those based on force and time taken for dilatation, twenty-one patients were studied and both categories of data were analysed.

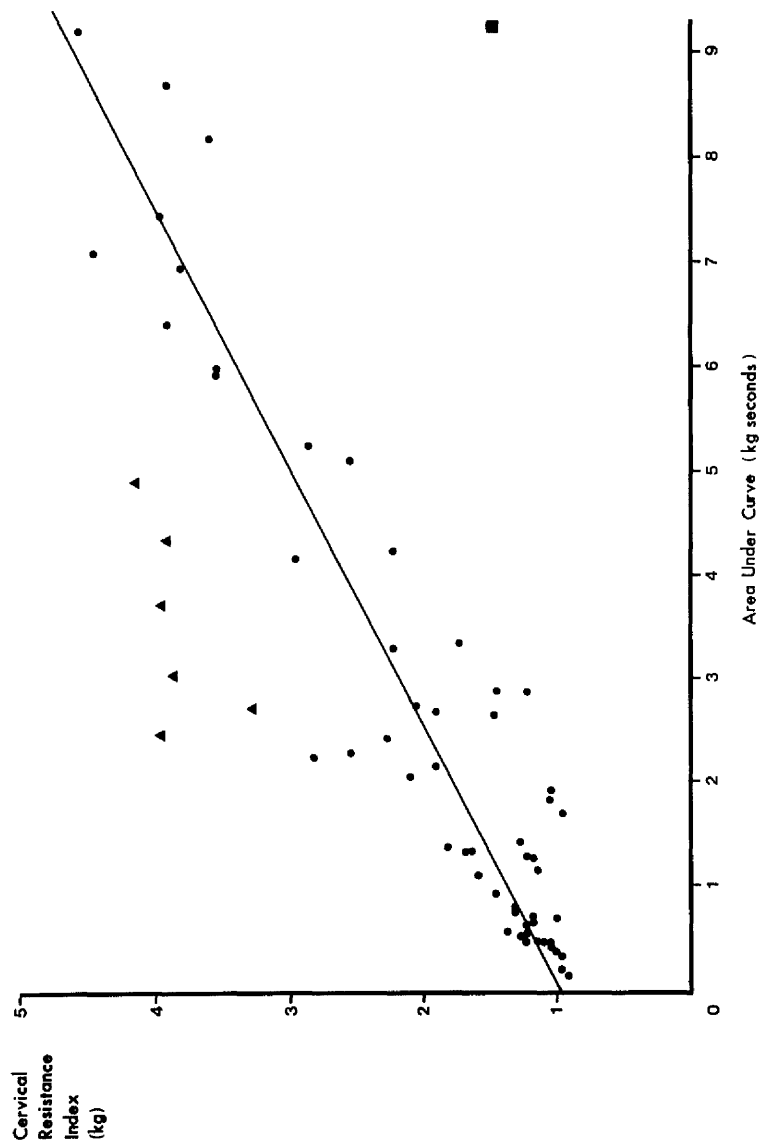
The instrument described in Chapter 3 was used in conjunction with a Nascom 2 computer which was programmed to measure the area under the curve in each deflection. As the passage of a dilator took about two seconds the computer

analysed the data fifty times per second and produced a summation of these measurements for each deflection.

Dilatation of the cervix in the twenty-one patients produced sixty-two recordings of resistance to a dilator. Figure 4.1 shows the relationship between peak height in kilograms and area under the curve in kilogram seconds. The correlation factor between peak height and area under the curve was 0.77 - indicating that the time taken to pass the dilator had been fairly uniform. As the force to pass a dilator has both elastic and viscous elements, measurement of peak height was as reliable as measurement of the force-time integer.

From the graph of peak height against area under the curve, it can be seen that the correlation line does not run through zero. This was probably due to the detection threshold of the input to the computer.

There were seven recordings (▲■) which were widely scattered from the correlation line. In three of the patients the dilator passed through the cervix unusually quickly, but the cervix did not sustain any apparent damage. Four of these recordings occurred when dilatation of the cervix with that particular dilator, produced the usual increasing pattern and then the next dilator produced a marked reduction



in the force required to pass it through the cervix. In three patients (▲) the dilator passed through the cervix unusually quickly and in one (■) dilatation was difficult and took much longer than usual. It seems likely that these four cases sustained cervical tears of the type described by Hulka and Higgins (1961). Measurement of CRI identified dilatations which required considerable force, whereas measurement of the force-time integers would not identify these cases if the time taken for dilatation was unduly short. While every effort was made to use a standard technique of passing the dilator, these seven cases illustrate the difficulties in attempting to standardise the time taken to pass a dilator through the cervix. By introducing time into the calculation of force-time integers, one is introducing another variable which cannot be precisely controlled.

Dilatation Characteristics in Non-Pregnant Patients.

In (Figure 4.2) the median force for each dilator size has been plotted against the size of dilator. This shows a curved relationship between force and dilatation. Black et al. (1975b) have shown that the slope of the curve may be used as a measure of the "dilatability of the cervix".

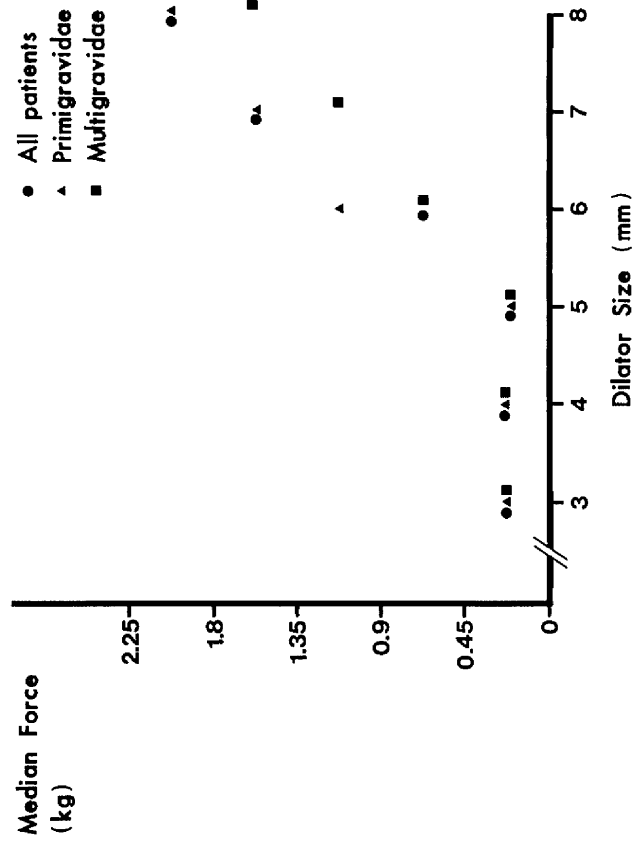


FIGURE 4.2—THE EFFECT OF PARITY ON THE MEDIAN FORCE FOR EACH DILATOR

To obtain the slope of the curve, it is necessary to plot log dilatation force against log of dilatation and this gives a straight line.

The effect of parity on CRI will be discussed in Chapter 5. Further analysis of the force dilatation curves (Figure 4.2) show that primigravid patients had higher median force for each dilator size, compared to multigravid patients. The effect of hormone status on the force dilation curves is seen in Figure 4.3. Again it was seen that patients with higher CRI (post menopausal women) showed a different slope of curve to those with lower CRI (patients on Depo-Provera). It was interesting that groups of patients in whom the summated force for dilatation was high, show higher values of force with each dilator and similarly those with lower resistance, again showed low resistance with each dilator. This finding validated the use of summation of the force required to dilate the cervix to 8 mm, since similar patterns of force dilatation curves were seen in all groups of non-pregnant patients studied.

The Effect of the Diameter of the Cervical Canal on the Force Required to Dilate the Cervix.

The cervical resistance at a given diameter is dependant on the diameter of the cervical canal prior to dilatation and on the compressibility of the cervical tissue.

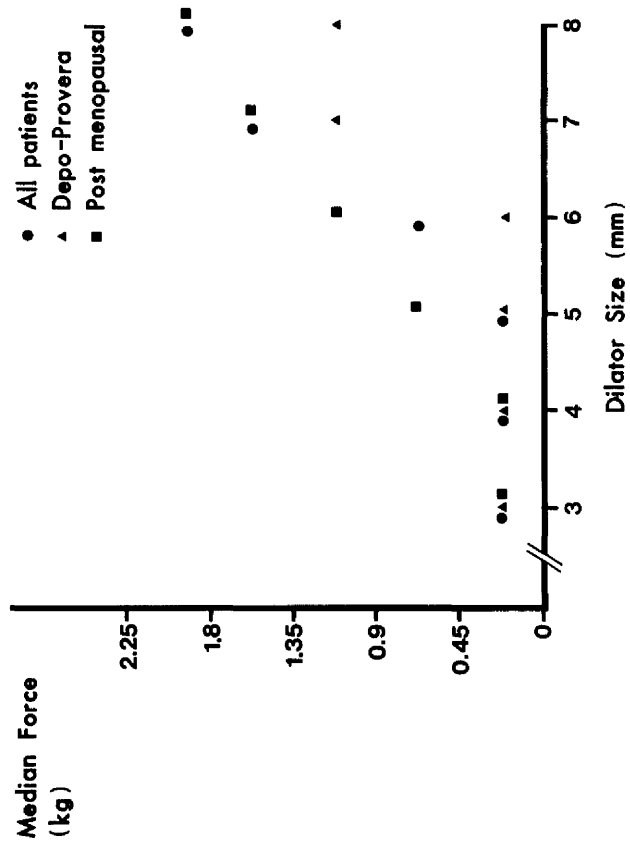


FIGURE 4.3—THE EFFECT OF HORMONE STATUS ON THE MEDIAN FORCE FOR EACH DILATOR

Halliday, Jacobs and Heyns (1958) and Johnstone et al. (1974) have shown that the diameter of the cervical canal is influenced by the number of pregnancies that the patient has had.

