show that H.A.A. persistence in these patients is probably not the result of gross deficiency in the host immune response.

The authors acknowledge the technical help of Miss Praful Damani and the help of Steven Lwanga with statistics. Dr. John Ziegler provided valuable help in the preparation of the text.

This work is supported by contract No. PH43-67-1343 from the National Cancer Institutes, Bethesda, Maryland, U.S.A.

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Coagulation Changes during Termination of Pregnancy by Prostaglandins and by Vacuum Aspiration

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British Medical Journal, 1973, 1, 19-21

Summary

Serial studies on coagulation factors were performed on 12 patients having termination of mid-trimester pregnancy by extra-amniotic prostaglandin $F_{2\alpha}$ and 11 patients terminated by vacuum aspiration during the first trimester. A significant change in the activity of factors V, VII and X, VIII, and X, and a decrease of the prothrombin time and platelet count were found with prostaglandin termination but no such changes occurred during vacuum aspiration. These findings suggest that the coagulation system is activated during induction of mid-trimester abortion with extra-amniotic prostaglandin $F_{2\alpha}$. This is probably related to the physiological changes in the coagulation mechanism which occur by the second trimester of pregnancy. Termination of pregnancy in the mid-trimester may, however, be expected to give rise to defective blood coagulation and thromboembolic complications.

Introduction

Thromboembolic complications constitute one of the major hazards of pregnancy and delivery. The blood clotting system is the chief mechanism involved in thromboembolism but little is

known about changes in blood coagulation during termination of pregnancy.

After intra-amniotic injection of hypertonic saline to induce mid-trimester abortion, changes in coagulation factors have been reported which are consistent with disseminated intra-vascular coagulation (Stander *et al.*, 1971). In view of this we investigated the coagulation system during induction of mid-trimester abortion with prostaglandin $F_{2\alpha}$ and the termination of pregnancy in the first trimester by vacuum aspiration.

Patients and Methods

Twelve patients were studied aged 18 to 37 years (mean 23 years) and parity one to seven, having termination of pregnancy at 14 to 20 weeks' gestation (mean 17 weeks) by extra-amniotic prostaglandin $F_{2\alpha}$. Eleven patients were studied aged 18 to 39 years (mean 24 years) and parity one to four, having termination of their pregnancies by vacuum aspiration at eight to 12 weeks' gestation (mean 10 weeks).

Termination by Extra-amniotic Prostaglandin $F_{2\alpha}$.—A Foley catheter was inserted through the cervix into the extra-amniotic space and the bulb was inflated with 40 ml of distilled water. A test dose of 250 μ g of prostaglandin $F_{2\alpha}$ was injected into the extra-amniotic space via the Foley catheter. If no side effects occurred 750 μ g was instilled at two-hourly intervals until abortion took place. Samples of venous blood (18 ml) were withdrawn into a plastic syringe at the following stages: 1, before administration of prostaglandin $F_{2\alpha}$; 2, when uterine contractions were established two to four hours after the first instillation of prostaglandin; 3, immediately after the expulsion of the products of conception; and 4, twenty-four hours after abortion.

Termination by Vacuum Aspiration.—This operation was carried out under general anaesthesia by using a Karman suction curette. Venous blood samples (18 ml) were withdrawn

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at the following stages: 1, before operation; 2, immediately after completion of vacuum aspiration; and 3, twenty-four hours after operation.

COAGULATION TESTS

A 9-ml sample of blood was added to 1 ml of 3.8% sodium citrate for coagulation assays, 5 ml to 0.05 ml of aprotinin (5,000 units/ml) for assay of fibrin degradation products, and 4 ml to edetic acid for platelet counting.

Prothrombin time was measured by the method of Quick (1966) and partial thromboplastin time by using Bell and Alton's (1954) platelet substitute. Fibrin degradation products were assayed by the tanned red cell haemagglutination method (Merskey *et al.*, 1966; Bonnar *et al.*, 1969). Platelets were counted on a Coulter counter. Factors V and VII and X were assayed by the method of Stefanini and Dameshek (1962). Factor VIII was assayed by the two-stage method of Biggs *et al.* (1955). Factor X was assayed as described by Denson (1961).

STATISTICAL ANALYSIS

The factors were subjected to Wilcoxon's signed ranks test to determine the statistical significance of changes in the clotting factors.

Results

In the prostaglandin group a significant decrease in prothrombin time occurred during uterine contractions and at the time of abortion (table I). No significant changes were found with vacuum termination (Wilcoxon's signed ranks test).

