Effect of *Eschericia coli* infection of the bovine uterus from the whole animal to the cell

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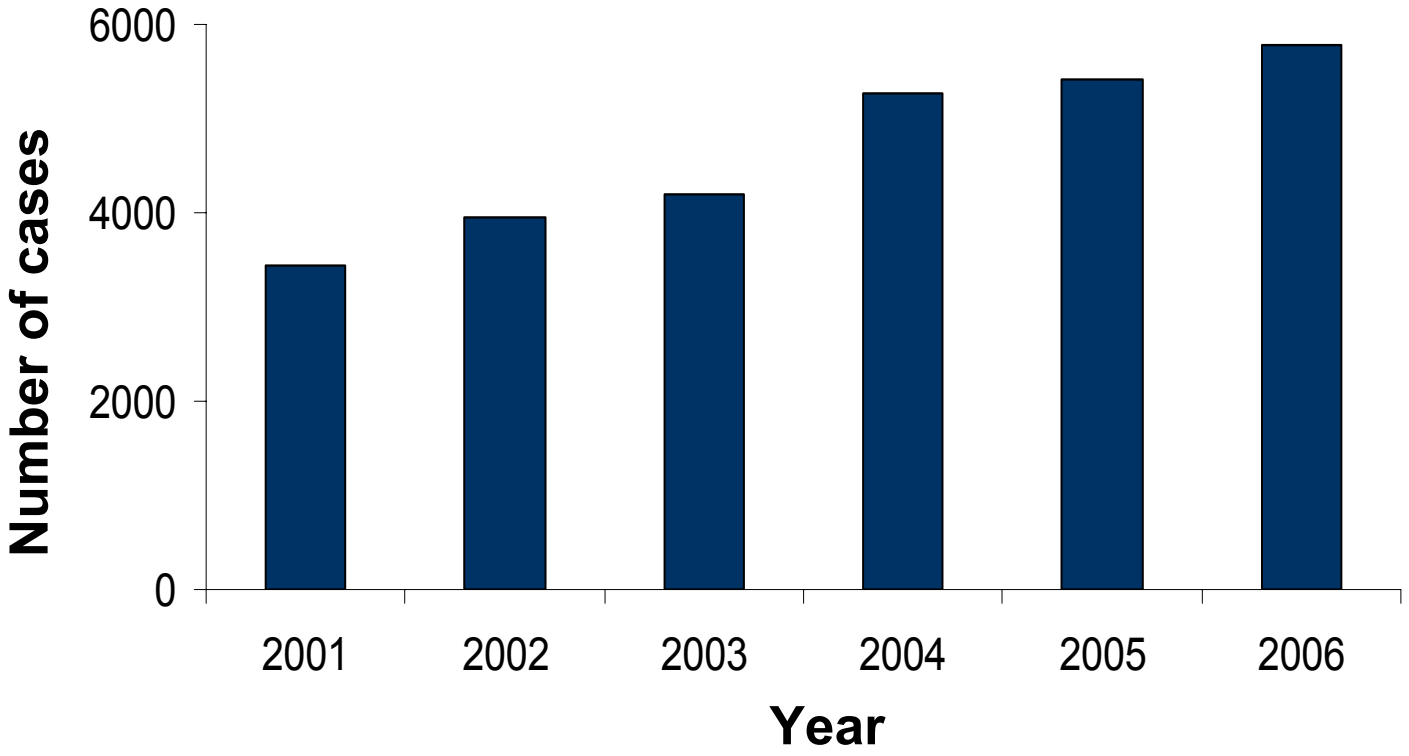
NADIS
National Animal Disease Information Service

Bacterial Infections of the Reproductive Tract

- Long term consequences include infertility
- Infections common
  - At coitus / insemination
  - After parturition
- Ubiquitous in cattle after parturition
- Associated with subfertility

Uterine disease in cattle – on the up!



Number of animals per year requiring direct intervention by a veterinarian. Data does NOT reflect subclinical cases.

Data generously supplied by NADIS

Clinical uterine disease (endometritis)

- Costs the dairy industry millions per year
  - Longer Ca-Cn intervals
  - Increased no. serves/conception
  - Increased number of culls
  - Subfertility

- High numbers of bacteria in the postpartum uterus result in reduced growth and function of the first postpartum dominant follicle

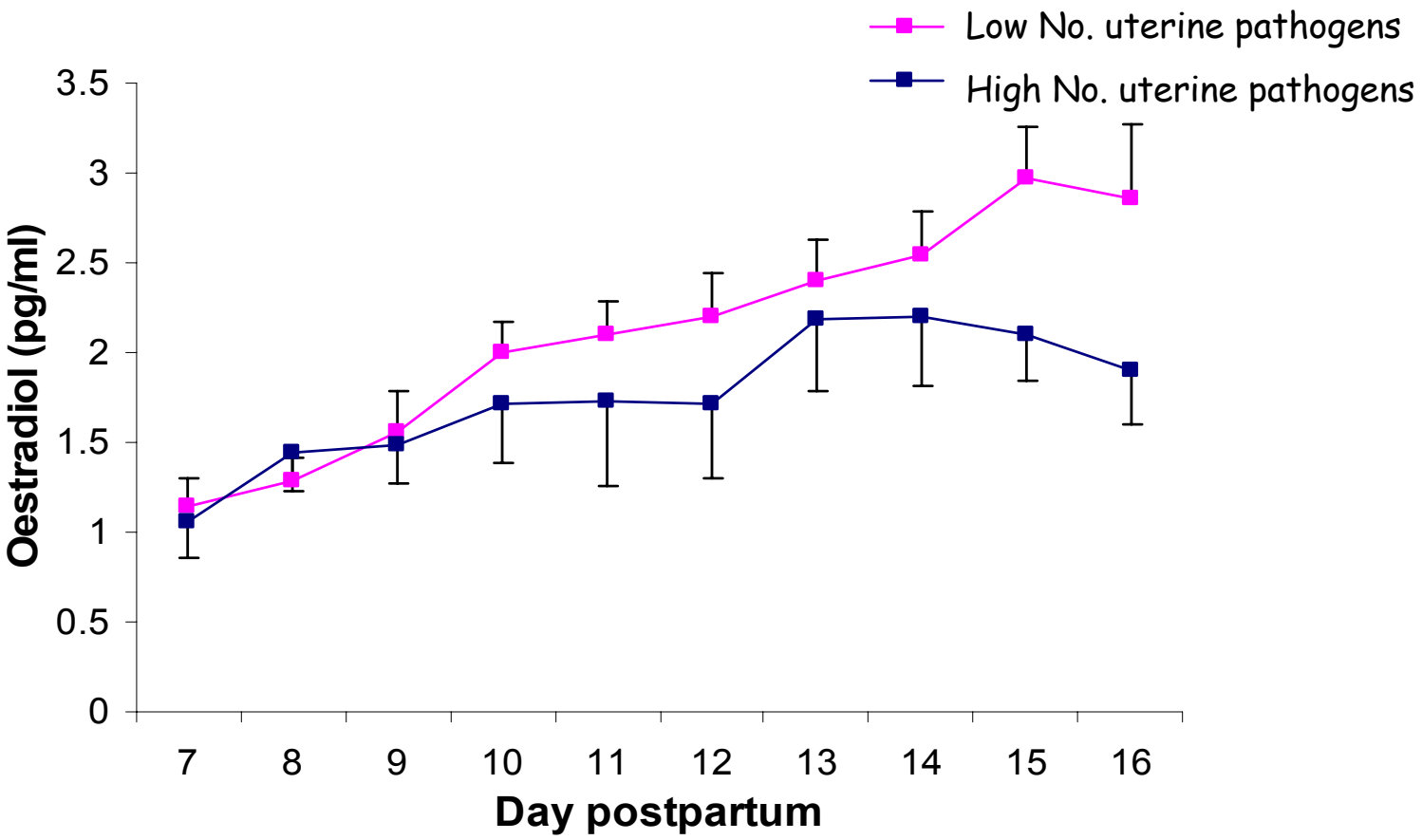
Sheldon *et al*, 2002

Uterine bacterial profile

Table 1. Categorization of bacteria, isolated by aerobic and anaerobic culture of uterine swabs from cattle, based on their potential pathogenicity

