

Understanding the Peritoneal Micro-environment in Endometriosis

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What is the Peritoneum?

- Largest serous membrane in the human body (Figure 1). Two layers:
 - Visceral - encases visceral organs;
 - Parietal - the outer layer, attached to the abdominal and pelvic walls.
- Potential space between the two layers contains peritoneal fluid (volume fluctuates 5-50ml).
- This fluid contains surfactant, immune cells (macrophages, NK cells, T cells, B cells), and inflammatory mediators (cytokines and prostaglandins).

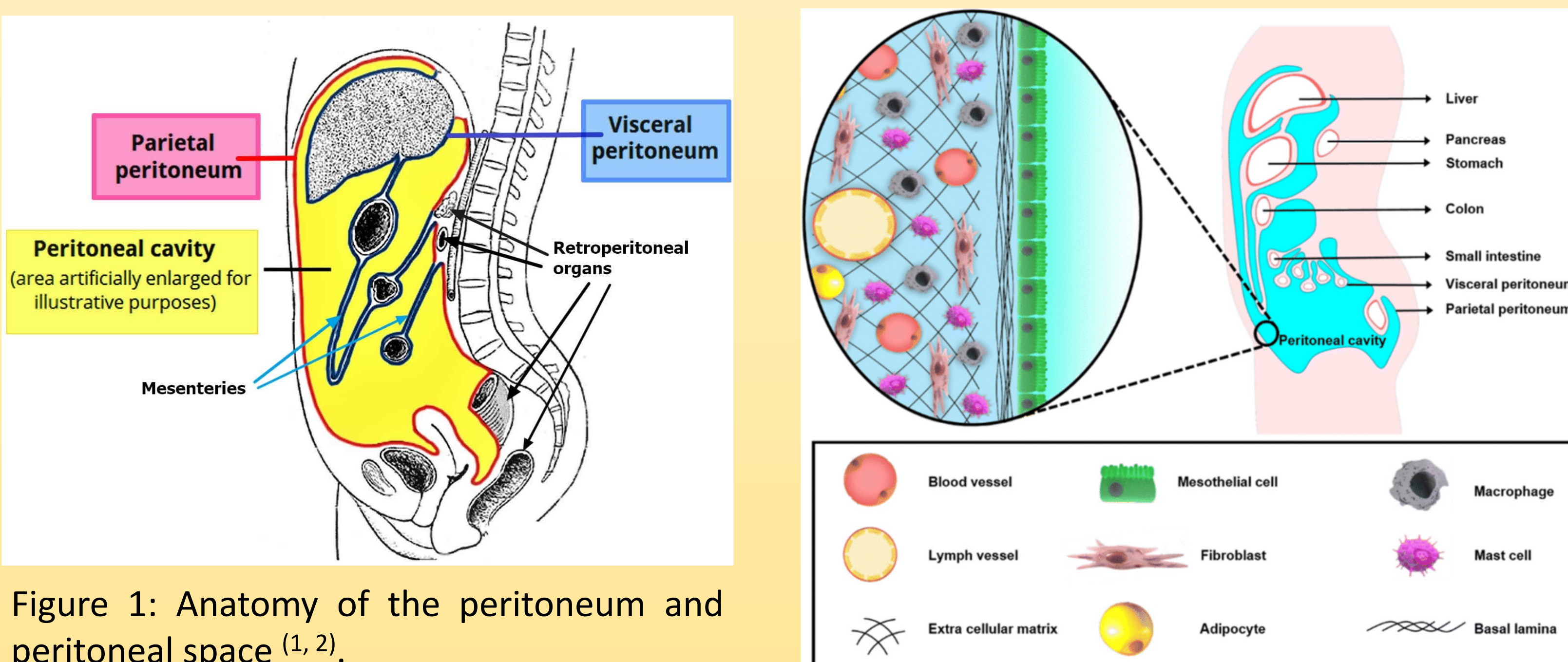


Figure 1: Anatomy of the peritoneum and peritoneal space^(1, 2).

Methods

- Peritoneal fluid (n=16) and washings (n=61) were obtained from 68 women with and without endometriosis at laparoscopy. Care was taken to avoid blood contamination where possible from insertion of the primary port.
- Samples were centrifuged and the supernatant frozen at the time of collection.
- Sample pH, osmolality, and total protein were measured using the accumet® pH Meter, Osmomat and Nanodrop spectrophotometer respectively. Glucose and protease activity were evaluated using colorimetric ELISA kits.
- Data were tested for normality and analyzed using Mann-Whitney U or unpaired t-tests.

References

¹ <https://teachmeanatomy.info/abdomen/areas/peritoneal-cavity/>, ² Ramírez-Pavez *et al.* Int J Mol Sci. 2021 Oct 6;22(19):10792, ³ Alavi *et al.* Pharm Res. 2020 37(6): 119; 1-24., ⁴ Whitaker *et al.* Pilot Feasibility Stud 7, 19 (2021). ⁵ <https://www.endometriosis-india.com/peritoneal-endometriosis/>, ⁶ Dückelmann *et al.* Arch Gynecol Obstet. 2021 Jul;304(1):143-155.

Why is it Important in Endometriosis?

- Endometriosis is a condition that primarily affects the peritoneum³.
- The majority of endometriotic lesions exist within the peritoneal cavity.
- 80% of endometriosis exists as superficial peritoneal disease⁴.
- Excision of disease involves excision of the peritoneum (Figure 2).



