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## تغییرات باکتریولوژیک و هیستولوژیک رحم گاو ان مبتلا به آندومتريت

مزمن درمان شده با  $PGF2\alpha$

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### خلاصه

تغییرات باکتریولوژیک و هیستولوژیک رحم در ۲۳ راس گاو شیری نژاد هلشتاین با سابقه آندومتريت مزمن مطالعه شد. گاو ان در طول سال ۱۳۶۵ جهت درمان به بخش مامائی و بیماریهای تولید مثل دام بیمارستان شماره ۱ دانشکده دامپزشکی دانشگاه تهران آورده شده بودند. از رحم گاو ان، قبل و بعد از درمان با يك آنالوگ  $PGF2\alpha$  در خلال فاز لوتئال سیکل استروس، نمونه های باکتریولوژیک و هیستولوژیک گرفته شد. انواع میکروارگانیسم ها از رحم جدا شد. در بعضی موارد پس از درمان جمعیت باکتریائی کاهش یافت لیکن باکتریها و قارچهای دیگری جانشین آنها شد. فقط ۸ راس از ۲۳ راس گاو (۳۵٪) درمان شدند. بروسلا آبورتوس از رحم يك راس گاو که از نظر سرمی سه مرتبه پیپای منفی اعلام شده بود، جدا گردید.

بیست و يك نمونه بیوپسی (۹۱٪) قبل از درمان تغییرات هیستولوژیک شدید نشان داد. بعد از درمان در ۸ نمونه بهبودی چشمگیری مشاهده شد (۳۴/۵٪). تعداد ۹ نمونه تغییرات پاتولوژیک خفیفی داشت (۳۹٪) و در ۴ نمونه تغییری مشاهده نشد (۷۵/۵٪).

نتیجه اینکه درمان مکرر با  $PGF2\alpha$  در فاز لوتئال سیکل استروس در گاوهای که مبتلا به آندومتريت مزمن هستند موجب کاهش جمعیت باکتریائی رحم شده و واکنش های التهابی آندومترיום را کاهش میدهد.

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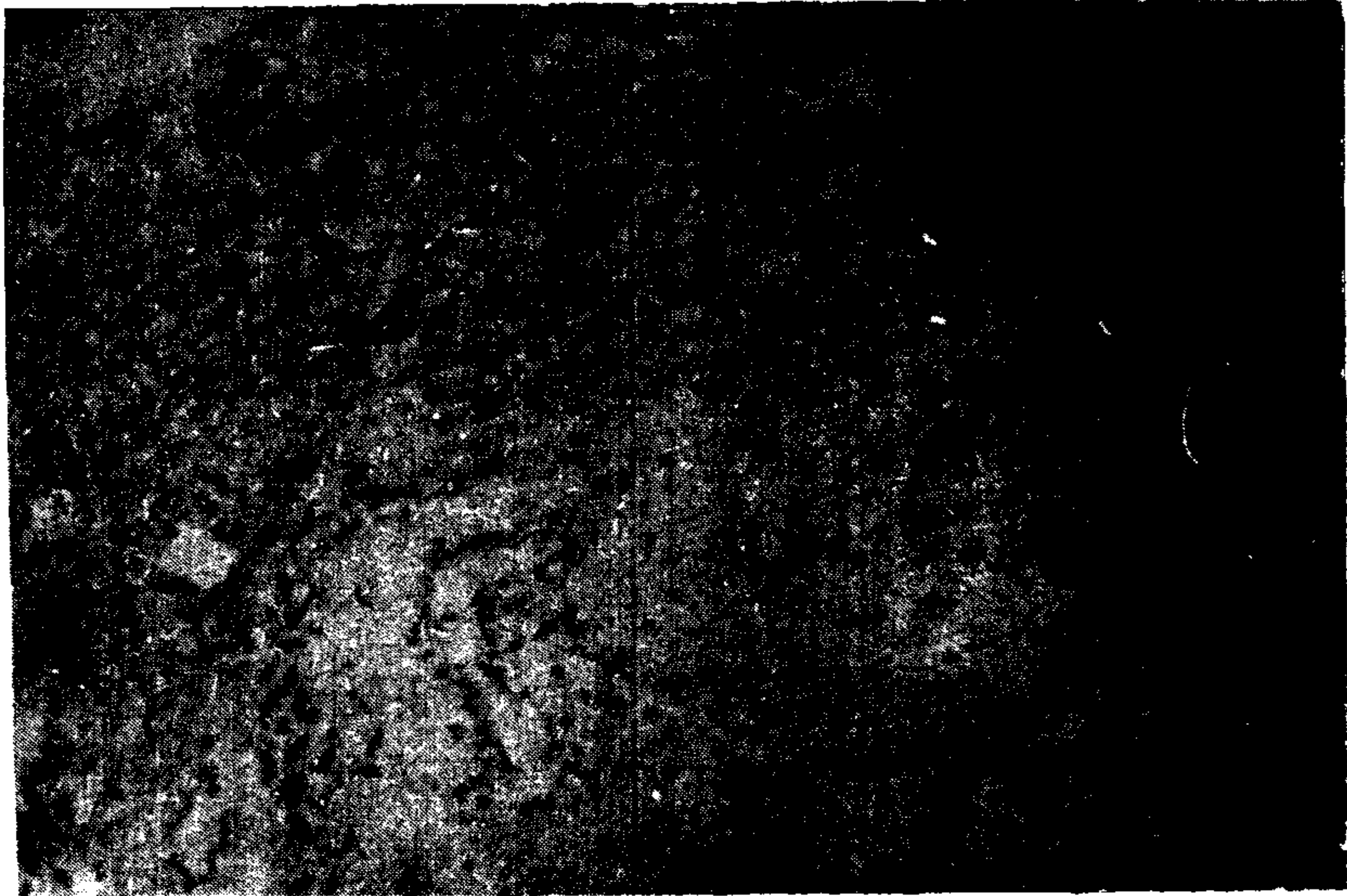