Bacterial category		
Uterine pathogens	Potential pathogens	Opportunist contaminants
Arcanobacterium pyogenes	*Acinetobacter* spp	*Aerococcus viridans*
Prevotella spp	*Bacillus licheniformis*	*Clostridium butyricum*
Escherichia coli	*Enterococcus faecalis*	*Clostridium perfringens*
Fusobacterium necrophorum	*Haemophilus somnus*	*Corynebacterium* spp
Fusobacterium nucleatum	*Mannhiemia haemolytica*	*Enterobacter aerogenes*
	Pasteurella multocida	*Klebsiella pneumoniae*
	Peptostreptococcus spp	*Micrococcus* spp
	Staphylococcus aureus (coagulase +)	*Providencia rettgeri*
	Streptococcus uberis	*Providencia stuartii*
		Proteus spp
		Proprionobacterium granulosa
		Staphylococcus spp (coagulase –)
		α-Haemolytic Streptococci
		Streptococcus acidominimus

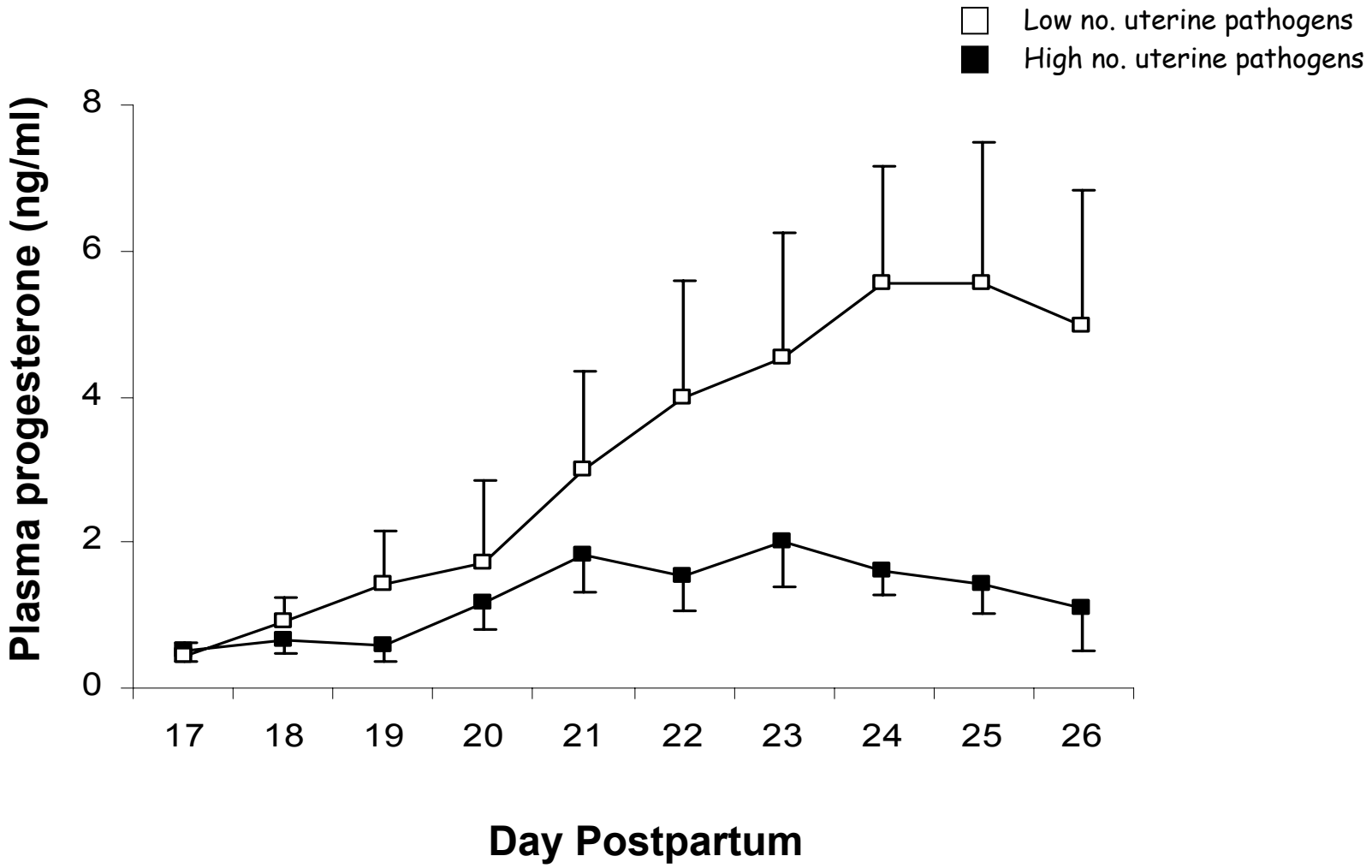
Ovarian follicles grow slower and produce less estradiol in animals with high numbers of uterine pathogens



(n = 82) *P < 0.05

Williams *et al*, 2007

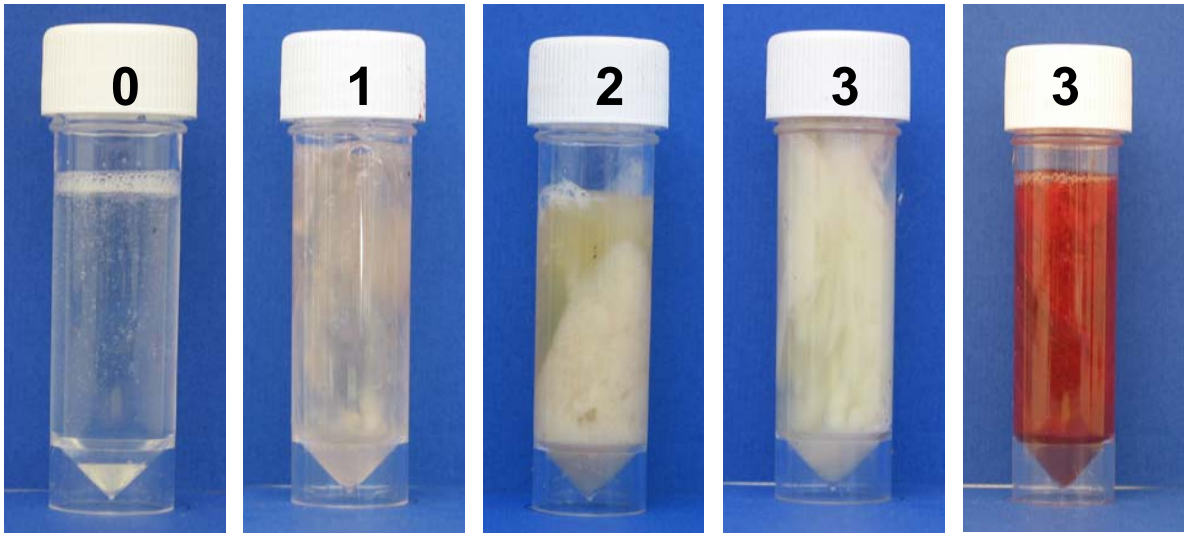
Corpora lutea grow slower and produce less progesterone in animals with high numbers of uterine pathogens



Williams *et al*, 2007

Uterine bacterial profile

- *E. coli* most commonly isolated
- Associated with increased AGP concentrations
- Associated with more severe clinical disease



- LPS detected in uterus, follicle and peripheral circulation

Question:

Are the effects of infection on postpartum fertility mediated by LPS?