In order to assess the effect of the diameter of the cervical canal on cervical resistance measurements, the relationship between the first dilator to meet resistance and the cervical resistance index has been studied. These parameters were compared in 172 non-pregnant multiparous patients and the results are shown in Table 4.1.

First Dilator to meet resistance.	No. of Patients.	C.R.I. Mean \pm S.D.
3 mm	20	9.63 \pm 4.49
4 mm	18	6.86 \pm 3.30
5 mm	36	6.30 \pm 2.75
6 mm	47	3.96 \pm 1.89
7 mm	38	1.99 \pm 1.15
8 mm	13	0.76 \pm 1.01

Table 4.1 : The relationship between CRI and first dilator to meet resistance.

The correlation coefficient between the first dilator to meet resistance and CRI is 0.72. This is a significant

relationship ($P < 0.0005$). This finding is hardly surprising since the greater the diameter of the cervical canal, the fewer dilators there will be to meet resistance. The standard deviations of the mean CRI are large for each dilator, indicating the wide scatter of values of CRI for that dilator. The CRI measurements for patients in which the 5 mm dilator was the first to meet resistance, varied between 1.27 and 11.53. The wide scatter of values for any given diameter of the cervical canal, indicates the variation that is present in the elasticity of cervical tissue.

Summation of the force required to dilate the cervix to 8 mm, therefore takes into account the elasticity of the tissue and the diameter of the canal. Since the diameter of the cervical canal is not known until dilatation is undertaken, measurement of CRI gives an indication of the ease with which the cervix may be dilated.

In considering drug therapy aimed at reducing cervical resistance, further analysis of the data may be necessary to identify which element of resistance is being affected by the therapy.

Summation of the force to dilate the cervix to 8 mm (which we have called CRI) therefore takes account of the many variable factors which influence the passage of a dilator through the cervix.

CHAPTER 5.

CERVICAL RESISTANCE IN NON-PREGNANT PATIENTS.

This chapter describes a study of cervical resistance in non-pregnant patients. The instrument described in Chapter 3 has been used in 200 non-pregnant patients.

Patients and Methods.

Two hundred patients undergoing diagnostic curettage for a variety of symptoms and conditions were studied. The indications for diagnostic curettage are shown in Table 5.1.

	Number of Patients.		
	Nulliparous	Multiparous	Total
Menstrual Symptoms	10	38	48
Pelvic Pain	4	5	9
Vaginal discharge	2	11	13
Postmenopausal bleeding	0	16	16
Infertility	8	2	10
IUCD	0	4	4
Sterilisation	2	92	94
Reversal of Sterilisation	0	6	6
TOTALS	26	174	200

Table 5.1 : Indications for operation in patients studied.

None of the patients had conditions directly related to the cervix. All patients were studied under general anaesthesia, using the technique described in Chapter 3.

The CRI was calculated as described in Chapter 4. All results are expressed in kilograms \pm standard error of the mean (SEM). A sample of venous blood was withdrawn prior to operation and the plasma levels of progesterone and 17β -oestradiol were measured with specific radioimmunoassays. Statistical comparisons between the results in different groups of patients were made using the Student's t-test for unpaired data.

RESULTS.

Parity.

The effect of parity on CRI is seen in Table 5.2. A lowering of CRI was seen with increasing parity.

Parity	No. of Patients	CRI (Mean \pm SEM)
0	26	7.18 \pm 0.91
1 or 2	83	4.59 \pm 0.41
≥ 3	91	4.45 \pm 0.36
All parities	200	4.92 \pm 0.20

Table 5.2 : The effect of parity on CRI in non-pregnant patients.

The CRI was significantly lower in women with parity of 3 or more, compared with nulliparous women ($P < 0.05$).

This may in part be explained by the findings of Johnstone et al. (1974) who found that the diameter of the internal os increased with increasing parity.

Age of Patients.

The age of the patient was not an important variable. Increasing age may expose patients to an increasing number of pregnancies. The correlation coefficients of CRI with age were 0.26 and 0.24 in nulliparous and multiparous women respectively. When parity is taken into account, age has no significant effect on CRI.

Phase of the Menstrual Cycle.

Those pre-menopausal patients who were not receiving hormonal contraception were ascribed to the proliferative, secretory or menstrual groups according to the endometrial histology. The effect of the phase of the menstrual cycle on CRI is shown in Table 5.3. The lowest resistance was seen in the menstrual group but there were no significant differences between any of the groups.

Phase of Cycle	Number	CRI (Mean \pm SEM)
Proliferative phase	48	4.45 \pm 0.55
Secretory phase	43	5.45 \pm 0.59
Menstrual phase	11	4.32 \pm 1.77
All phases	102	4.91 \pm 0.41

Table 5.3 : The effect of the phase of the menstrual cycle on CRI.

Johnstone et al.(1974) observed a significantly greater diameter of the internal os at the time of menstruation but in our study the cervical resistance did not significantly differ from other phases of the cycle.

Youseff (1953) in a study of hystero-graphy, noted that in the proliferative phase of the cycle, the cervix appeared to be moderately dilated, dye remained in the uterus for about three hours and then ran out through the Fallopian tubes and the cervix. In the luteal phase, the cervix was much narrower and dye remained in the uterus for up to eight hours before emptying through the Fallopian tubes into the peritoneal cavity. About two days prior to menstruation, the cervix became more dilated again, dye only remained in the uterus for about thirty minutes before running out through the cervix.

Johnstone et al. (1974) studied the diameter of the cervical canals in seven women throughout the menstrual cycle. He found a similar pattern of change in the diameter of the canal to those reported by Youseff. In Johnstone's study, the diameter of the cervix was significantly lower at ovulation and in the luteal phase compared with the diameter in the proliferative phase of the cycle.

The results in our study follow the pattern of change described by Youseff, although the differences are not significant despite the large number of patients studied.

In 71 of the 102 women with regular menstrual cycles, the date of the last period was known. The mean cervical resistance for each day of the menstrual cycle is shown in Figure 5.1. There is no significant difference in the CRI on any particular day of the menstrual cycle. This is in keeping with the data based on endometrial histology.

Hormone Status of the Patient.

The CRI for each patient was plotted against the circulating levels of progesterone (Figure 5.2) and 17β -oestradiol (Figure 5.3). The correlation coefficients were 0.13 and -0.05 respectively. Progesterone and 17β -oestradiol play an important role in the modification of cervical collagen which is associated with cervical softening in late pregnancy (Calder 1980). The present study has failed to show any direct correlation between CRI and the circulating levels of these hormones in the non-pregnant state. It may be that the circulating levels of these hormones do not reflect their influence and activity at the cervix itself.

The group of 102 normal cycling women were compared with a group of patients using combined oral contraceptives;

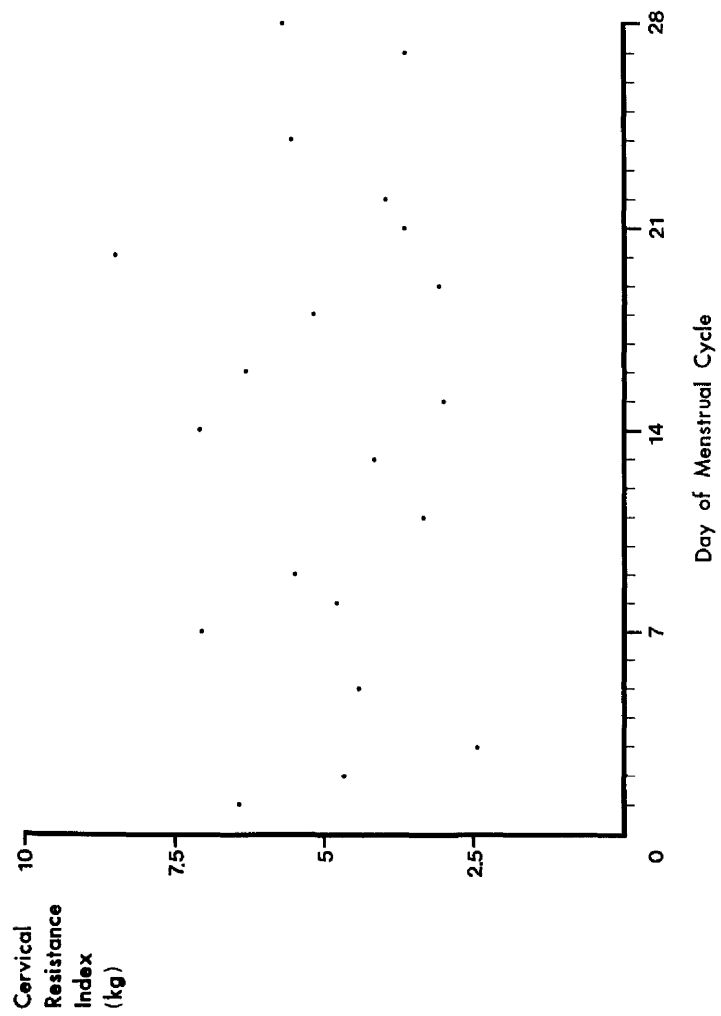


FIGURE 5.1 —THE EFFECT OF THE MENSTRUAL CYCLE ON C.R.I.