Figure 1⁽³⁾ - Superficial endometriosis overlying right uterosacral ligament.
Figure 2⁽³⁾ - Peritoneum of the UV fold after excision.

Results

- Peritoneal fluid and wash pH were consistent between women with and without endometriosis, averaging at 7.9 ± 0.1 and 7.5 ± 0.1 respectively (Figure 3a).
- No significant difference was observed when measuring osmolality between the two groups, ranging from 0.28 to 0.34mOsm/kg (Figure 3b).
- Equally, glucose averaged at $5.4 \pm 3\text{mmol/L}$.
- There was a large inter-subject variation in protein content, with concentrations 6-fold higher in peritoneal fluid compared to washes (Figure 3c).
- Protease activity was below the limit of detection in most samples. Where a reading was detected (n=19), total protease activity ranged from 127-8614ng/ml (Figure 3d). Again, no significant difference was noted between groups.

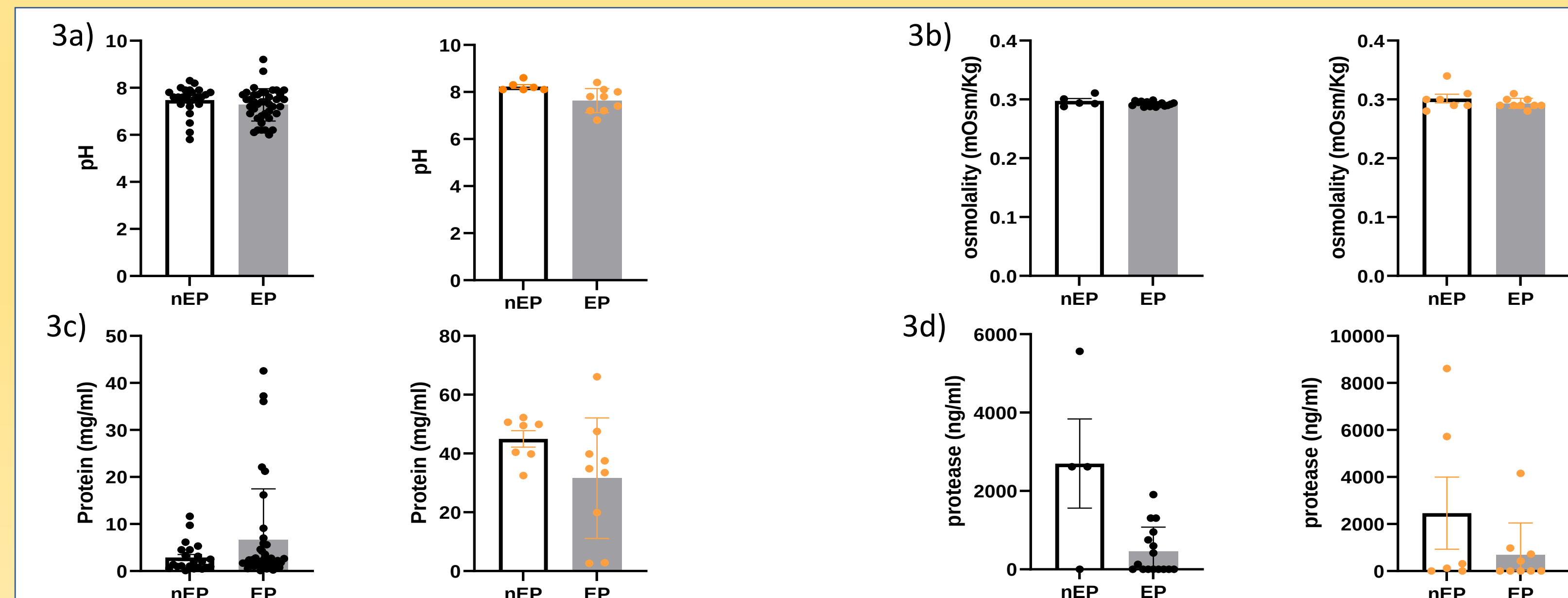


Figure 3: The a) pH, b) osmolality, c) total protein and d) protease activity of peritoneal fluid (●) and peritoneal wash samples (●) from women with (EP) and without (nEP) endometriosis.

Why Do We Need to Know About it?

- An understanding of the conditions of the microenvironment within the peritoneal cavity is vital for considering how drugs may behave if locally administered.
- Also important for considering drug delivery systems.
- Do the same conditions apply for women without disease to those with?
- Does the disease itself change the basic conditions of the peritoneum?



Figure 5 – Endometriosis prior to peritoneal excision⁽⁵⁾. Figure 6 – Appearance following excision⁽⁶⁾.

Conclusions

- The findings show no significant difference in the peritoneal micro-environments of those with and without endometriosis.
- This is positive regarding the development of potential drug treatments that could be delivered intra-peritoneally (e.g. at laparoscopy).
- Drug treatments can be developed and considered for use universally, regardless of 'stage of disease' or even the presence of absence of endometriosis.
- Drug treatments could be trialled for those with pelvic pain, without confirmed diagnosis of endometriosis.
- The finding of low protease is also positive when considering drug delivery systems, particularly if a biodegradable hydrogel is used, as this is likely to be broken down slowly and universally.

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