Intervention study

- 8 nulliparous Holstein heifers
  - Normal genital tract and oestrous cycles
  - No bacterial contamination of the uterus
- Randomised crossover design

- Intrauterine infusion
  - Vehicle, 0.3 or 3 μg/kg *E.coli* LPS per infusion

Williams *et al*, unpublished

Ovarian events

LPS μg/kg per infusion	Days to follicular dominance from PG_2	Number of animals ovulated
0	3.2 ± 0.6	7/8
0.3	6.4 ± 0.5 *	2/8 *
3	7.9 ± 1.0 **	3/8 **

All animals displayed oestrous behaviour

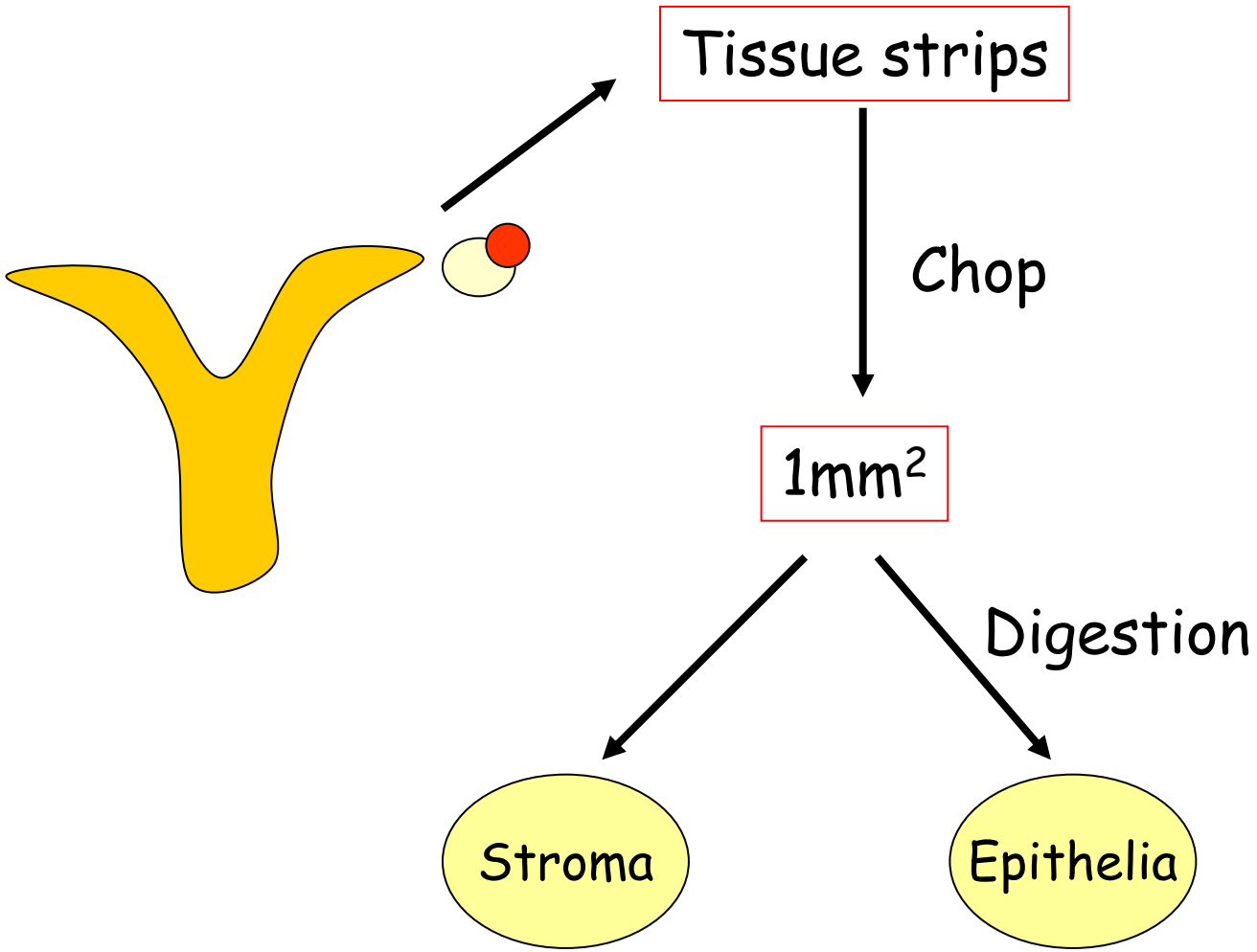
(n = 8) Values are mean ± SEM. *P < 0.05, **P ≤ 0.01 difference from control

Williams *et al*, unpublished

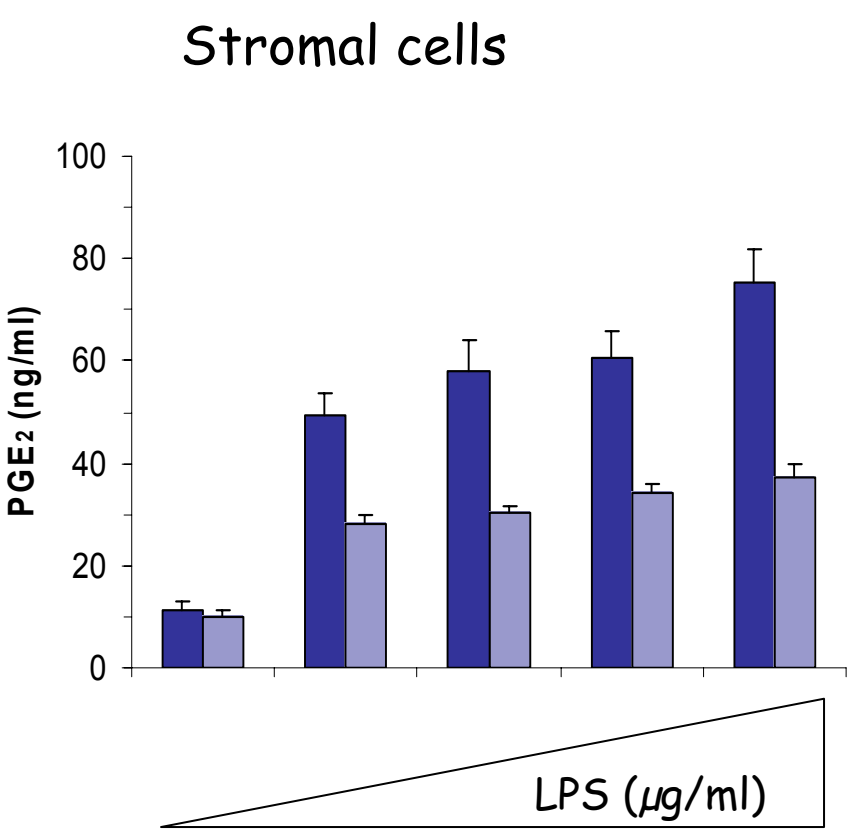
Question:

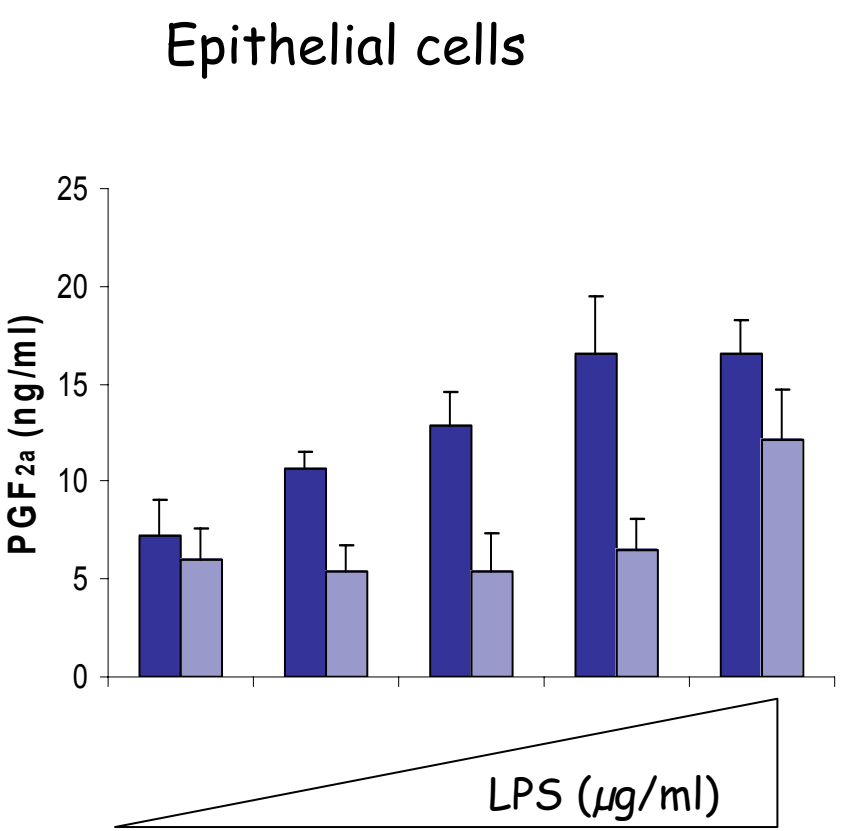
Does LPS act locally to affect the physiological function of uterine and/or ovarian cells?