Fig 6: Reduction of leukocyte in filtration following treatment





Fig 4: Reduction of periglandular fibrosis and cystic dilation of treatment



Fig 5: Stromal leukocyte infiltration of uterus prior to treatment



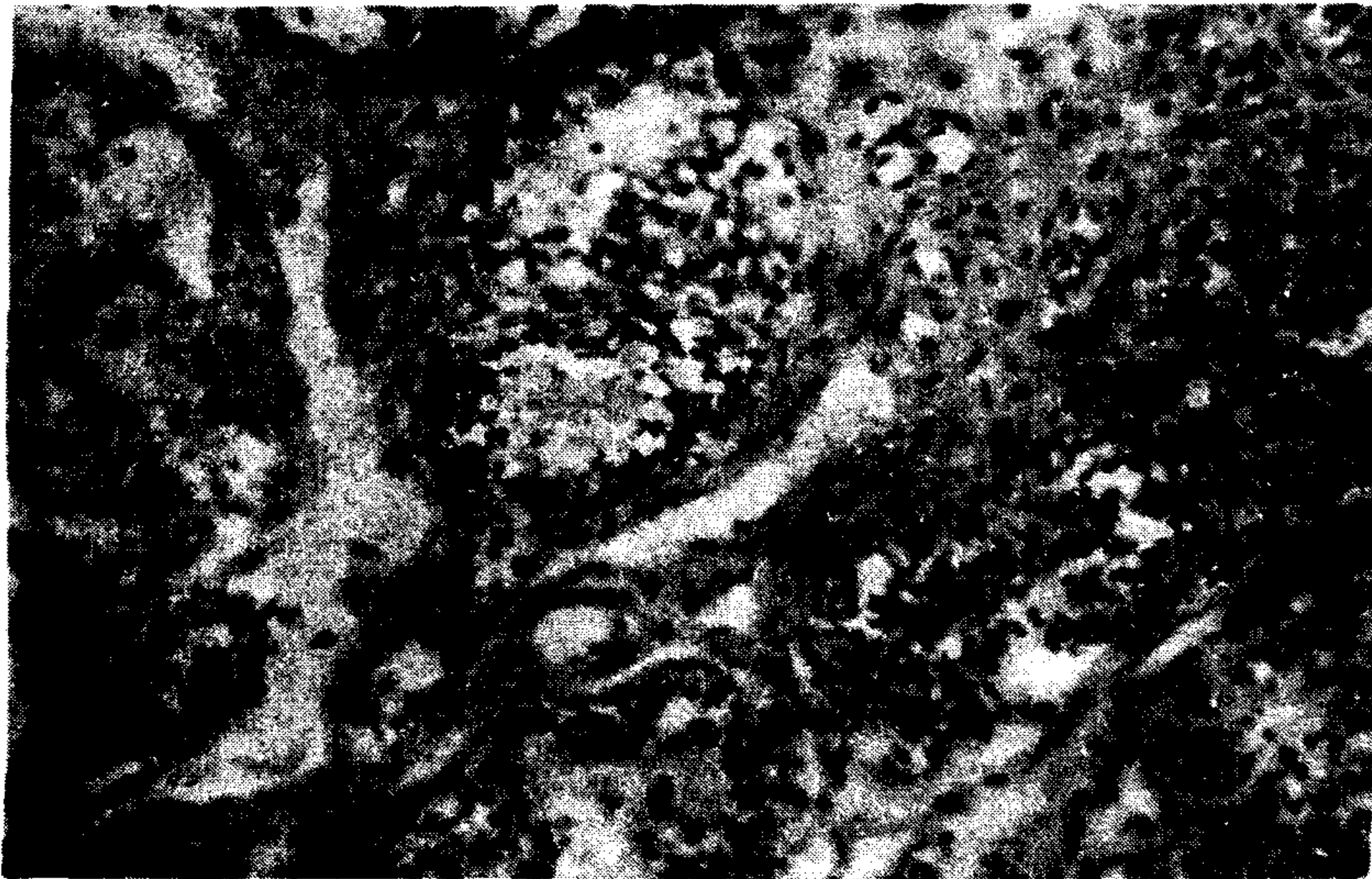


Fig 2: Cystic dilation of endometrial glands with moderate fibrosis prior to treat-