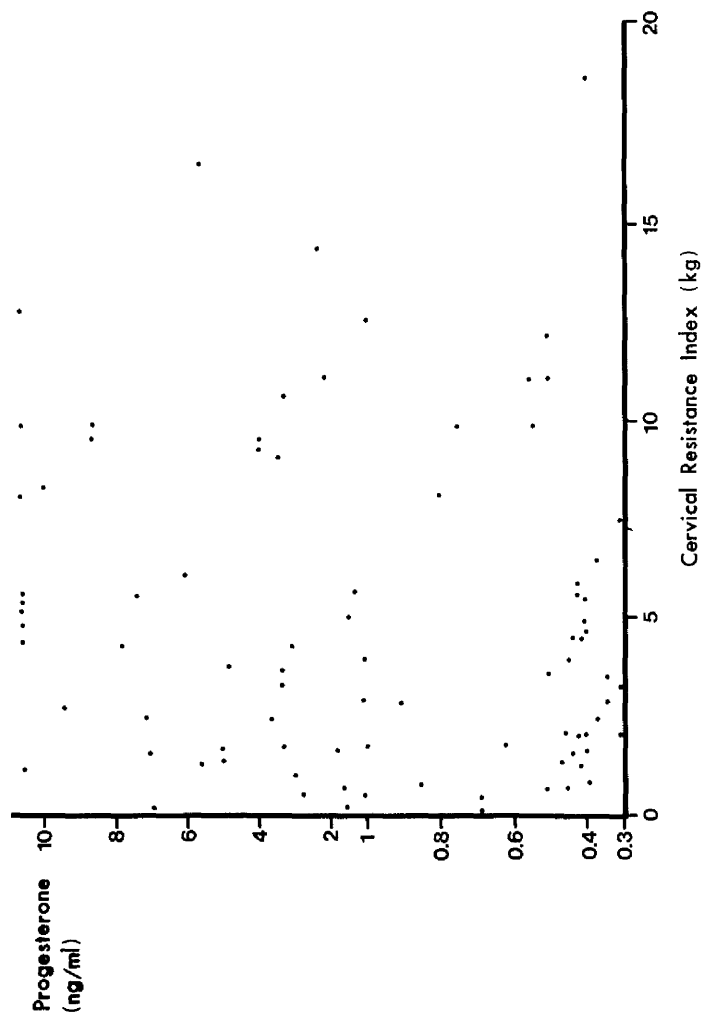


FIGURE 5.2—THE RELATIONSHIP BETWEEN SERUM PROGESTERONE CONCENTRATION AND C.R.I.

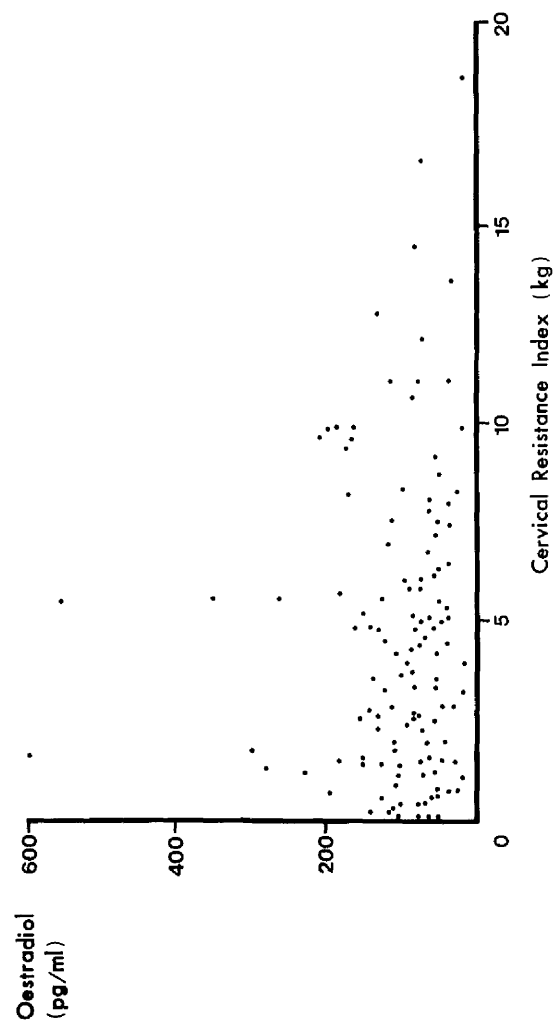


FIGURE 5.3—THE RELATIONSHIP BETWEEN SERUM OESTRADIOL CONCENTRATION AND C.R.I.

a group using intrauterine contraceptive devices and a group receiving intramuscular medroxy-progesterone acetate, (Depo-Provera) for contraceptive purposes (Table 5.4).

Sixteen women admitted for investigation of postmenopausal bleeding were studied. None of these patients had endometrial or cervical malignancy.

Category	Number	Mean Parity	C.R.I. (Mean \pm SEM)
Cycling	102	2.5	4.91 \pm 0.41
Contraception:			
(a) Combined Pill	39	2.2	4.32 \pm 0.45
(b) IUCD	7	2.4	5.45 \pm 2.23
(c) Depo-Provera	18	2.0	2.68 \pm 0.64
Postmenopausal	16	3.5	7.45 \pm 1.27

Table 5.4. : The influence of hormone status on the Cervical Resistance.

The postmenopausal women showed significantly higher CRI than the cycling group ($P < 0.05$). These women were of higher parity than the cycling group. In pre-menopausal women, increasing parity led to lower cervical resistance. This finding is at variance with the findings of Youseff(1958). He found the cervix to be more dilated, a finding which he attributed to atrophy of the muscle content of the cervix. In clinical practice the cervix is usually relatively firm and rigid after the menopause.

Patients on combined oral contraception showed slightly low cervical resistance than the cycling group, while those using an IUCD, had slightly higher cervical resistance. These differences were not significant. Patients receiving Depo-Provera showed significantly lower cervical resistance than the cycling group ($P < 0.0025$). Depo-Provera is often used for contraception in women of low social class and high parity, who are unreliable in their use of other methods of contraception. This finding of lower CRI cannot be explained on the basis of parity, since they had a lower mean parity than the cycling group. Progestogens are known to relax smooth muscle. The small amount of smooth muscle in the cervix has generally been considered of little importance to cervical function. Depo-Provera may be affecting the cervical smooth muscle or alternatively, it may be affecting the ground substance. This observation requires further investigation.

The results presented here, establish baseline values for cycling, contracepting, and postmenopausal women.

CHAPTER 6.

THE EFFECT OF EXOGENOUS HORMONES
ON CERVICAL RESISTANCE
IN EARLY PREGNANCY.

Termination of pregnancy in the first trimester involves dilatation of the cervix prior to suction curettage. Damage sustained by the cervix during dilatation may result in an increased rate of spontaneous mid-trimester abortion (Wright, Campbell and Beazley 1972) and pre-term labour in future pregnancies, (Richardson and Dixon 1976).

Since the introduction of the Abortion Act, 1976, the number of first trimester abortions has greatly increased. In Scotland the number rose by 47.58 per cent between 1970 (5,254) and 1979 (7,754), (Scottish Health Statistics 1979). In young single nulliparous women under the age of twenty, the incidence of abortion virtually doubled from 4.9 per 1,000 women in 1970 to 9.7 per 1,000 women in 1979. Atienza, Burkman and King (1980) found that nulliparous women were ten times more likely to sustain cervical laceration during dilatation of the cervix than multiparous women. With the increased numbers of women seeking abortion, the number who may have problems in future pregnancies will almost certainly rise, (Kuhn and Pepperall 1977).

This Chapter describes studies of the effects of exogenous treatment with oestradiol, progesterone, medroxy-progesterone acetate and prostaglandin E₂ on the

Cervical Resistance Index (CRI).

Three hundred and fifty-five patients were studied during dilatation of the cervix prior to suction curettage. All patients had a gestational age of twelve weeks or less. The size of the largest dilator used varied between 8 mm and 10 mm depending on the gestational age of the pregnancy. To allow comparison between groups and against non-pregnant patients, the force required to dilate the cervix from 3 mm to 8 mm has been calculated (CRI). Under general anaesthesia, the force required to dilate the cervix from 3 mm to 8 mm was measured using the instrument described in Chapter 3.

One hundred patients were used as controls with which to compare the hormone treated groups. The control group included sixty patients who received no treatment prior to measurement of CRI and forty patients who received a pessary of polyethylene glycol (the base used in the preparation of the hormone pessaries). There was no significant difference in CRI between these two groups of patients and they have therefore been combined to form the control group. The control group were compared with a group of two hundred non-pregnant patients described in Chapter 5, in order to assess the effect of pregnancy on CRI.

The Effect of Pregnancy on CRI.

The control group of patients were compared with 200 non-pregnant patients to assess the effect of pregnancy on CRI.

	Cervical Resistance Index (mean \pm SEM)	
	Non-pregnant	Pregnant
Nulliparous	7.18 \pm 0.91 (26)	5.13 \pm 0.43 (55)
Multiparous	4.55 \pm 0.41 (174)	4.30 \pm 0.42 (45)
All patients	4.92 \pm 0.20 (200)	4.77 \pm 0.30 (100)

Table 6.1 : The effect of pregnancy on CRI.

Pregnant patients showed a lower CRI than non-pregnant patients. When groups were divided into nulliparous and multiparous patients, the nulliparous pregnant patients showed significantly lower CRI than the nulliparous non-pregnant patients, ($P < 0.05$). This lowering of CRI in pregnancy is in accord with the common clinical impression that the cervix is soft in early pregnancy.

The effect of parity seen in non-pregnant patients was also seen in pregnant patients. The CRI in multiparous patients was significantly lower than that seen in nulliparous patients ($P < 0.05$).

Gestational Age.