Uterine cell culture



Response to LPS

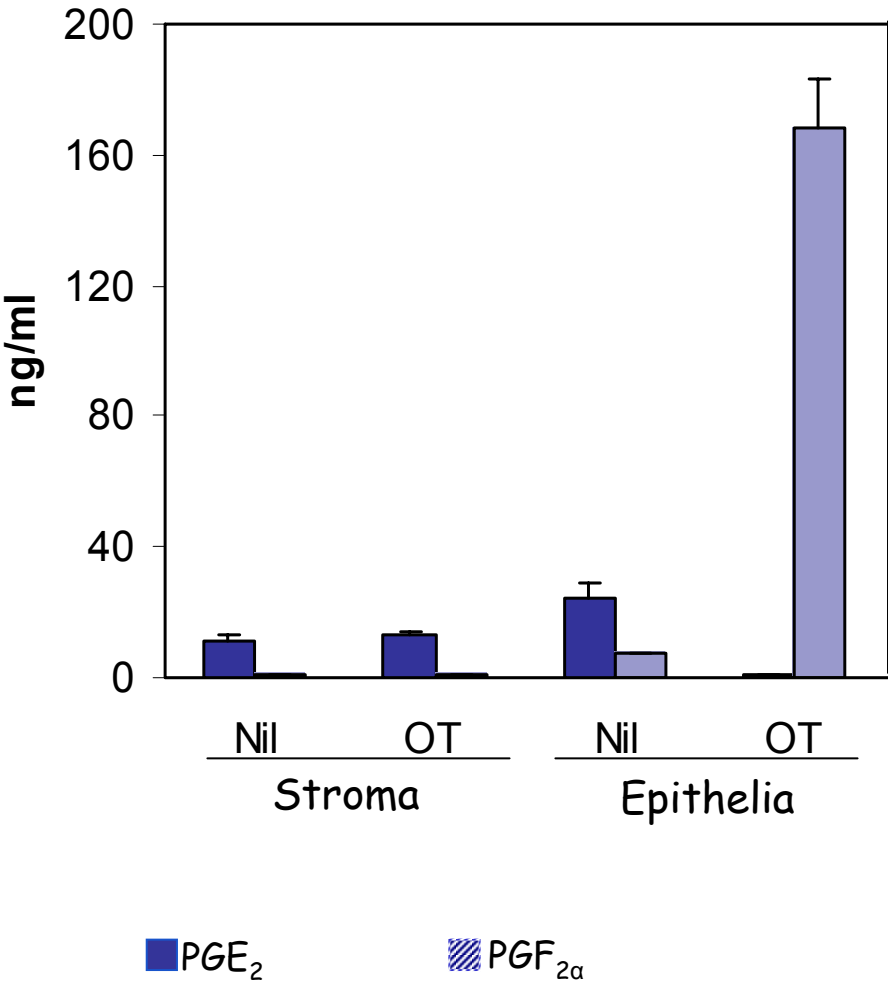




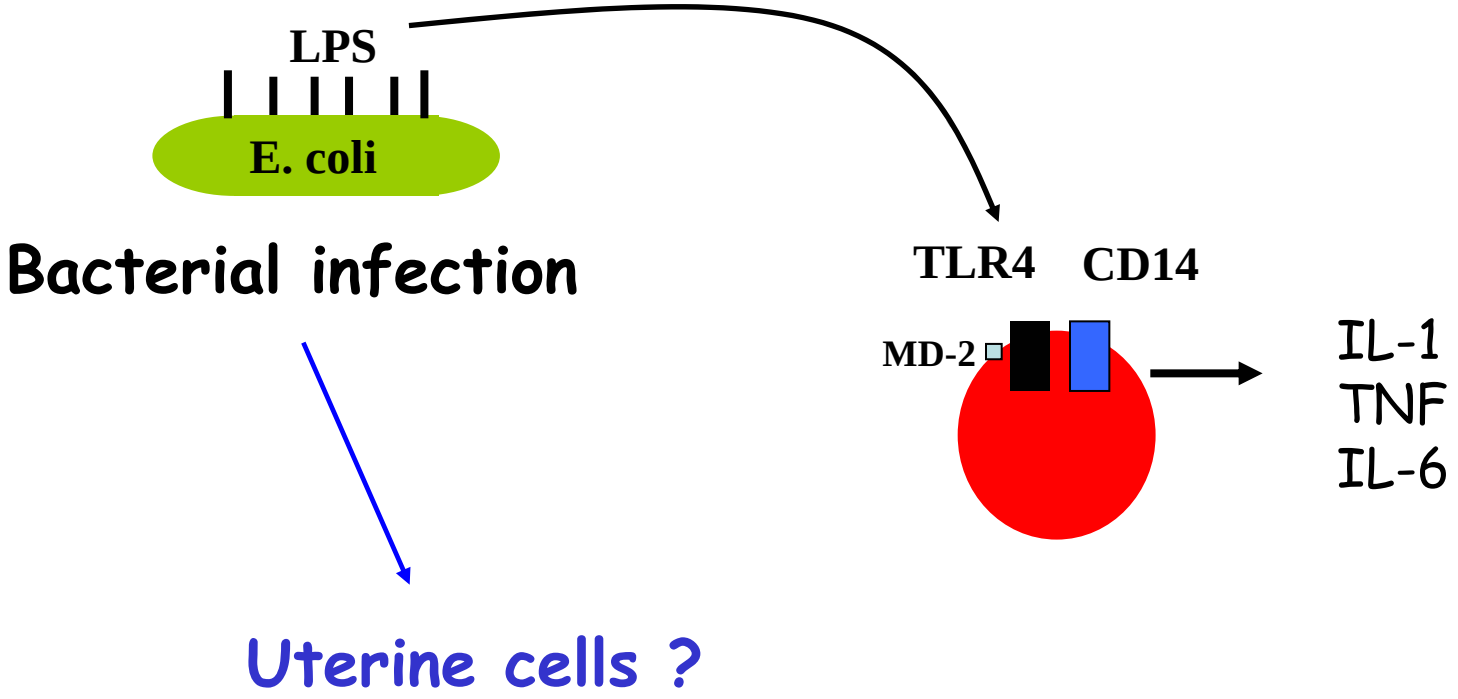
E.Coli LPS LPS + PMB

Herath *et al*, 2006

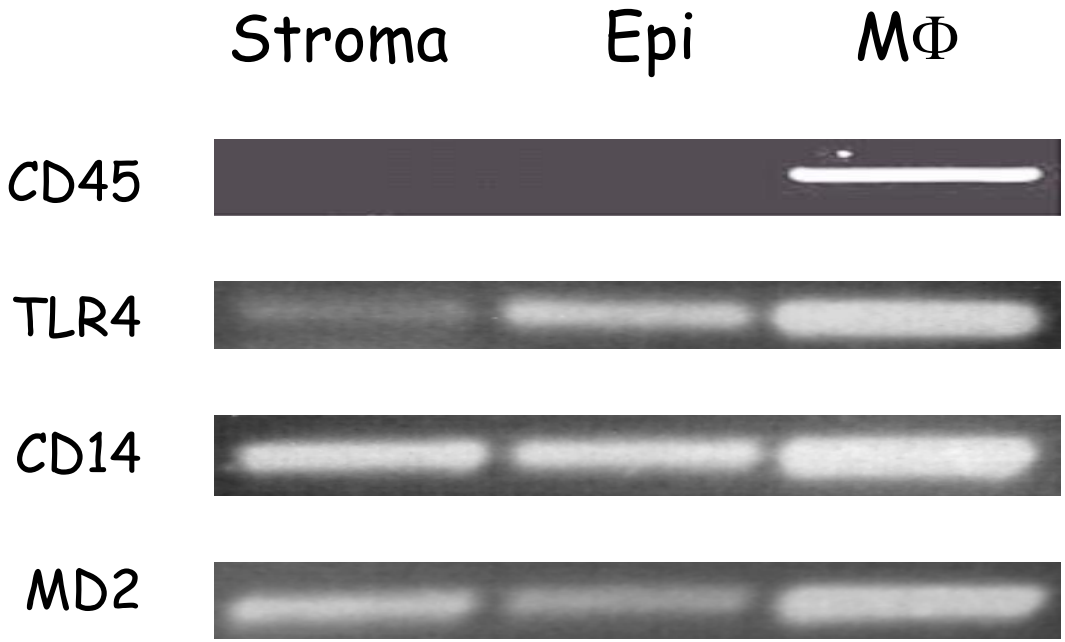
Response to LPS - $PGF_{2\alpha}$:PGE_2 ratio



Herath *et al*, 2006

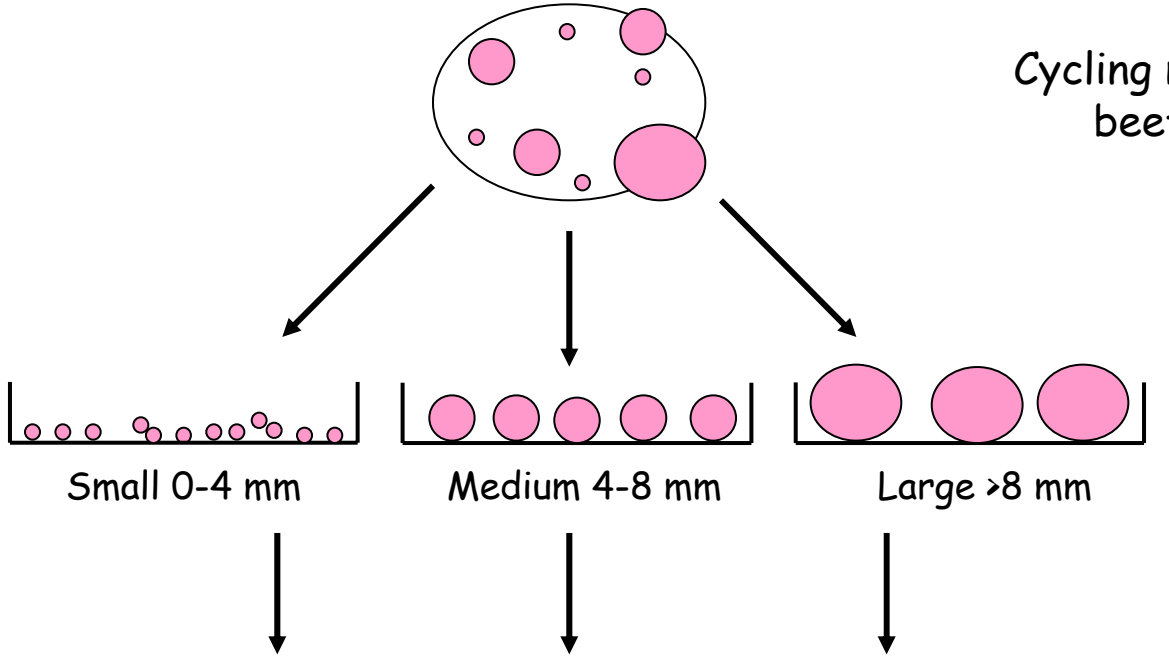

LPS
E. coli
Bacterial infection
TLR4
CD14
MD-2
IL-1
TNF
IL-6
Uterine cells ?