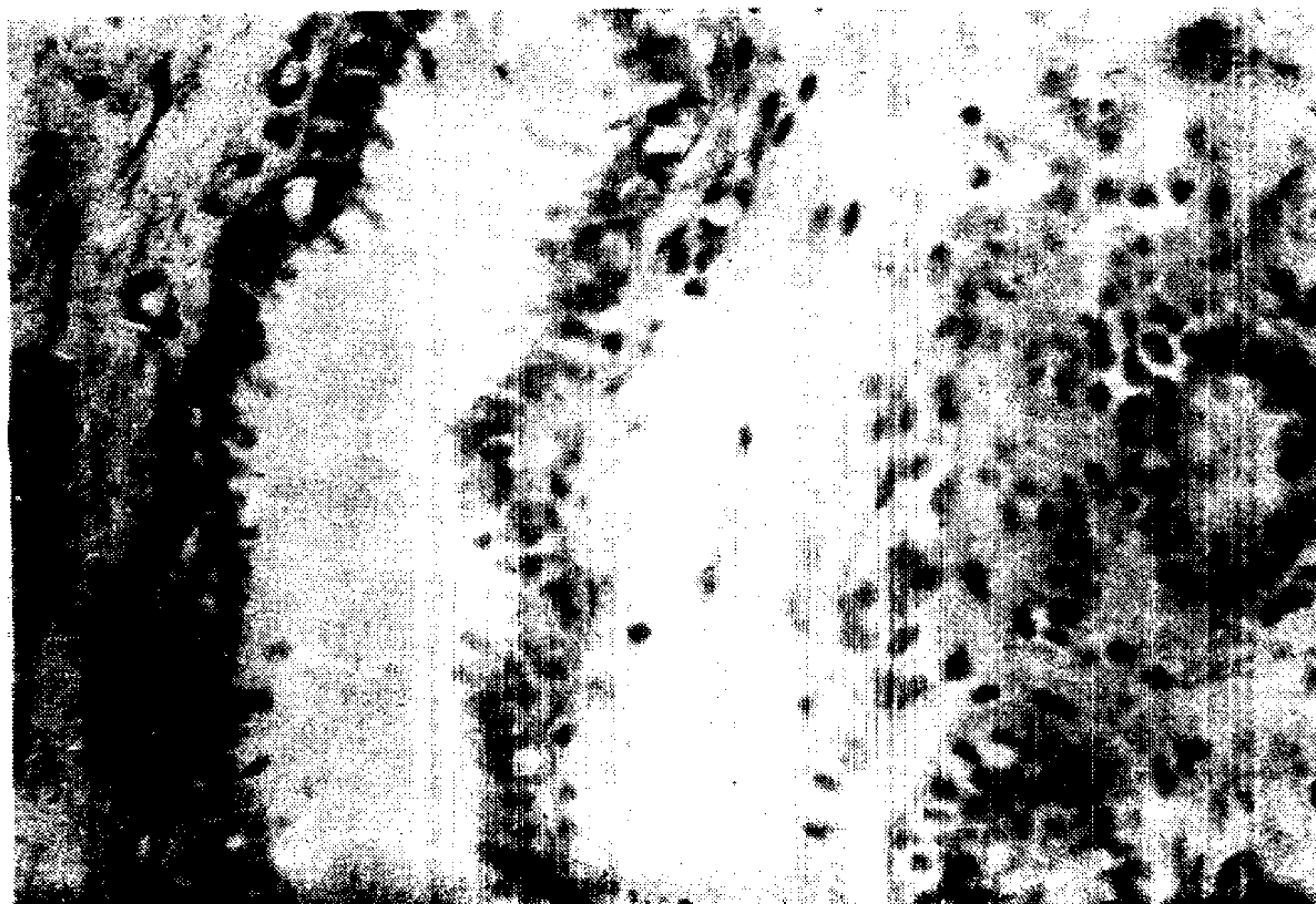


Fig 3: Reduction of periglandular fibrosis and cystic dilation after treatment