The correlation coefficients of CRI with gestational age were -0.51 and -0.11 in nulliparous and multiparous women respectively. There is no significant correlation between gestational age and CRI. This finding is at variance with the findings of Hulka et al. (1974). Hulka, in a study of only thirty-five nulliparous women, found that increasing gestational age was associated with reduction of the cervical resistance, however, only five of the patients were beyond ten weeks gestation and two of them had gestational ages of thirteen and fourteen weeks respectively.

The Effect of Hormone Treatment on Cervical Resistance.

Two hundred and fifty-five patients received hormone pessaries as shown in Table 6.2. All pessaries were placed in the posterior vaginal fornix, twelve hours prior to measurement of CRI. The pessaries which used polyethylene glycol as the base, were prepared by the Pharmacy Department in Glasgow Royal Infirmary. The progesterone pessaries used were commercially available "Cyclogest" pessaries. The lactic acid based pessaries were generously provided by Upjohn Ltd. These pessaries contain 3 mg PGE_2 and the patients who were treated with 6 mg received two 3 mg pessaries.

The patients who received a pessary were questioned about the occurrence of vaginal bleeding, uterine activity and gastro-intestinal upset prior to administration of the anaesthetic premedication.

Hormone	Type of Pessary	No. of Patients
Oestradiol	50 mg in Polyethylene Glycol	40
Progesterone	200 mg in Glyceride base (Cyclogest)	40
Medroxy-progesterone acetate	200 mg in Polyethylene Glycol	40
Prostaglandin E ₂	0.5 mg in Polyethylene Glycol	40
	3 mg in Polyethylene Glycol	35
	3 mg in Lactic Acid (Upjohn)	30
	6 mg in Lactic Acid (Upjohn)	30

Table 6.2 : Pessaries given prior to measurement of CRI.

Statistical comparisons between the results in different groups of patients were made using the Student's t-test for unpaired data.

The Effect of Oestradiol, Progesterone and Medroxy-progesterone Acetate on CRI.

The effect of these hormones on CRI is shown in table 6.3. Oestradiol had no effect on CRI in nulliparous or multiparous patients in the first trimester of pregnancy. Oestradiol administered by the extra-amniotic route in late pregnancy

has been shown to cause cervical ripening (Gordon and Calder 1977; Stewart et al 1981). In the non-pregnant sheep cervix, our group has produced changes similar to those seen in late pregnancy, with a combination of oestrogen and progesterone. These changes did not occur when oestrogen or progesterone alone were administered. It may be that in the first trimester of human pregnancy, there is insufficient progesterone in the cervical tissue to mediate the oestrogen response seen in late pregnancy.

Pessaries	Cervical Resistance Index (Mean \pm SEM)	
	Nulliparous	Multiparous
Control Group	5.13 \pm 0.43 (55)	4.30 \pm 0.46 (45)
Oestradiol 50 mg	5.64 \pm 0.62 (22)	4.26 \pm 0.89 (18)
Progesterone 200 mg.	6.77 \pm 0.95 (21)	5.55 \pm 0.86 (19)
Medroxy-progesterone acetate 200 mg.	7.05 \pm 1.05 (16)	4.00 \pm 1.09 (24)

Table 6.3 : The effect of exogenous hormones on CRI.

The apparent rise in CRI in both nulliparous and multiparous patients following progesterone therapy was not significant. Progesterone is known to relax smooth muscle but the small amount of smooth muscle in the cervix has generally been considered to play little part in cervical physiology. In our sheep experiments, progesterone alone

did not produce the reduction in density of the collagen fibres that was seen with combined oestrogen and progesterone therapy. Since the collagen fibre matrix probably is responsible for the compliance of cervical tissue, it is not surprising that progesterone had little effect on CRI.

Long term systemic medroxy-progesterone acetate (Depo-Provera) was shown to lower CRI in multiparous patients in the non-pregnant state (Chapter 5). When this hormone was given vaginally to patients in the first trimester of pregnancy, nulliparas showed a rise in CRI, while no effect was seen in multiparas. The difference in nulliparous patients is not significant. Depo-Provera in non-pregnant patients, abolishes ovulation for up to four months. Most of the patients studied in Chapter 5 had been receiving Depo-Provera for at least one year. Perhaps the twelve hours of treatment used in the pregnant patients is too short a time to see an effect on CRI.

Jeffrey and Koob (1980) have shown that in the rat uterus, progesterone and Depo-Provera prevent degradation of collagen and inhibit the production of collagenase. The effect of these actions is to make the collagen fibres matrix more rigid and therefore more difficult to dilate. Hillier (1977) has shown that progesterone inhibits collagenase

activity in cultures of human cervical tissue. These observations may explain the rise seen in CRI when patients were treated with progesterone and medroxy-progesterone acetate.

The Effect of Prostaglandin E₂ on CRI.

The CRI in prostaglandin treated patients are compared with the control group in table 6.4.

	Cervical Resistance Index (Mean \pm SEM)	
	Nulliparous	Multiparous
Control	5.13 \pm 0.43 (55)	4.30 \pm 0.42 (45)
0.5 mg in PEG	3.55 \pm 0.54 (19)	3.03 \pm 0.55 (21)
3 mg in PEG	4.78 \pm 0.65 (20)	2.85 \pm 0.65 (15)
3 mg in Lactic Acid	5.90 \pm 0.66 (16)	2.95 \pm 0.56 (14)
6 mg in Lactic Acid	5.33 \pm 1.17 (15)	2.05 \pm 0.52 (15)

Table 6.4 : The Effect of Prostaglandin E₂ on CRI.

The pessaries containing 0.5 mg PGE₂ in polyethylene glycol produced significant lowering of CRI in nulliparous and multiparous patients ($P < 0.05$). The 3 mg. pessary in polyethylene glycol produced a significant lowering of CRI only in multiparous patients ($P < 0.005$).

The 3 mg. pessaries in lactic acid produced no change in CRI in nulliparous patients but significantly lowered

the CRI in multiparous patients ($P < 0.05$). The 6 mg pessaries produced no effect in nulliparous patients while the CRI in multiparous patients was significantly lowered ($P < 0.005$).

No prostaglandin related side effects were noted in the 0.5 mg group. Four patients who received the 3 mg pessary in polyethylene glycol complained of uterine cramp on questioning - three nulliparous and one multiparous patient. One nulliparous patient who received 3 mg lactic acid pessary complained of cramp. The 6 mg pessaries produced side effects in eight patients. One nulliparous and four multiparous patients complained of cramp, while three nulliparous patients complained of nausea the following morning.

Mackenzie and Fry (1981) in a study using 5 mg, 10 mg and 15 mg PGE_2 pessaries, one to six hours prior to operation, found the cervix to be easier to dilate, on subjective assessment, with 10 mg and 15 mg PGE_2 pessaries. Nine patients who received 15 mg pessaries and four who received 10 mg pessaries, had to be given intramuscular Papavertum to relieve abdominal discomfort. Many of our patients were admitted as day cases having inserted the pessary at home. The occurrence of pain requiring sedation, obviously makes the use of such large doses of prostaglandin E_2 unacceptable for

outpatient care.

Prostaglandin E_2 is now widely recognised as being capable of producing softening of the cervix in pregnancy. Stys et al. (1981) inserted pressure balloons in the cervical os of pregnant sheep between days 124 and 142 of pregnancy. Ten milligram of PGE_2 in K-Y jelly was inserted into the cervical canal three times, at four hourly intervals. Within 8 to 12 hours the compliance of the cervix had increased to the levels seen at spontaneous parturition. The cervical compliance of those ewes which did not go into labour, returned to normal in 24 to 72 hours, after ceasation of the treatment. Conrad and Ueland (1979) subjected strips of human cervix, after spontaneous, oxytocin-induced and prostaglandin E_2 induced labour, to stretching. The stretch modulus of prostaglandin induced patients was significantly lower than the other two groups, indicating that prostaglandin E_2 had produced softening of the cervical tissue.

Dingfelder et al. (1975) compared cervical resistance in patients treated with 50 mg $PGF_{2\alpha}$ and 20 mg PGE_2 , three hours prior to cervical dilatation for therapeutic abortion. The resistance was reduced with PGE_2 and significantly reduced with $PGF_{2\alpha}$. Gastro-intestinal side effects were

noted in 60 per cent of patients treated with PGE_2 and 40 per cent of patients treated with $\text{PGF}_{2\alpha}$. Ten per cent of patients in both groups required sedation for painful uterine activity. Recently 16, 16 - dimethyl - trans $-\Delta^2$ - PGE_1 (16 me E_1) has been given as a pessary prior to abortion by Nakano et al. (1980) and Welch and Elder (1982). Nakano et al., inserted a 1 mg pessary of 16 me E_1 at three hourly intervals and found that after five pessaries 56.6 per cent had aborted, while in a further 26.1 per cent, the cervix had dilated to 10 mm. Welch and Elder (1982) found a significant reduction in cervical resistance using a 1 mg me E_1 pessary but 44 per cent of patients experienced mild to moderate pain and bleeding between $1\frac{1}{2}$ and 3 hours after insertion of the pessary.

In the current study, patients were often treated as outpatients. Large doses of PGE_2 , while having the desired effect on the cervix, produce uterine activity (MacKenzie and Fry 1981), thus rendering them unsuitable for outpatient use. The use of 16 me E_1 produced complete abortion in a large number of cases (Nakano et al. 1980) and this again makes the technique unsuitable for outpatient use.

The four dosage regimes used in this Chapter have produced a significant fall in CRI of multiparous patients, compared to the control. It is thus relatively easy in

multiparous patients to facilitate dilatation of the cervix by the administration of prostaglandins.

