The Effect of the Polyethylene Intrauterine Device on Peritoneal Fluid Cell Distribution of Adult Female Mice (37713)

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Administration of dextran (1, 2) or bacterial capsular polysaccharide (3) into the abdominal cavity to invoke inflammation produced characteristic changes in the cellular population of mouse peritoneal fluid. Since the contraceptive effect of an intrauterine device (I. U. D.) may be related to polymorphonuclear leukocytes within the uterine lumen, the present study attempts to determine if the uterine cavity I. U. D.-induced inflammation extends into the abdominal cavity, *i.e.*, the polymorphonuclear leukocytes may change the peritoneal cavity cell distribution.

Materials and Methods. Adult female CF-1C mice were smeared once daily by vaginal lavage to determine estrus. Each mouse was then anesthetized with ether, and a piece of polyethylene intramedic tubing (1.3 cm long, P. E. 60, 0.030 mm i. d., 0.048 mm o. d., free from tissue reaction, Clay-Adams) was fixed in place by suture within each uterine horn from the animal's ventral body surface. In the control animal, a silk suture alone (without an I. U. D.) was sutured into each horn. Twenty-one days later, all mice were placed on an Electronic Activity Monitor (EAM) for 10 min, and the movements per minute were recorded. Peritoneal fluid specimens (sometimes only a drop) were then aspirated from the animal's ventral surface using a 1.0-ml tuberculin syringe attached to a 27-gauge needle. The specimens were then placed on an albumin-coated slide and placed in 95% alcohol for 2 hr. After fixation, the slides were stained using the Papanicolaou Technique (4), and 200 cells were randomly counted and grouped as mesothelial cells, histiocytes, polymorphonuclear leukocytes, monocytes, lymphocytes, mast cells, bare nuclei, and daisy cells. The random counting of a fixed number, rather than counting the number of cells in an absolute fluid volume, eliminates the extreme variation resulting from counting cells per unit volume because of the small amount of fluid aspirated. The average values represent % distribution of each cell type in a 200-cell count. Final body weight and percent I. U. D. expulsions were recorded at autopsy.

Results. The sutured-in polyethylene I. U. D. produced a significant increase in peritoneal fluid histiocyte and polymorphonuclear leukocyte proportions: histiocytes increased from 9.5 ± 0.9 to 17.5 ± 0.9% (83.8% increase) and polymorphonuclear leukocytes increased 89.2% from 12.0 ± 0.8 (controls) to 22.7 ± 1.5% (I. U. D. group). Mesothelial cells decreased 34% in the presence of the I. U. D. However, the percent distribution of control mesothelial cells were somewhat higher than we usually record. Daisy cells were only noted in animals having an I. U. D. No significant change was observed in lymphocyte or monocyte distributions.

While the I. U. D. produced a definite abdominal inflammatory effect as evidenced by the cellular response, it produced no apparent animal discomfort as recorded by the spontaneous activity measured on the EAM. The movements per minute were 63.9 ± 3.0 for controls as compared to 60.5 ± 2.9 for I. U. D.-bearing animals, a change of only 5.5%. Twenty-five percent (7/28) of the intrauterine devices were expelled from the uterus despite our fixing the device within the lumen. The I. U. D. produced no change in body weight over the experimental period.

Discussion. Polyethylene I. U. D-induced

TABLE I. Effect of Sutured-in Polyethylene Intrauterine Devices on Peritoneal Fluid Cell Distribution of CF-1C Mice.

	Sham-operated controls	Polyethylene sutured IUD	p	% Change
No. of mice	15	14	—	—
Final body weight (g)	28.1 ± 0.1[a]	29.1 ± 0.2	>0.5	+3.4
Movements/minute	63.9 ± 3.0	60.5 ± 2.9	>0.5	−5.5
% expulsion of I.U.D.	—	7/28 (25%)	—	—
Cell type		% Distribution of cells		
Mesothelial cells	70.2 ± 1.4	52.4 ± 1.7	<0.001	−34.0
Polymorphonuclear leukocytes	12.0 ± 0.8	22.7 ± 1.5	<0.001	+89.2
Histiocytes	9.5 ± 0.9	17.5 ± 0.9	<0.001	+83.2
Lymphocytes	4.3 ± 0.3	3.6 ± 0.4	>0.5	−20.4
Monocytes	3.5 ± 0.3	3.6 ± 0.4	>0.1	+2.0
Mast cells	0.2	0.1	—	—
Bare nuclei	0.1	0.2	—	—
Daisy cells	—	0.04	—	—

[a] ± Standard error of the mean.

inflammation poses an interesting problem to gynecologists because the antifertility response may involve the leukocytic increase within the uterine lumen, which agrees with the increase in the percent polymorphonuclear leukocytes within the pelvic cavity. The mode of action of the I. U. D. might be defined in terms of the inflammatory response seen in uterine and abdominal fluids. The macrophages in contact with the I. U. D. may produce a hostile uterine environment in which sperm become phagocytized by macrophages (polymorphonuclear leukocytes and histiocytes). Part of the hostile enviroment contributing to contraception may be due to a polyethylene I. U. D. causing excess mucosal enzymes being secreted into the uterine fluid which interferes with the maturation and/or the survival of the blastocyst (5). The increased antifertility activity produced by copper wire wrapped around the polyethylene I. U. D. may be related to an increased inflammatory response (6, 7). One wonders about the degree of response needed for contraceptive effectiveness. It would seem desirable to produce a mild mucosal effect (adding of small amounts of enzymes into uterine fluid) by an I. U. D. without the increase in percent polymorphonuclear leukocytes in peritoneal fluid signifying inflammation as seen in the present study. Certainly, one should determine whether or not a massive white-blood-cell increase in uterine fluid is essential for a maximum contraceptive effect. Despite our "suturing-in," about 25% of the intrauterine devices were expelled, in part due to a foreign body response. The I. U. D. becomes covered with a purulent material which possibly alters the I. U. D. and facilitates expulsion. Future studies must focus on improved tolerance of the I. U. D. as well as the mechanism of action.

Summary. Polyethylene intrauterine devices sutured into the uterine cavity of CF-1C mice for 21 days produced an alteration in peritoneal fluid cell distribution as shown by the percent increase in polymorphonuclear leukocytes and histiocytes, but with no change in animal movement.

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Received May 18, 1973. P.S.E.B.M., 1973, Vol. 144.