with PGF2 (H.T.E x 400)

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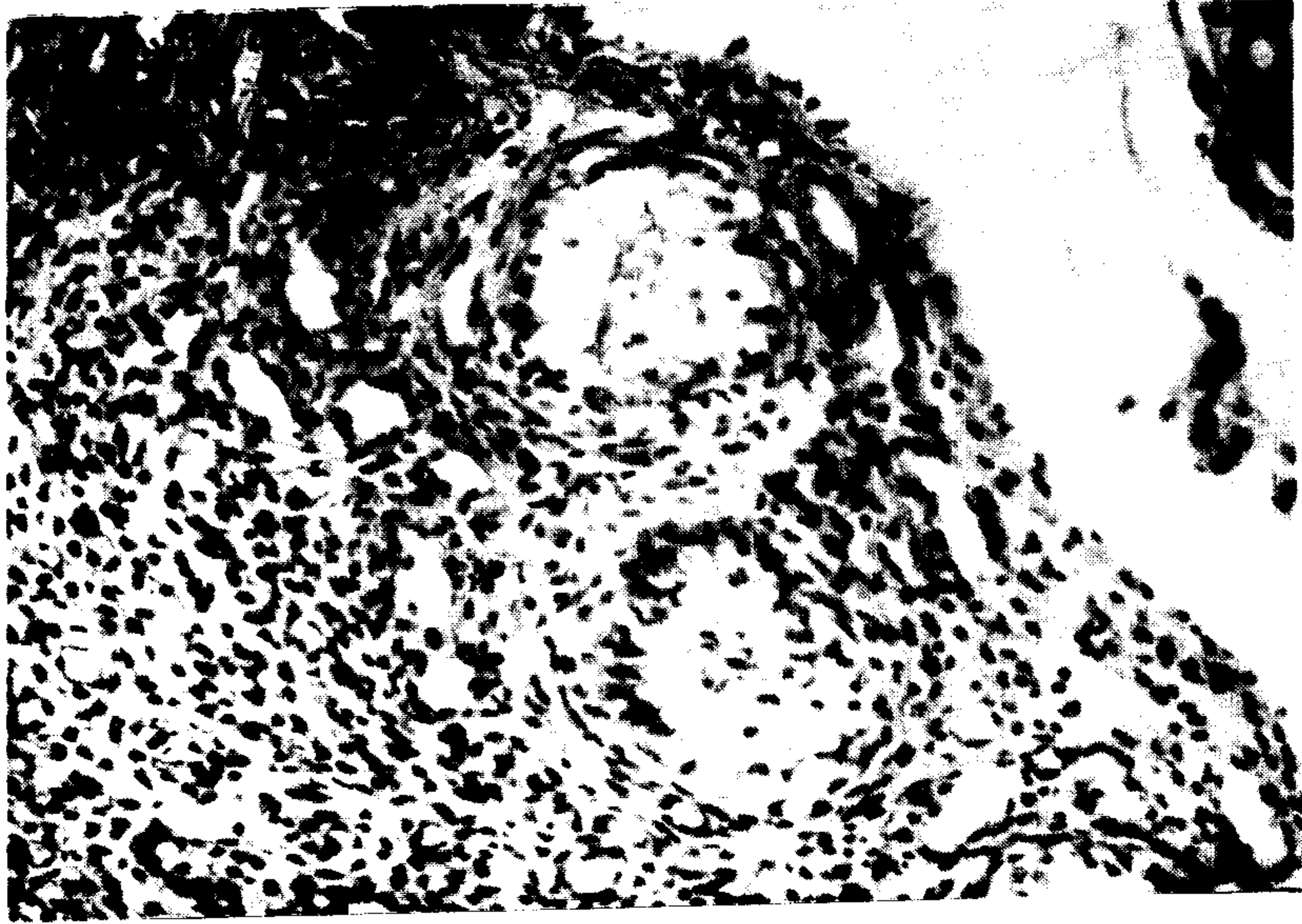