In both the prostaglandin and vacuum aspiration groups no significant changes in partial thromboplastin time, platelet count, and levels of fibrin degradation products occurred.

During prostaglandin termination the levels of coagulation factors rose in most of the patients, and the increase of factors V, VIII, and X were significant during uterine contractions and at the time of abortion. Virtually no changes occurred with vacuum termination (table II). As shown in the chart the initial levels of coagulation factors X and VII and X in patients having prostaglandin termination were significantly higher

Coagulation factor changes during termination of pregnancy by vacuum aspiration in first trimester and by extra-amniotic prostaglandin $F_{2\alpha}$ in second trimester. Wilcoxon's signed ranks test was used to establish statistical significance of changes in clotting factors. For sample stages, see text.

than the preoperative levels in patients undergoing vacuum termination. Twenty-four hours after abortion the levels of coagulation factors in the prostaglandin group had returned to the preinduction values.

Discussion

Normal pregnancy is accompanied by major changes in the haemostatic mechanism, particularly an increase in the levels of certain coagulation factors and a noticeable decrease in fibrino-

TABLE I—Coagulation System Changes during Mid-trimester Abortion with Extra-amniotic Prostaglandin $F_{2\alpha}$

Test	Venous Blood Sample			
	Stage 1* (Mean $\pm$ S.D.)	Stage 2 (Mean $\pm$ S.D.)	Stage 3 (Mean $\pm$ S.D.)	Stage 4 (Mean $\pm$ S.D.)
Prothrombin time (sec)	13.58 $\pm$ 0.95	13.2 $\pm$ 1.19	12.77 $\pm$ 0.96	13.55 $\pm$ 1.01
Partial thromboplastin time (sec)	79.91 $\pm$ 12.55	83.45 $\pm$ 18.83	79.08 $\pm$ 16.82	78.00 $\pm$ 12.87
Platelet count	178 $\times 10^3 \pm 35$	160 $\times 10^3 \pm 38$	164 $\times 10^3 \pm 52$	175 $\times 10^3 \pm 43$
Fibrin/fibrinogen degradation product (μ g)	4.47 $\pm$ 0.82	5 $\pm$ 1.17	4.75 $\pm$ 1.53	5.37 $\pm$ 1.95
Factor V (% normal)	81 $\pm$ 20	102 $\pm$ 28	125 $\pm$ 48	83 $\pm$ 19
Factor VII and X (% normal)	126 $\pm$ 19	126 $\pm$ 19	140 $\pm$ 31	108 $\pm$ 18
Factor VIII (% normal)	88 $\pm$ 34	102 $\pm$ 33	132 $\pm$ 56	115 $\pm$ 57
Factor X (% normal)	188 $\pm$ 39	229 $\pm$ 94	289 $\pm$ 122	218 $\pm$ 92

*For explanation of sample stages, see text.

TABLE II—Coagulation System Changes during First-trimester Abortion by Vacuum Aspiration

Test	Venous Blood Sample		
	Stage 1* (Mean $\pm$ S.D.)	Stage 2 (Mean $\pm$ S.D.)	Stage 3 (Mean $\pm$ S.D.)
Prothrombin time (sec)	13.5 $\pm$ 1.04	13.72 $\pm$ 0.93	14.13 $\pm$ 1.26
Partial thromboplastin time (sec)	70.77 $\pm$ 8.39	74.27 $\pm$ 12.71	70.68 $\pm$ 8.62
Platelet count	180 $\times 10^3 \pm 24$	154 $\times 10^3 \pm 30$	155 $\times 10^3 \pm 29$
Fibrin/fibrinogen degradation products (μ g)	3.52 $\pm$ 1.66	3.86 $\pm$ 1.71	4.2 $\pm$ 1.28
Factor V (% normal)	88 $\pm$ 26	95 $\pm$ 25	86 $\pm$ 15
Factor VII-X (% normal)	104 $\pm$ 30	100 $\pm$ 24	93 $\pm$ 23
Factor VIII (% normal)	92 $\pm$ 28	92 $\pm$ 37	95 $\pm$ 18
Factor X (% normal)	103 $\pm$ 34	105 $\pm$ 27	102 $\pm$ 31

*For explanation of sample stages, see text.

lytic activity. Such changes have been interpreted as a physiological development to provide for effective haemostasis and preservation of the maternal blood volume during parturition (Bonnar *et al.*, 1971). The increased levels of coagulation factors associated with pregnancy have been reported as occurring, in the main, in the third trimester.