Expression of the LPS recognition receptor



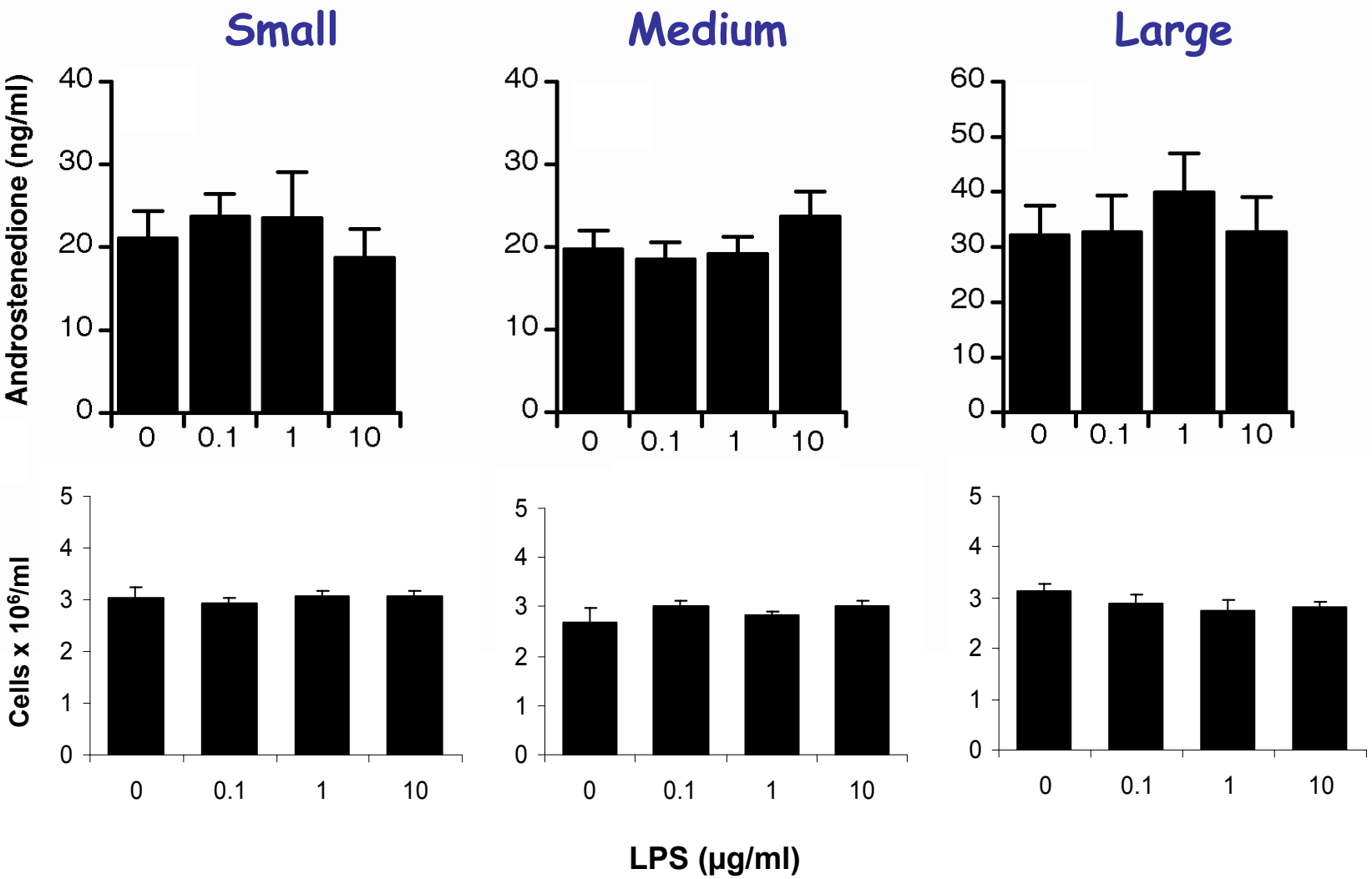
Herath *et al*, 2006

Ovarian cell culture



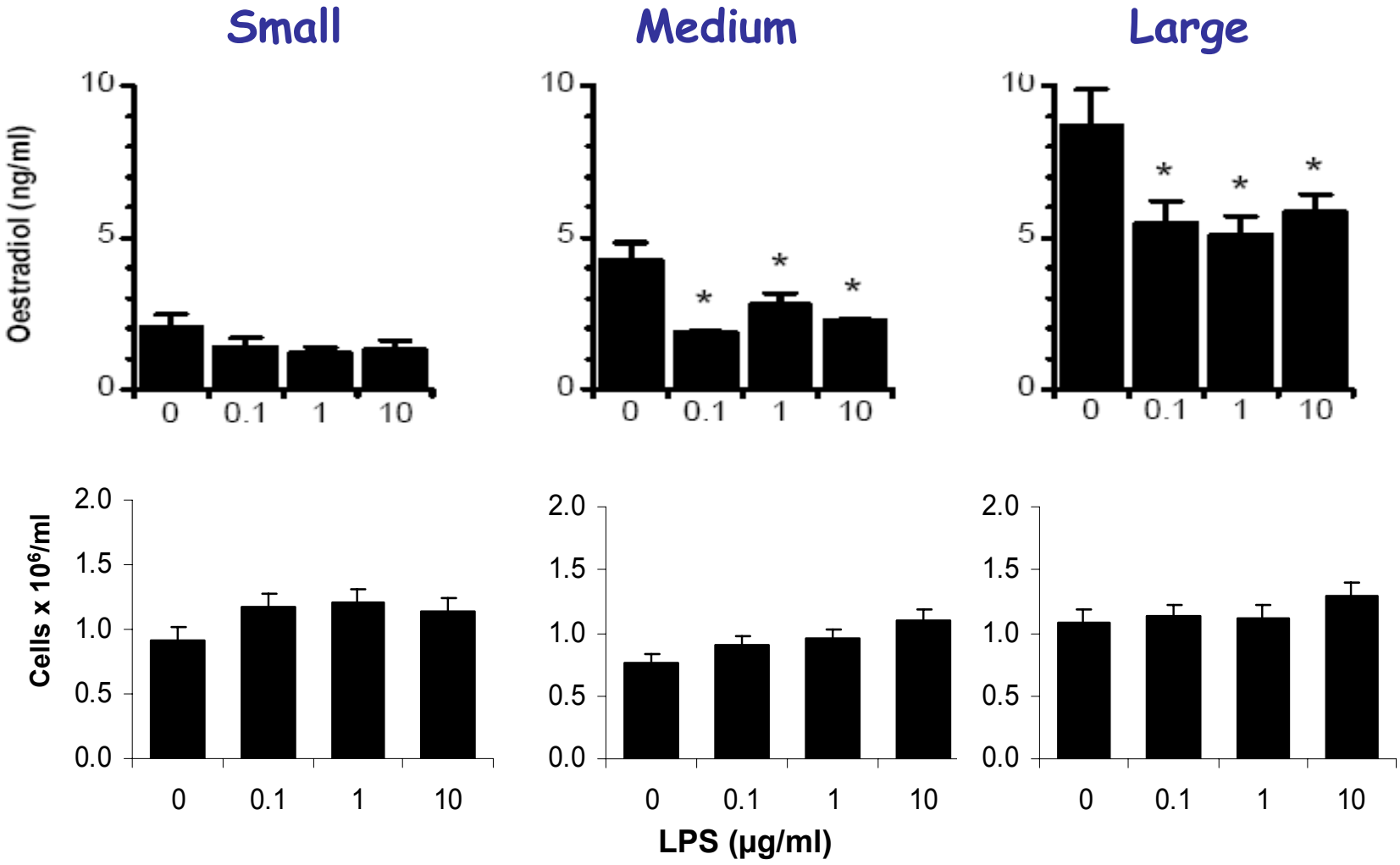
Gutierrez *et al*, 1997; Marsters *et al*, 2003; Glister *et al*, 2005