Fig 1: Periglandular and perivascular fibrosis with leukocytic infiltration of uterus prior to treatment with  $\text{PGF}_{2\alpha}$  in a cow (H.T.E x 400)



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Table (5)- The association between histopathological changes and presence of the microorganisms in samples taken from the uteri after treating the cows with PGF2  $\alpha$  . Faculty of Vet.Med.Univ. of Tehran-IRAN

Microorganisms	Histopathological changes		Total
	Present	Absent	
Present No(%)	3(13)	12(52)	15(65)
Absent No(%)	2(9)	6(26)	8(35)
Total	5(22)	18(78)	23(100)

\*The association was not statistically significant



Table (4)- The association between histo-pathological changes and presence of the microorganisms in samples taken from the uteri prior to treating the cows with PGF2 $\alpha$  . Faculty of Vet.Med.Univ. of Tehran,IRAN

Microorganisms	Histopathological changes		Total
	Present	Absent	
Present No(%)	23(100)	—	23(100)
Absent No(%)	—	—	—
Total	23(100)	—	23(100)

\* The association was not statistically significant

Table (3) -Lesions of the uteri prior to and after treating the cows with PGF2 $\alpha$  in luteal follicular phase. Faculty of Vet. Med. Univ. of Tehran- IRAN

phase	Uterine lesions						Total
	Prior to treatment			After treatment			
	Present	Reduce	Absent	Present	Reduce	Absent	
Luteal No(%)	21(91)	—	—	4(17.5)	9(39)	8(34.5)	21
Follicular No(%)	2(9)	—	—	—	—	2(9)	2
Total							23

Table (2)- Occurrence of different groups of microorganisms in the uteri of repeat breeder cows prior to and after treatment with PGF2<sup>a</sup>. Faculty of Vet.Med.Univ. of Tehran. IRAN

	Microorganism groups			No isotation	Total
	specific	Non-specific	Non pathogenic		
Control No. (%)	4(17.5)	14(61)	5(21.5)	--	23(100)
Treatment No. (%)	--	13(56.5)	2(8.5)	8(35)	23(100)



Table (1) -Microorganisms isolated from the uteri in repeat breeder cows prior to and after treatment with PGF2  $\alpha$  . Faculty of Vet.Med. Univ. of Tehran. IRAN.