It is difficult to explain our failure to produce a consistent effect in nulliparous patients. In pregnancy the amount of cervical secretion increases. Cervical secretions are alkaline and while this might interfere with the release of prostaglandin from the lactic acid based pessaries, it is difficult to explain why these pessaries produced an effect in multiparous patients and not in nulliparous patients.

In the multiparous patients the effect of PGE_2 on CRI seems to be dose related. It is difficult to explain why 3 mg PGE_2 in polyethylene glycol has produced no response *2.88 10.11* when 0.5 mg PGE_2 in the same base, produced a significant *3.03 10.11* reduction in CRI. Dingfelder et al. (1975) were unable *4.0 10.11* to significantly reduce cervical resistance in patients using a dose of 20 mg PGE_2 . This dose of PGE_2 did produce uterine activity in 10 per cent of patients, although it was only given three hours prior to operation.

Mode of Action of Prostaglandin.

In order to study which element of cervical resistance was being affected by treatment with Prostaglandin E_2

pessaries, the diameter of the cervical canal prior to dilatation has been studied. The first dilator to meet resistance was noted in the control group and in all prostaglandin treated groups. The diameter of the cervical canal prior to dilatation in nulliparous patients is shown in table 6.5. Statistical comparisons between the results in different groups of patients were made using Chi-Square test of significance.

	CRI (Mean \pm SEM)	Diam. of the cervical canal (Mean \pm SEM)
Control Group	5.13 \pm 0.43	5.65 \pm 0.13
PGE ₂ 0.5 mg in PEG	3.55 \pm 0.54	5.84 \pm 0.19
PGE ₂ 3 mg in PEG	4.78 \pm 0.65	5.65 \pm 0.20
PGE ₂ 3 mg in Lactic Acid	5.90 \pm 0.66	5.56 \pm 0.16
PGE ₂ 6 mg in Lactic Acid	5.33 \pm 1.17	6.53 \pm 0.35

Table 6.5 : The diameter of the cervical canal (millimetres), prior to dilatation in nulliparous patients.

No significant changes in diameter of the cervical canal were seen in nulliparous patients despite prostaglandin 0.5 mg having produced a significant change in CRI.

The diameter of the cervical canal prior to dilatation in multiparous patients is shown in table 6.6.

	CRI (Mean \pm SEM)	Diam. of the cervical canal. (Mean \pm SEM)
Control Group	4.30 \pm 0.42	5.69 \pm 0.15
PGE ₂ 0.5 mg in PEG	3.03 \pm 0.55	6.29 \pm 0.35
PGE ₂ 3 mg in PEG	2.85 \pm 0.65	5.73 \pm 0.33
PGE ₂ 3 mg in Lactic Acid	2.95 \pm 0.56	6.43 \pm 0.37
PGE ₂ 6 mg in Lactic Acid	2.05 \pm 0.52	6.73 \pm 0.30

Table 6.6 : The diameter of the cervical canal (millimeters) prior to dilatation in multiparous patients.

All groups showed a significant reduction in CRI, compared with the control group ($P < 0.05$) but only those patients who received 6 mg PGE₂ showed a significant increase in the diameter of the cervical canal ($\chi^2 = 13.0$)

Prostaglandin E₂ while having some effect on the diameter of the cervical canal, would appear to mainly effect the compliance of the cervix.

Provision of outpatient abortion care, limits the dose of prostaglandin which can be administered. We have opted for a smaller dose of prostaglandin administered a relatively long time prior to operation, in the hope that a gradual effect of this hormone would minimise side effects. Little is known about the mode of absorption of prostaglandins and

other hormones from the vagina. It may be that a more direct application of PGE_2 to the cervical canal would limit systemic side effects including myometrial stimulation, while at the same time produce changes in the cervical tissue.

Nulliparous patients are most at risk for cervical damage and it is to this group of patients that further attention must be directed.

CHAPTER 7.

CERVICAL RESISTANCE IN PATIENTS
WITH PREVIOUS SPONTANEOUS
MID-TRIMESTER ABORTIONS.

Attention has already been drawn in Chapter 2 to the difficulty of making a diagnosis of cervical incompetence. In practice the clinical diagnosis of cervical incompetence relies heavily on the history of the previous abortions. The classical picture is of premature rupture of the membranes, little or no bleeding, followed by a relatively painless expulsion of the pregnancy (Palmer and Lacomme, 1948). Often however the history is obscure or atypical, so that a confident clinical diagnosis cannot be made.

The techniques which have been recommended to establish a diagnosis of cervical incompetence were discussed in Chapter 2. In this Chapter the results of a study of cervical resistance in thirty-five patients with a history of previous spontaneous mid-trimester abortions are presented. The obstetric performance of those patients who have subsequently become pregnant is also described.

Patients and Methods.

The study was conducted on thirty-five patients with a history of one or more spontaneous mid-trimester abortions. The cervical resistance has been measured not less than twelve weeks after the most recent abortion. Thirty-one patients were studied because of a history of spontaneous

mid-trimester abortion. The remaining four patients were also noted to have such a history, when admitted for diagnostic curettage. A record of all previous gynaecological procedures and a detailed obstetric history was taken from all patients by the author. Where possible, the previous hospital case records were scrutinised.

Under general anaesthesia, the cervix was inspected for evidence of cervical trauma and then the force required to dilate the cervix from 3mm to 8 mm inclusive, was measured with the instrument described in Chapter 3. These data were compared with those from a group of 102 patients with normal menstrual cycles, identified in Chapter 5. Statistical evaluation of the results was made by the Student's t-test for unpaired data.

RESULTS.

The patients were studied with particular regard to past obstetric history, previous procedures likely to cause cervical damage and cervical resistance.

Previous Obstetric Performance.

The 35 patients had had a total of 129 pregnancies of which only 29 resulted in a live infant. Of the 100

unsuccessful pregnancies (range 1 - 8 per patient), 67 ended in mid-trimester abortion (range 1 - 4 per patient).

History of the Previous Abortions.

Particular attention was paid to the details of the previous mid-trimester abortions. Patients with a history of premature rupture of the membranes, followed by a relatively painless expulsion of the foetus, were considered to have a history suggestive of cervical incompetence. Those patients who had a history of vaginal bleeding, painful uterine activity and absence of premature rupture of the membranes were considered to have a history that was not suggestive of cervical incompetence. Nineteen patients were found to have a history suggestive of cervical incompetence. The remaining sixteen patients had a history which was not suggestive of cervical incompetence.

Past Procedures Likely to Cause Cervical Trauma.

Twelve patients had undergone procedures which might have predisposed to cervical trauma. Three patients had undergone suction termination of pregnancy at seven weeks, eleven weeks and twelve weeks gestation. These abortions were the patient's first pregnancies and were followed by mid-trimester losses. Three of the patients had had a diagnostic curettage performed. The indications for

diagnostic curettage were: investigation of primary infertility, missed abortion and primary dysmenorrhoea at the age of fifteen. Four patients had been delivered by mid-cavity forceps in the pregnancy preceding the spontaneous abortions. One patient had had an assisted breech delivery at term followed by four mid-trimester losses. This patient was noted to have a cervical tear extending to the level of the internal os. The twelfth patient had had two spontaneous vaginal deliveries at term, followed by a sixteen week spontaneous abortion and then delivered at twenty-eight weeks - the baby survived. This patient was also noted to have a cervical tear extending to the level of the internal os.

Cervical Resistance Studies.

The cervical resistance in the thirty-five patients is compared with the normal cycling group in Table 7.1.

Patient Group	Number	CRI (Mean \pm SEM)
Normal Cycling Group	102	4.91 \pm 0.41
Previous mid-trimester abortion.	35	2.83 \pm 0.82
History suggestive of cervical incompetence	19	2.09 \pm 0.55
History not suggestive of cervical incompetence	16	3.70 \pm 0.82

Table 7.1 : Cervical Resistance Index in patients studied.

The CRI in the study group was significantly lower than the cycling group ($P < 0.01$). Nineteen patients in the study group had a typical history of cervical incompetence. These patients had significantly lower CRI than the cycling group ($P < 0.005$). Sixteen of the patients had vaginal bleeding and painful uterine activity without early rupture of the membranes. These patients had lower CRI than the cycling group, but this was not a significant difference. There was no significant difference between those with a classical history and those without the classical history of cervical incompetence.

Twelve of the patients did not conform to this pattern, (Figure 7.1). Four patients with a typical history had high resistance of 8.27, 7.0, 4.36 and 4.18 respectively. Eight of the patients without a typical history had low CRI of zero in four cases, 1.0, 2.09, 2.27 and 2.82.

The effect of the number of spontaneous mid-trimester abortions on CRI is shown in Figure 7.1. There was no apparent relationship between CRI and the number of mid-trimester abortions, regardless of whether or not the history was suggestive of cervical incompetence. When the cervix has an intrinsic weakness, patients are likely to suffer recurring abortions. These abortions do not seem to further weaken the cervix.