Response to LPS - Theca



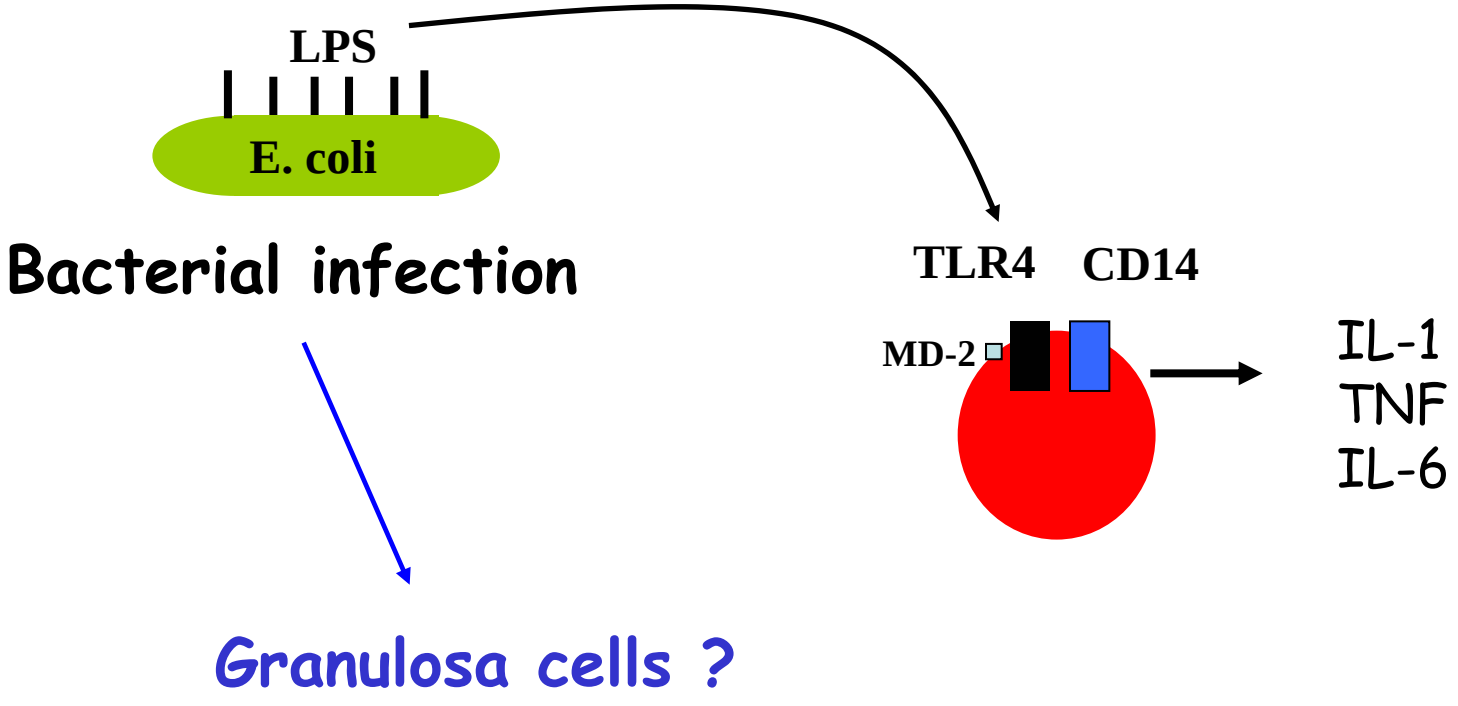
Herath and Williams *et al*, 2007 (*in press*)

Response to LPS - Granulosa



* P<0.05

Herath and Williams *et al*, 2007 (*in press*)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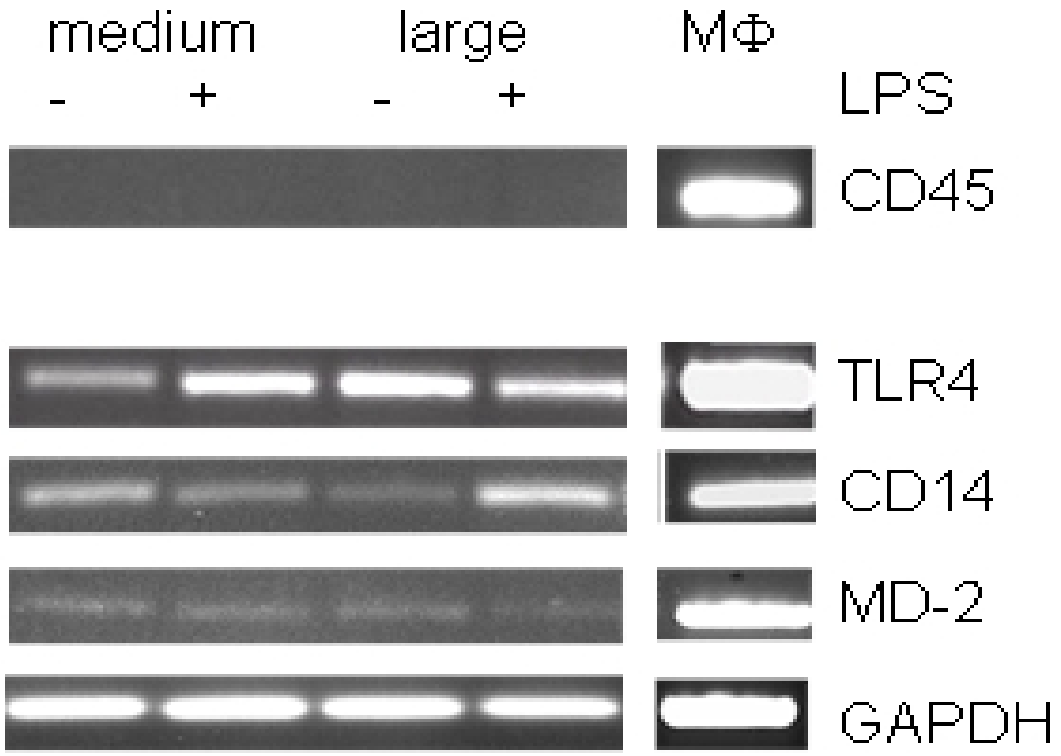
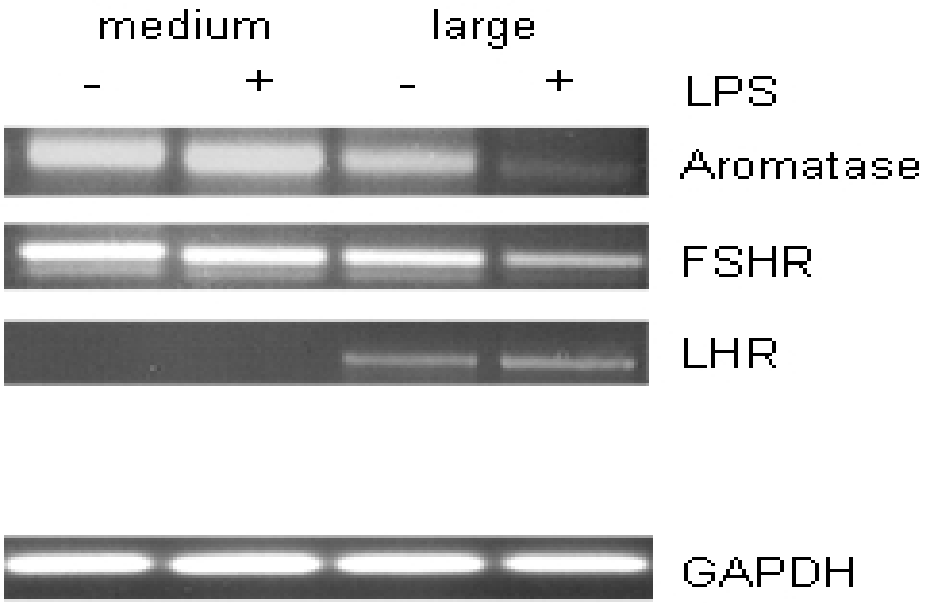
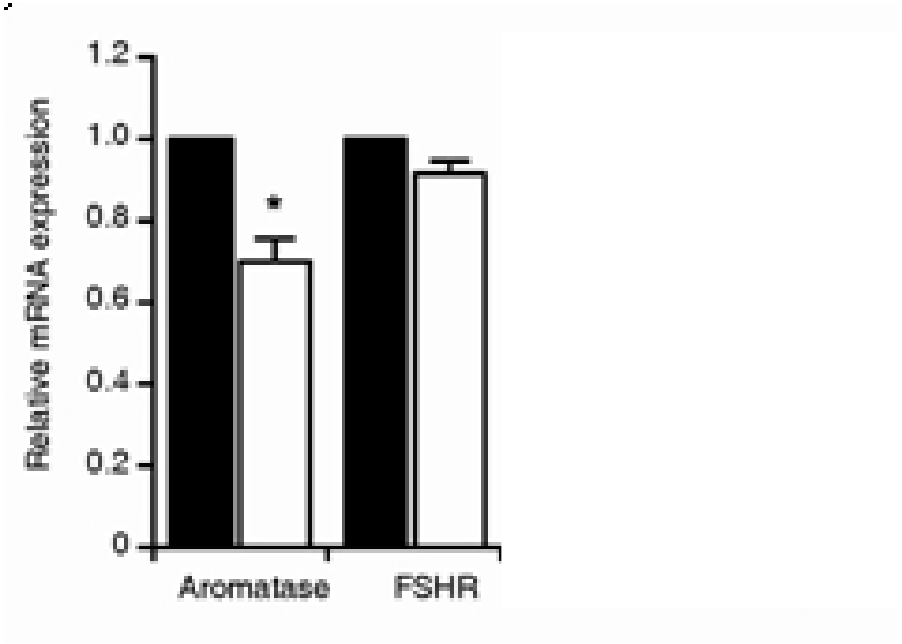