Type of the microorganism	Prior to treatment No.(%)	After treatment No.(%)
<u>B.abortus &amp; E.coli</u>	1(4.5)	-
<u>Mycoplasma sp. &amp; Aspergilus sp.</u>	1(4.5)	-
<u>Mycoplasma sp.</u>	1(4.5)	-
<u>C.fetus, C.bovis &amp; B.macerance</u>	1(4.5)	-
<u>E.coli</u>	11(48)	6(26)
<u>C.pyogenes</u>	1(4.5)	-
<u>P.aeroginosa</u>	-	1(4.5)
<u>Staph. sp</u>	-	2(4.5)
<u>Strep. sp</u>	-	2(8.5)
<u>Aspergilus sp &amp; yeasts</u>	2(8.5)	1(4.5)
<u>B.macerance</u>	5(21.5)	3(13)
Negative	-	8(35)
Total	23(100)	23(100)

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tool. However, it may not be always practical in farm. Shortening the oestrus cycles regularly, with a luteolytic agent (PGF $2\alpha$ ) increases the uterine contractility, changes the abnormal endometrial tissue to the normal state and reduces the population of the microorganisms. Intrauterine infusions may introduce bacteria and fungi into the uterus that are mostly persistent to the available antibiotics. Thus, treatment of such cows with PGF $2\alpha$  may remain the method of choice specially in valuable animals.

all 23 uteri(100%) showed infiltration of lymphocytes in the endometrium, of which only 4 uteri(17.5%) did not respond to the treatment and in 8 uteri(35%) there was a significant reduction in lymphocytes. Seven uteri(30.5%) showed neutrophils in abundance before treatment and all disappeared in response to the treatment except one(8.5%). Infiltration of the eosinophils in the endometrial stroma was found in 3(13%) of the uteri which was still present in two (8.5%) after treatment.

The uterine lesions were present in all 21 (91%) of the specimens taken in the luteal phase before treatment. These lesions were still present in 4 (17.5%), reduced to 9(39%) and completely disappeared in 8(34.5%) of the uteri after treatment. Two specimens(9%) which were also taken in follicular phase before treatment, were completely free of these lesions after treatment(table 3).

Data which are presented in table 4 and 5 show that the association between histopathological changes and the presence of the microorganisms in the uteri was not statistically significant both prior to and after treating the cows with  $PGF2\alpha$ .

In conclusion, since the adverse economic consequences of chronic endometritis affects the management of dairy herds, it is very important to confirm the problem. Bacteriological examination may not be very practical and is less reliable than uterine biopsy. Uterine biopsy may be applied as an effective diagnostic



others (3).

Brucella abortus was isolated from the uterus of three consecutive seronegative tests. This cow had a previous abortion. This has also been reported by others (2) Escherichia coli was isolated from 11 uteri (48%) prior to treatment and resisted in only 6 ones (26%) after treatment (table 1).

In 4 (17.5%), 14 (61%) and 5 (21.5%) of the uteri, specific (B. abortus, C. fetus etc.) non-specific and non pathogenic microorganisms were isolated respectively prior to the treatment. However, after treatment specific pathogens were not isolated. In 13 (56.5%) and two (8.5%) uteri, non-specific and non pathogenic microorganisms were still present (table 2). Presence of non-specific bacteria in the uterus around the period of mating may not be very important in producing infertility. However, the duration of infection is very important (6).

Histopathological examination of the endometrium showed significant alterations in the tissue after treatment. Preglandular fibrosis (fig.1) of the endometrium was observed in 16 (69.5%) of the specimens which persisted in 6 (26%) after treatment. In 6 specimens (26%), cystic dilation of the endometrial glands (Fig 2) was present prior to treatment and all disappeared following treatment. Fibrosis around the endometrial blood vessels of 4 (17.5%) uteri was reduced to one (4.5%) and thrombosis of these vessels which was present in 2 (8.5%) specimens, disappeared after treatment (fig 3).

Uterine tissues were collected in 70 per cent alcohol or 10 per cent formalin solution to the laboratory for histopathological studies. Cows were then observed for signs of Oestrus and the nature of discharge from the vulva. The same sampling procedures were used on day 11 or 12 after treatment, when a mature CL could be palpated in an ovary.