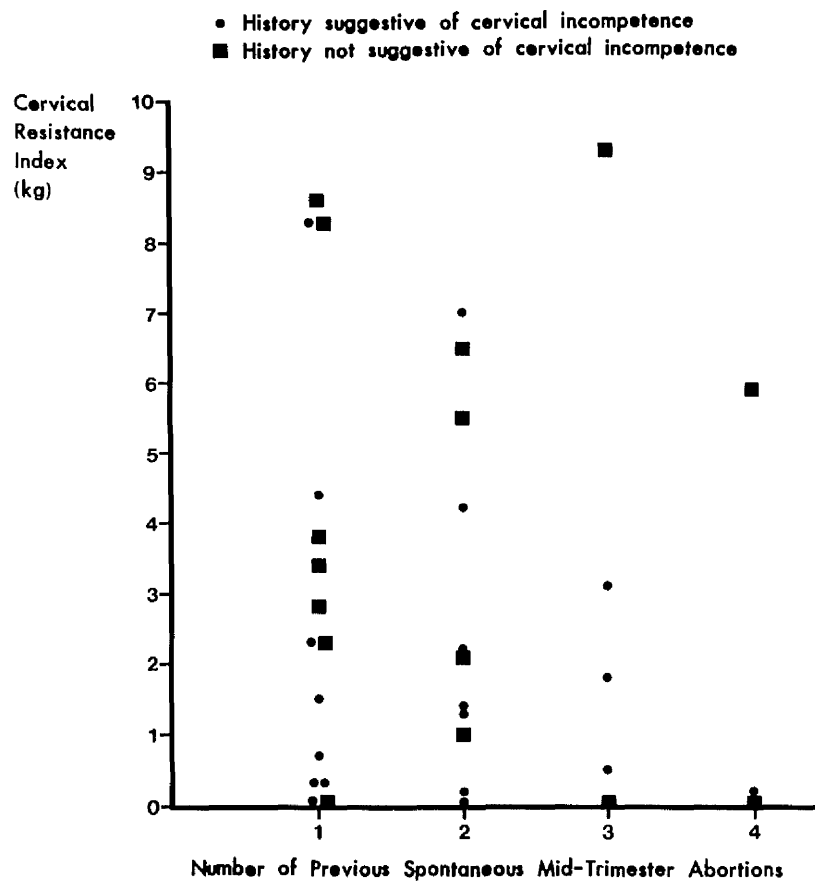


FIGURE 7.1 — THE EFFECT OF THE NUMBER OF SPONTANEOUS MID-TRIMESTER ABORTION ON C.R.I.

Subsequent Pregnancies.

Nine of the study patients have become pregnant again since measurement of CRI. Eight patients are now delivered and one patient is currently pregnant.

The first patient had two previous mid-trimester abortions, one with a classical history and one without. The CRI was low at 1.4. In view of this, cervical cerclage was performed at fifteen weeks in the subsequent pregnancy. The pregnancy was uneventful and the suture was removed at thirty-eight weeks gestation. Removal of the suture was followed at once by the onset of labour and spontaneous vaginal delivery of a healthy female infant.

The second patient had had three previous abortions, all in the second trimester, but without typical histories of cervical incompetence. In the third pregnancy cervical cerclage had been performed at seventeen weeks because of the history of two previous mid-trimester losses. This pregnancy ended at twenty weeks with vaginal bleeding and painful uterine activity. The CRI was above average at 9.3. In the subsequent pregnancy, cerclage was not performed and the patient had an uncomplicated pregnancy which ended with a spontaneous vaginal delivery at term of a healthy male infant.

The third patient had had seven pregnancies, six having ended spontaneously between twelve and thirty weeks gestation. Pregnancies four and five had shown signs of cervical incompetence at twenty-eight and thirty weeks gestation. In the sixth pregnancy cerclage was performed and the outcome was a spontaneous delivery of a healthy infant at term. In the seventh pregnancy cerclage was again performed at fourteen weeks gestation but bleeding and abortion ensued at sixteen weeks. The CRI was very low at 0.2. In the subsequent pregnancy there was bleeding at ten weeks which quickly settled. Cerclage was performed at twelve weeks but recurrent bleeding at fourteen weeks led to removal of the suture and abortion.

The fourth patient had had two successful deliveries at term followed by four second trimester abortions and one first trimester abortion. The history did not point to cervical incompetence. Examination of the cervix at CRI measurement, revealed a cervical tear extending to the level of the internal os. The CRI was zero. In view of this, trachelorrhaphy was performed. The patient showed no signs of cervical incompetence during her subsequent pregnancy but developed severe hypertension and was delivered of a live infant at thirty-six weeks gestation, by caesarean section.

The fifth patient had had two previous mid-trimester losses, at fourteen and twenty-one weeks gestation. The history was not...

suggestive of cervical incompetence and the CRI was normal at 5.5. It had not been planned to offer this patient cervical cerclage but the Consultant in charge of this patient entered her in the MRC/RCOG randomised cervical cerclage trial. She was allocated to the suture group and this was inserted at twelve weeks gestation. The patient developed premature rupture of the membranes at thirty-three weeks gestation and labour ensued four days later. The suture was removed at the onset of uterine activity and she was delivered by mid-cavity forceps of a live child weighing 2.14 Kilogrammes.

The sixth patient had a previous history of one spontaneous mid-trimester abortion which was not of the classical type. The CRI was zero. Cervical cerclage was performed at fifteen weeks gestation. The suture was removed at thirty-eight weeks gestation and the cervix immediately dilated to 4 cms. Spontaneous labour was established four days later. After a labour of three and a half hours she had a spontaneous vaginal delivery of a live male child.

The seventh patient started her reproductive life with two spontaneous mid-trimester abortions at fourteen and sixteen weeks respectively. Both these abortions were proceeded by vaginal bleeding. In her third pregnancy a cervical suture was inserted and she had a spontaneous vertex delivery at term.

A cervical suture was inserted in the fourth pregnancy at fourteen weeks. This patient had vaginal bleeding at sixteen weeks and twenty-two weeks gestation and then had premature rupture of the membranes at twenty-four weeks. This was followed by the onset of labour, the suture was removed and the patient aborted. The cervical resistance was normal at 5.9. In the subsequent pregnancy she was given prophylactic bed rest until fourteen weeks gestation. She had vaginal bleeding at seventeen weeks gestation and the following week, ultrasound examination showed a missed abortion. This pregnancy was terminated with extra-amniotic PGE₂.

The eighth patient had had a spontaneous abortion at twelve weeks in her first pregnancy. In her second pregnancy she went into premature labour at twenty-six weeks gestation. The membranes remained intact but efforts to abolish labour were unsuccessful and she was delivered by caesarean section of a baby weighing 1.08 Kilogrammes. This baby died from Respiratory Distress Syndrome, two days later. The CRI was normal at 3.36. In the subsequent pregnancy, cervical cerclage was not performed and after an uneventful pregnancy she was delivered by repeat caesarean section at thirty-eight weeks gestation because of a breech presentation.

A further patient is still pregnant. She had a history of three spontaneous mid-trimester abortions. Her second

pregnancy, twins, ended at twenty-one weeks with a typical history of cervical incompetence. The CRI was normal at 4.2. This patient has not been offered cervical cerclage and is currently thirty-four weeks pregnant. There have been no complications in this pregnancy.

The patients were studied between pregnancies for two reasons. It has been shown in Chapter 6 that CRI is significantly lower in pregnancy compared with the non-pregnant state. Those patients with low resistance in the non-pregnant state could therefore be expected to have even lower resistance when they become pregnant. The possibility of provoking abortion in such high risk patients, precluded application of this technique during pregnancy.

Conclusion.

Selection of patients for cervical cerclage on the basis of the cervical resistance findings may prove no better than selection based on the history of the previous abortions. Although the number of patients who have subsequently conceived is small, already there are indications that identification of patients with low CRI may enable better selection for cervical cerclage. The obstetric performance of those who have become pregnant (seven successful pregnancies out of nine) is much better than the performance of the study group prior to measurement of CRI (twenty-nine successful pregnancies out of

one hundred and twenty-nine).

In time it is hoped that more patients will be studied and that more of the patients studied will become pregnant. This will allow a better evaluation of selection for cervical cerclage, based on the cervical resistance findings.

CHAPTER 8.

CONCLUSIONS.

For as long as gynaecologists have been performing dilatation of the cervix there has been an awareness that this procedure can, in some patients, be difficult. As Gream (1865) so eloquently put it, "Dilatation of the cervix may prove hurtful, indeed may be dangerous to life, but not when properly performed." Over 100 years later this warning by Gream still holds good. Today one would add that performing the procedure properly should include the anticipation of difficulty in dilatation, particularly in the nulliparous patient. The awareness of clinicians of the amount of force required to dilate the cervix varies greatly. When difficulty is encountered, during dilatation, the force required for dilatation can be reduced by increasing the time taken to dilate the cervix. This can be achieved by dilating the cervix more gradually, using half-sized dilators. Subjective assessment of the ease with which the cervix may be dilated suffers from the disadvantage that it is not possible to compare observations made by different clinicians. The development of the instrument described in Chapter 3 of this thesis has enabled comparisons to be made between different groups of patients.

In Chapter 5, the study of non-pregnant patients has confirmed the clinical impression that the cervix is permanently changed after the first pregnancy. The multiparous cervix is easier to dilate than the nulliparous and this

substantiates the evidence that the nulliparous cervix is at greater risk of damage during surgical dilatation.

The studies of the effect of the menstrual cycle on CRI has failed to show any significant difference in CRI during the various phases of the menstrual cycle. This finding is reflected in the absence of any significant change in CRI on each day of the menstrual cycle.

Oestrogen and progesterone are known to affect the cervix in late pregnancy, but the circulating levels of these hormones, in the non-pregnant state, do not show any correlation with the CRI findings. The finding of significantly higher CRI in postmenopausal women compared to normal cycling women is in accord with the clinical finding of a firm cervix after the menopause.

The most interesting finding in non-pregnant patients is the effect which systemic medroxy-progesterone acetate (Depo-Provera) had in reducing the cervical resistance. Depo-Provera has been shown to prevent degradation of collagen and inhibit production of collagenase in the rat uterus. These changes would be expected to make the cervix firmer and not softer as has been shown in Chapter 5.