Herath and Williams *et al*, 2007 (*in press*)

Expression of functional genes

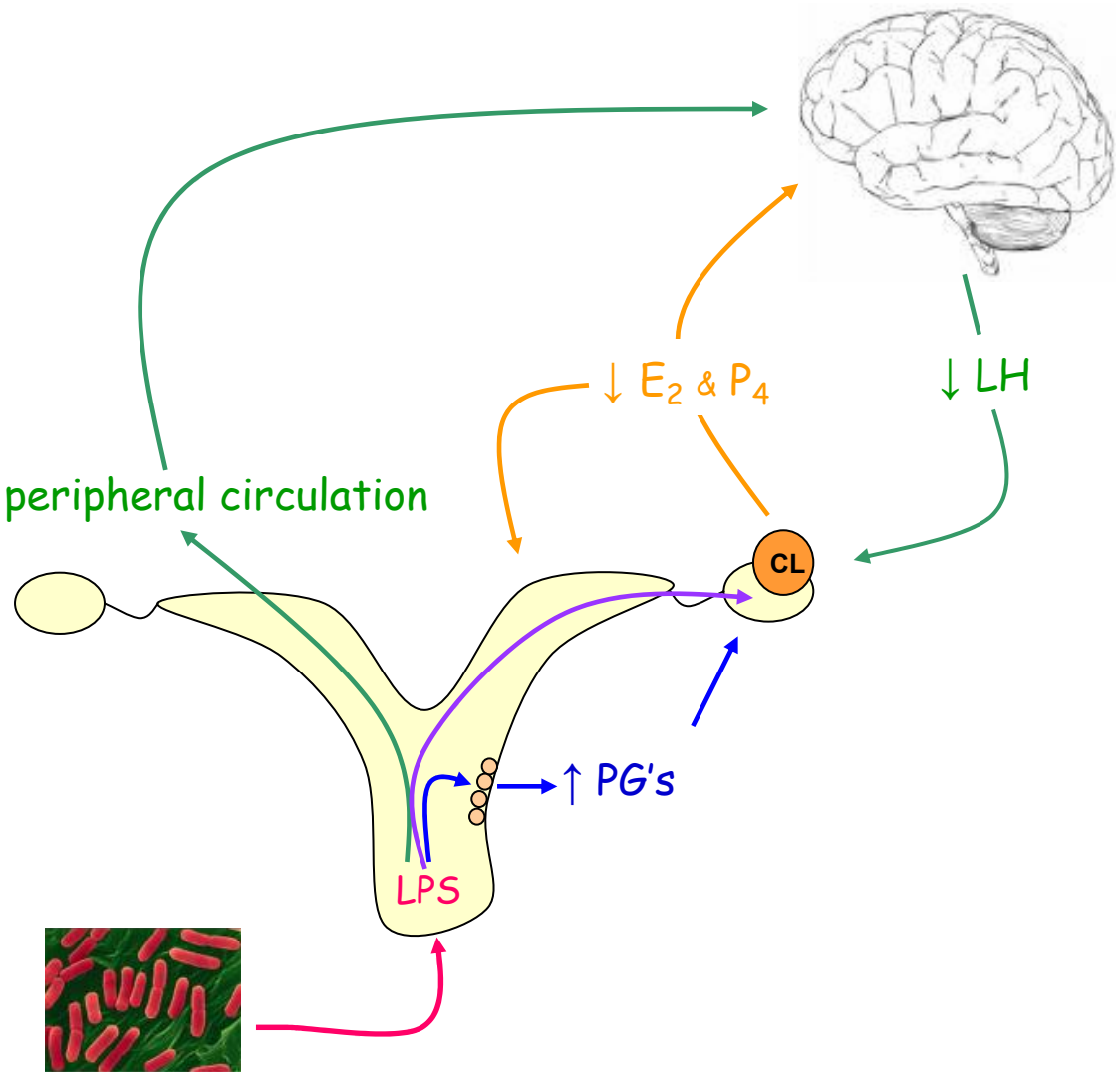




* P<0.05

Herath and Williams *et al*, 2007 (*in press*)

The story so far….



Conclusions

- E.coli is the most commonly isolated uterine pathogen and preceeds infection with other organisms
- LPS is detected in the uterus, peripheral circulation and in follicular fluid of infected cows
- LPS affects the physiological function of uterine and ovarian cells
  - Prostaglandin production affected
  - Aromatase expression and estradiol production down-regulated
- Mechanisms may be partly responsible for the subfertility in postpartum dairy cattle

THANK YOU!