In the present study factors VII and X were found to be increased early in the second trimester. An increase of similar magnitude in the activity of these factors at an unspecified time during the second trimester was reported by Nilsson and Kullander (1967). Already there are reports emphasizing the haemorrhagic complications of therapeutic abortion, and it is likely that in some instances defective blood coagulation may be responsible.

The increase in the activity of factors V, VIII, and X which were found during induction of abortion in mid-trimester pregnancy by extra-amniotic prostaglandin $F_{2\alpha}$ indicates that activation of the coagulation system is taking place. In particular the increase of factor X may be due to the escape of thromboplastin substances from the placental site during uterine contractions and especially at the time of placental separation. It has been shown in hamsters that thromboplastin material enters both the maternal and fetal circulation during placenta separation (Brown and Stalker, 1969). During placental separation at term in normal pregnancies increased levels of coagulation factors V and VIII have been found in both peripheral and uterine blood (Bonnar *et al.*, 1970). Stander *et al.* (1971) suggested that induction of abortion by intra-amniotic injection of hypertonic saline initiates disseminated intravascular coagulation. They reported more extensive changes than were found in the present study.

It is of interest that virtually no changes in the coagulation system were found during termination of early pregnancy by vacuum aspiration. It seems, therefore, that when pregnancy is terminated in the mid-trimester, whether by hypertonic saline instillation or by extra-amniotic prostaglandin, coagulation system changes in the circulating blood take place. These are most probably related to the physiological changes which have

taken place in the haemostatic system in the second trimester. Coagulation changes associated with abortion will establish a vulnerable state for intravascular clotting and thromboembolic complications. It is likely, therefore, that in susceptible patients termination of pregnancy after the first trimester may give rise to such complications as defective haemostasis or thromboembolic complications.

We wish to thank the consultant staff of the division of obstetrics and gynaecology for allowing us to study patients under their care. We gratefully acknowledge gifts of prostaglandin $F_{2\alpha}$ from Dr. R. Jacob, of the Upjohn Company.

One of us (M.H.H.B.) was on study leave from the department of obstetrics and gynaecology, Al Azhar University, Cairo, and was in receipt of a Ford Foundation Fellowship. This investigation has been supported in part by the Agency for International Development contract No. AID/Csd 2837 (granted to K.H. and M.P.E.).

We thank Mr. M. Haddon and Mrs. J. Fairweather for expert technical help.

Requests for reprints should be sent to Dr. M. H. H. Badraoui, Al Azhar University, Cairo, Egypt.

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Problem of the Old and the Cold*

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British Medical Journal, 1973, 1, 21-24

Summary

A pilot winter study of body temperatures using new measuring techniques was tested on 72 volunteers aged 65 or more living in Portsmouth. The body temperatures were related to their environmental temperature and living conditions. No case of serious hypothermia was found, but the study confirms that elderly people have

lower body temperatures and suggests that the coldest individuals tended to be the least aware of discomfort from the cold; this may well place them "at risk" for developing hypothermia.

Introduction

The incidence of hypothermia of the elderly is uncertain, with estimates varying from the hundred or so returns on the Registrar General's death certificates to over 20,000 deaths annually (Taylor, 1964). A committee of the Royal College of Physicians (1966) estimated that in a three-month winter period in Britain there could be 9,000 hospital admissions with hypothermia (rectal temperature $< 35^{\circ}\text{C}$).

Mouth temperature was advocated for the diagnosis of hypothermia (a deep body temperature below 35°C (95°F)) by a special committee for the British Medical Association (1964). In the winter survey undertaken by the Society of Medical Officers of Health (1968), 11.4% of all mouth temperatures of elderly people living at home were 35°C or below. In another similar survey (Williams, 1968), 5.1% of mouth temperatures were below 35°C and 17.8% were below 35.5°C (95.9°F). Many of the

* This work was one of two pilot studies preceding a major study on 2,000 elderly people in 1972. It is hoped to publish the results of the main study, which was a collaboration between the Centre for Environmental Studies (Professor D. Donnison and Mr. M. Wicks), the Medical Research Council (Dr. R. H. Fox and Miss P. M. Woodward), University College Hospital (Dr. A. N. Exton-Smith), and the Royal Free Hospital (Dr. M. F. Green), early in 1973.

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