The literature review on first trimester termination of pregnancy has clearly shown that complications are less

likely to occur the earlier the pregnancy is terminated. The finding that the cervical resistance index did not reduce with advancing gestation adds further weight to this argument. The index is assessed over the 3 mm to 8 mm dilatation range and continuing dilatation beyond 8 mm clearly adds further to the force applied to the tissue and consequently to the potential damage inflicted. In order to carry out termination as early as possible, patients must be educated to seek medical help as early as possible when they are considering termination of pregnancy. The medical profession have also a duty to ensure that there is the minimum of delay between the patient consulting her general practitioner and the procedure being carried out. To minimise trauma to the cervix, dilatation should be kept to the minimum necessary to carry out the procedure, particularly in nulliparous patients.

In Chapter 6, it has been shown that prostaglandin E_2 will significantly lower the CRI in multiparous patients. The absence of a consistent effect of prostaglandin E_2 in nulliparous patients is difficult to explain. Since it is these patients who are most likely to suffer cervical damage, our efforts to make termination of pregnancy safer for them must continue. Prostaglandin administered vaginally, probably acts locally on the cervix and after absorption through the vaginal mucosa, has a systemic effect on the

uterus. Perhaps a system which delivers prostaglandin more directly to the cervical canal would have the desired effect on the cervical tissue without producing the systemic effects. It is the systemic effects of prostaglandins which limit their use for outpatients.

Cervical incompetence presents two perplexing problems to the clinician. The first problem is the diagnosis of this condition. Many diagnostic aids have been described but there is still considerable reliance on the history of the previous abortions when deciding to insert a suture. The study in Chapter 7 has shown that patients with a history suggestive of cervical incompetence have significantly lower CRI than normal cycling women. Despite this generalisation, twelve out of the thirty-five patients studied did not fit this pattern. Identification of patients with abnormally low CRI may enable a more rational selection of patients for treatment of cervical incompetence. As more patients are studied and more of the patients become pregnant, it should be possible to see if this encouraging initial impression is substantiated.

The second dilemma facing clinicians, dealing with cervical incompetence, is the value of cervical cerclage in the treatment of these patients. The current M.R.C/R.C.O.G. trial will hopefully throw light on the uncertainty of this

procedure's value.

THE MAIN CONCLUSIONS OF THIS THESIS ARE:-

1. The nulliparous cervix in pregnant and non-pregnant patients is significantly more difficult to dilate than the multiparous cervix.
2. The cervix in postmenopausal women is more difficult to dilate than in pre-menopausal women.
3. Long-term systemic Depo-Provera significantly reduces CRI.
4. Prostaglandin E₂ given vaginally in the first trimester of pregnancy, reduces CRI in multiparous patients.
5. Measurement of CRI in patients with a history of spontaneous mid-trimester abortions will identify patients with abnormally low values. This may assist in making a confident diagnosis of cervical incompetence.

Direction of Future Studies.

The results of the research indicate that we should approach dilatation of the cervix in the nulliparous patient with caution, particularly at termination of pregnancy. This procedure has the potential of causing damage to the cervix, which may impair the patient's future reproductive life. The search must continue for agents which increase

cervical compliance in nulliparous patients in early pregnancy. Studies should be directed towards a more direct application of prostaglandin E_2 to the cervical canal, which would hopefully produce changes in the cervical tissue without the systemic side effects of this hormone. Wingerup, Andersson and Ulmsten (1979) have shown that a single intracervical application of PGE_2 in a viscous gel, produced ripening of the cervix in late pregnancy.

The action of long-term systemic Depo-Provera on cervical tissue requires further investigation. An electron-microscopy study of cervical tissue from patients undergoing sterilisation, after using Depo-Provera for contraception, might help elucidate the effect that this hormone has on the collagen fibre matrix.

The initial results of the study of CRI in patients with a history of spontaneous mid-trimester abortion suggests that the technique may be of value in diagnosing cervical incompetence. Further patients with such a history should be studied and as more of the patients studied become pregnant an evaluation of this technique in the diagnosis of cervical incompetence could be made.

This thesis began with Gream's warning about the dangers of dilatation of the cervix. We must continue to use the operation with care. When problems in dilating the cervix are anticipated, we should consider treatment aimed at increasing cervical compliance and therebyⁿ reducing the chances of the patient suffering damage to this vital structure.

REFERENCES.

ANDERSON, A.B.M., FRASER, I.S., HAYNES, P.J.

TURNBULL, A.C., (1978): Prostaglandin synthetase inhibitors in the treatment of primary dysmenorrhoea. Lancet 1, 345 - 348.

ASCHOFF, L., (1905): Zur Cervix Frage; Nachtrag zu der Arbeit des Herrn Dr. Hohmeir. Monatsschrift für Geburtshilfe and Gynäkologie 22, 611 - 615.

ATIENZA, M.F., BURKMAN, R.T., KING, T.M., (1980): Forces associated with cervical dilatation at suction abortion: in Dilatation of the Uterine Cervix, eds. Naftolin, F., Stubblefield, P.G., p. 343 - 354. NEW YORK: RAVEN PRESS.

BATES, J.L., CROPLEY, T., (1977): Complications of Shirodkar suture. Lancet 2, 1035.

BARRETT, J.M., BOEHM, F.H., KILLAM, A.P., (1981): Induced abortion, a risk factor for placenta praevia. AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY 141, 769 - 772.

BENTOV, I., STUBBLEFIELD, P.G., (1980): Measurement of the tangential force required for dilatation of the human cervix for abortion: in Dilatation of the Uterine Cervix, eds. Naftolin, F., Stubblefield, P.G., P 247 - 254 NEW YORK: RAVEN PRESS.

BERIC, B., KUPRESANIAN, M., HULKA, J.F., (1972): The Karman Catheter: A preliminary evaluation of an instrument for termination of pregnancy up to twelve weeks gestation. American Journal of Obstetrics and Gynecology 114, 273 - 275.

BIBBY, J.G., BRUNT, J., MITCHELL, M.D., ANDERSON, A.B.M., TURNBULL, A.C., (1979): The effect of cervical encirculation on plasma prostaglandin concentration during early human pregnancy. British Journal of Obstetrics and Gynaecology 86, 19 - 22.

BLACK, M.M., MELCHER, D.H., MELVILLE, H.A.H., MORGON, J. (1975): Some preliminary studies of the use of a vibrating and force measuring cervical dilator. Biomedical Engineering 10, 346 - 349.

- BLACK, M.M., MELCHER D.H., MELVILLE, H.A.H. (1975b):
Developments in cervical dilatation including the use
of vibratory techniques. Clinics in Obstetrics and
Gynaecology 2, 173 - 201.
- BROOK, I., FEINGOLD, M., SCHWARTZ, A., ZAKUT, H., (1981):
Ultrasonics in the diagnosis of cervical incompetence
in pregnancy. British Journal of Obstetrics and
Gynaecology 88, 640 - 643.
- CADESKY, K.I., RIVINSKY, E., LYONS, E.R. (1981): Dilatation
and Evacuation: A preferred method of mid-trimester
abortion. American Journal of Obstetrics and
Gynecology 141, 329 -332
- CALDER, A.A. (1980): Pharmacological management of the Unripe
cervix. Dilatation of the uterine Cervix, ed. Naftolin, F.
Stubblefield, P.G., p 317 - 334. NEW YORK: RAVEN PRESS.
- CATES, W., BOYD, C., HAVORSON BOYD, G., HOLCK, S., GILCHRIST, T.F.
(1981) : Death from amniotic fluid embolism and disseminated
intravascular coagulation after curettage abortion.
American Journal of Obstetrics and Gynecology 141, 346 - 348.
- CHARLES, D., EDWARDS, W.R., (1981) : Infectious complications
of cervical cerclage. American Journal of Obstetrics
and Gynecology 141, 1065 - 1071.
- COLE, S.K., (1982) : Cervical Suture in Scotland. British
Journal of Obstetrics and Gynaecology 89, 528 - 535.
- CONRAD, J.T., UELAND, K., (1979) : The stretch modulus of
cervical tissue in spontaneous, oxytocin induced and
prostaglandin E₂ induced labour. American Journal of
Obstetrics and Gynecology 133, 11 - 14.
- CREATSOS, G., PAVLATOS, M., LOLIS, D., ARAVANTINOS, D.,
KASKARELIS, D., (1981) : Bacterial contamination of
the cervix and premature rupture of the membranes.
American Journal of Obstetrics and Gynecology 139, 552 - 525.
- CUSHNER, I.M., (1963) : The management of cervical incompetence
with a purse-string suture. American Journal of Obstetrics
and Gynecology 87, 882 - 891.