Data were subjected to chi-square test for statistical analysis(9).

### **Results and Discussion**

Reproductive records showed that all the cows, except one, had previous normal parturitions. However, repeat breeding was the common untreated disorder involving nearly 65 per cent of the animals. The average interval between calving and sampling was approximately 8.3 months. In some cases the cows had been infertile for one to two years and mostly between 4 to 6 years of age (ten out of 23 cows, 43.5%).

Sixty one per cent of the cows showed a cloudy mucus discharge. However, 26 per cent and 12 per cent of the animals had a muco-purulent and a purulent discharge from the vulva respectively. Cows were generally cyclic, with regular (21 to 23 days) oestrus cycles.

After treatment, the population of the microorganisms was generally reduced in the uteri but it was replaced by other organisms in some cases (table 1). This indicates that a secondary contamination must have occurred during the sampling that has been also shown by

metrial changes, both bacteriologically and histologically in repeat breeder cows clinically suspected to have chronic endometritis, prior to and after treating the animals with a prostaglandin F<sub>2α</sub> analogue(4).

### **Material and Methods**

Twenty three Holstein cows, between 2.5 and 9 years of age, with the history of repeat breeding and long standing(Chronic) endometritis were selected from several herds in Tehran Province. All the cows had been chosen to cull for managemental purposes due to infertility. Careful study of the reproductive records revealed that the animals have mucopurulent discharges from their genital tracts after the last parturition.

All the animals were palpated rectally to determine their reproductive status. Twenty one cows were in diestrus and the remaining two were in metestrus of the oestrus cycle.

Cows in diestrus were treated with 2ml. of a PGF<sub>2α</sub> analogue(cloprostenol, "Estrumate"ICI.), immediately after taking bacteriological samples and biopsies from the uterus by a sterile well-protected biopsy instrument. Cows in metestrus were also sampled but were treated with 2ml. PGF<sub>2α</sub> in diestrus. Bacteriological samples were cultured in the appropriate media(Blood agar, Brucella agar, Mycoplasma and Saboroux agars and other routine isolating media) and cultures were studies(1).



negative cultures. *Brucella abortus* was isolated from a uterus despite the cow being seronegative on three consecutive tests.

Twenty one specimens had severe histological changes (91%) before treatment. After treatment 8 specimens showed marked improvement (34.5%), 9 specimens showed minor alterations (39%) and 4 specimens remained unchanged (17.5%). It was concluded that repeated prostaglandin therapy in luteal phase of the oestrous cycle could reduce the bacterial population and improve the inflammatory reactions of the endometrium.

### **Introduction**

Endometritis has been reported to be the most common cause of the reproductive failure and infertility in the cow (10). Abortion, dystocia, trauma to the birth canal, retained placenta and many other disorders have been shown to be responsible for the condition (5,6,7,8). However, it may occur following normal parturition (7). Rectal palpation and vaginal inspection are not always reliable methods to diagnose the condition. Bacteriological samples and histological specimens from the uterus have been demonstrated to have some value in the diagnosis. Both physiological and pathological alterations of the endometrium have been studied in the cow and a careful histo-pathological picture of the condition has been presented (11,12).

The aim of the present study was to compare endo -

Bacteriological and Histological Alteration  
of the Uterus Injected with PGF<sub>2</sub>α to treat  
chronic endometritis in cows.

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**Summary:**

Bacteriological and histological changes of the uterus were studied in twenty three Holstein dairy cows with the history of chronic endometritis. The cows had been presented for treatment to the Large Animal Clinic, Faculty of Veterinary Medicine in Tehran during the year 1986.

Bacteriological swabs and histological specimens were prepared from the uteri before and after treating the animals with a PGF<sub>2</sub>α analogue during the luteal phase of the oestrous cycle.

A wide variety of microorganisms were isolated from the uteri. In some cases the population of the bacteria was reduced and replaced with some other bacteria and fungi after treatment. Only 8 cows out of 23 cases (35%) responded to the treatment on the basis of

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