- DANFORTH, D.N., (1947): The fibrous nature of the human cervix and its relation to the isthmic segment in gravid and non-gravid uterus. American Journal of Obstetrics and Gynecology 53, 541 - 560.
- DANFORTH, D.N., (1954): The distribution and functional activity of the cervical musculature. American Journal of Obstetrics and Gynecology 68, 1261 - 1270.
- DANFORTH, D.N., BUCKINGHAM, J.L., RODDICK, J.W., (1960): Connective tissue changes incident to cervical effacement. American Journal of Obstetrics and Gynecology 80, 939 - 944.
- DINGFELDER, J.R., BRENNER, W.E., HENDRICKS, C.H., STAUROVSKY, L.G., (1975): Reduction of cervical resistance by Prostaglandin suppositories prior to dilatation for induced abortion. American Journal of Obstetrics and Gynecology 122, 25 - 30.
- DUNN, L.J., ROBINSON, J.C., STEER, C.M., (1959): Maternal death following suture of the incompetent cervix during pregnancy. American Journal of Obstetrics and Gynecology 78, 335 - 339.
- FISHER, J.J., (1959): The effect of amputation of the cervix uterii upon subsequent parturition. American Journal of Obstetrics and Gynecology 62, 644 - 648.
- FITZPATRICK, R.J., DOBSON, H., (1979): The cervix of sheep and goats during parturition. Physiology and Control of Parturition in Domestic Animals, eds. Ellendoh, F., Taverne, M., Smidt, D., p. 209 - 224 AMSTERDAM: ANIMAL REPRODUCTION SCIENCES.
- GORDON, A.J., CALDER, A.A., (1977): Oestradiol applied locally to ripen the unfavourable cervix. Lancet 2 1319 - 1321.
- GREAM, G.T., (1865): Dilatation or division of the cervix uteri. Lancet 381.
- GUIDOTTI, R.J., GRIMES, D.A., CATES, W., (1981): Fatal amniotic fluid embolism during legally induced abortion. U.S. 1972 - 1978. American Journal of Obstetrics and Gynecology 141, 257 - 261.

HALLIDAY, E.C., JACOBS, G.V.W., HEYNS, O.S., (1958):

Changes in the mechanical properties of the cervix under the influence of pregnancy. Journal of Obstetrics and Gynaecology of the British Empire 65, 409 - 413.

HARKNESS, M.L.R., HARKNESS, R.D., (1959): Changes in the physical properties of the uterus and cervix of the rat during pregnancy. Journal of Physiology 148, 527-547.

HARMAN, C.R., FISH, D.G., TYSON, J.E., (1981): Factors influencing morbidity in termination of pregnancy. American Journal of Obstetrics and Gynecology 141, 333 - 337.

HILLIER, K., (1977): Biochemical changes in the cervix in parturition. Paper presented to Blair Bell Research Society, Southampton, September, 1977.

HULKA, J.F., HIGGINS, G., (1961): Trauma to the internal cervical os during dilatation for diagnostic curettage. American Journal of Obstetrics and Gynecology 82, 913 - 919.

HULKA, J.F., LEFLER, H.T., ANGLONE, A., LACHENBRUCH, P.A., (1974): A new electronic force monitor to measure factors influencing cervical dilatation for vacuum curettage. American Journal of Obstetrics and Gynecology 120, 166 - 173.

JEFFREY, J.J., KOOB, T.J., (1980): Endocrine control of collagen degradation in the uterus. Dilatation of the Uterine Cervix, eds. Naftolin F., Stubblefield, P.G., p. 135 - 147. NEW YORK: RAVEN PRESS.

JOHNSTONE, F.D., BOYD, I.E., MCCARTHY, T.G., McCLURE-BROWNE, J.C., (1974): The diameter of the uterine isthmus during the menstrual cycle, pregnancy and the puerperium. Journal of Obstetrics and Gynaecology of the British Commonwealth 81, 558 - 562.

JOHNSTONE, F.D., BEARD, R.J., BOYD, I.E., MCCARTHY, T.G., (1976): Cervical diameter after suction termination of pregnancy. British Medical Journal 1, 68 - 69.

- KEIRSE, M.J.N.C., RUSH, R.W., ANDERSON, A.B.M.,
TURNBULL, A.C., (1978): Risk of pre-term delivery in
patients with previous pre-term delivery and or
abortion. British Journal of Obstetrics and Gynaecology
85, 81 - 85.
- KUHN., R.J.P., PEPPERALL, R.J., (1977): Cervical Ligation:
A review of 242 pregnancies. Australian and New
Zealand Journal of Obstetrics and Gynaecology 17, 79 - 83.
- LASH, A.F., LASH, S.R., (1950): Habitual abortion:
The incompetent internal os. American Journal of Obstetrics
and Gynecology. 59, 68 - 76.
- LASH, A.F., (1961): The incompetent internal os of the cervix.
Complications after repair. American Journal of Obstetrics
and Gynecology 81, 465 - 471.
- LIPSHITZ, J., (1975): Cerclage in treatment of the incompetent
cervix. Suid - Afrikaanse Mediese Tydskrif 49, 2013 - 2015.
- LIU, D.T.Y., MELVILLE, H.A.H., MARTIN, T., (1972): Subsequent
gestational morbidity after various types of abortion.
Lancet 2, 431 - 432.
- LIU, D.T.Y., BLACK, M.M., MELCHER, D.H., MELVILLE, H.A.H.,
CAMERON, S., MORGON, J., (1975): Dilatation of the parous
non-pregnant cervix. British Journal of Obstetrics and
Gynaecology 82, 246 - 251.
- MCDONALD, I.A., (1957): Suture of the cervix for inevitable
miscarriage. Journal of Obstetrics and Gynaecology of
the British Empire 64, 346 - 353.
- MCDONALD, I.A., (1963): The incompetent cervix as a cause
for recurrent abortion. Journal of Obstetrics and
Gynaecology of the British Commonwealth 70, 105 - 109.
- MCDONALD, I.A., (1980): Cervical cerclage. Clinics in
Obstetrics and Gynaecology 3, 461 - 479.

- McKENZIE, I.Z., FRY, A., (1981): Prostaglandin E₂ pessary to facilitate first trimester aspiration termination. British Journal of Obstetrics and Gynaecology 88, 1033 - 1037.
- MACNAUGHTON, M.C., (1961): Pregnancy following abortion. Journal of Obstetrics and Gynaecology of the British Commonwealth 68, 789 - 792.
- MANN, E.C., McLAREN, W.D., HAYT, D.B., (1961): The physiology and clinical significance of the uterine isthmus. American Journal of Obstetrics and Gynecology 81, 209 - 222.
- NAKANO, R., HATA, H., SASAKI, K., YAMOTO, M., (1980): Use of prostaglandin E₁ analogue pessaries in patients having first trimester abortions. British Journal of Obstetrics and Gynaecology 87, 287 - 291.
- PALMER, R., LACOMME, M., (1948): La béance de l'orifice interne. Gynécologie et Obstetrique 47, 905 - 906.
- PALMER, R., (1950): Le rôle de la beone de l'isthme utérion dans l'avortement habituee. Revue Francais de Gynécologie et d'Obstetrique 45, 218.
- PETERSON, H.B., GRIMES, D.A., CATES, W., RUBIN, G.L., (1981): Comparative risk of death from induced abortion ≤ 12 weeks gestation, performed with local versus general anaesthesia. American Journal of Obstetrics and Gynecology 141, 763 - 768.
- RICHARDSON, J.A., DIXON, G., (1976): The effect of vaginal termination in subsequent pregnancies. British Medical Journal 1, 1303 - 1304.
- ROBBOY, M.S., (1973): The management of cervical incompetence. Obstetrics and Gynecology 41, 108 - 112.
- RUBOVITZ, F.E., COOPERMAN, N.R., LASH, A.F., (1953): Habitual abortion: A radiographic technique to demonstrate the incompetent internal os of the cervix. American Journal of Obstetrics and Gynecology 66, 269 - 280.
- SARTI., D.A., Sample, W.F., HOBEL, C.J., STAISCH, K.J., (1979): Ultrasonic visualisation of the dilated cervix during pregnancy. Radiology 130, 417 - 420.

- SCOTTISH HEALTH STATISTICS, (1979): H.M.S.O. p. 78.
- SHIRODKAR, V.N., (1955): A new method of operative treatment for habitual abortion in the second trimester of pregnancy. Antiseptic 52, 299 - 300.
- STALLWORTHY, J.A., MOOLGAOKER, A.S., WALSH, J.J., (1971): Legal abortion: A critical assessment of it's risks. Lancet 2, 1245 - 1249.
- STEWART, P., KENNEDY, J.H., BARLOW, D.H., CALDER, A.A., (1981): A comparison of oestradiol and prostaglandin E₂ for ripening the cervix. British Journal of Obstetrics and Gynaecology 88, 236 - 239.
- STYS, S.J., CLEWELL, W.H., MESCHIA, G., (1981): The effect of prostaglandin E₂ on cervical compliance in pregnant ewes. American Journal of Obstetrics and Gynecology 140, 415 - 419.
- THURSTON, J.G., (1963): Rupture of the uterus following Shirodkar Suture. British Medical Journal 5342, 1392.
- VON MAILLOT, K., STUHLSTATZ, H.W., GENTSCH, H.H. (1981): Connective tissue changes in the human cervix in pregnancy and labour. The Cervix in Pregnancy and Labour. eds. Ellwood, D.A., Anderson, A.B.M., p 123 - 135. EDINBURGH: CHURCHILL LIVINGSTONE.
- WELCH, C., ELDER, M.G., (1982): Cervical dilatation with 16, 16 - dimethyl - trans Δ^2 PGE₁ methyl ester vaginal pessaries before surgical termination of first trimester pregnancy. British Journal of Obstetrics and Gynaecology 89, 849 - 852.
- WINGERUP, L., ANDERSSON, K-E, ULMSTEN, U., (1979): Ripening of the cervix and induction of labour in patients at term by single intracervical application of prostaglandin E₂ in viscous gel. Acta Obstetrica et Gynaecologica Scandinavica Supplement 84, 11 - 14.
- W.H.O. (1979): Gestation, birth weight and spontaneous abortion in pregnancy after induced abortion. Lancet 1, 142 - 145.

WRIGHT, C.S.W., CAMPBELL, S., BEAZLEY, J., (1972): Second trimester abortion after vaginal termination of pregnancy. Lancet 1, 1278 - 1279.

YOUSEFF, A.F., (1958): The uterine isthmus and it's sphincter mechanism: A radiographic study. American Journal of Obstetrics and Gynecology 75, 1305 - 1319.



