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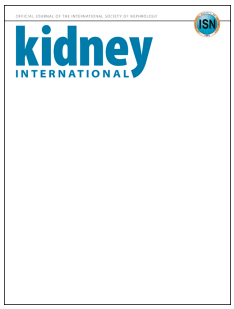

Measurement of innate immune response biomarkers in peritoneal dialysis effluent using a rapid diagnostic point-of-care device as a diagnostic indicator of peritonitis.

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Measurement of innate immune response biomarkers in peritoneal dialysis effluent using a rapid diagnostic point-of-care device as a diagnostic indicator of peritonitis.

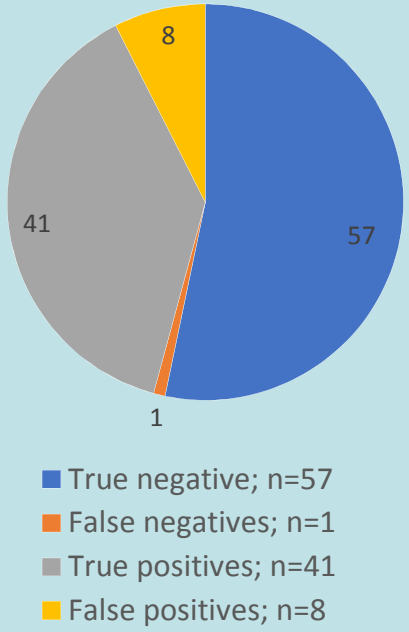
Problem

Peritonitis is a significant complication of PD. A point of care test which reliably diagnoses or excludes peritonitis would improve patient care.

Method

The PERiPLEX® device uses a lateral flow assay to detect MMP-8 and IL-6 in dialysate within minutes. We investigated the test characteristics of this device in 107 PD patients presenting with a requirement to diagnose or exclude peritonitis.

Results



The PERiPLEX® test

- had a high negative predictive value (98%).
- performed better than usual clinical signs, excluding peritonitis in 27 of 74 patients presenting with abdominal pain or a cloudy bag.
- required "number needed to test" of 6 to improve patient management compared to clinical assessment.
- had 8 false positives requiring additional testing

CONCLUSION:

The PERiPLEX® test could have significant clinical utility for diagnosis of peritonitis.

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Measurement of innate immune response biomarkers in peritoneal dialysis effluent using a rapid diagnostic point-of-care device as a diagnostic indicator of peritonitis.

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Abstract

Peritonitis is the commonest complication of peritoneal dialysis and a major reason for treatment failure. Current diagnosis is based on clinical symptoms, cloudy effluent and a dialysate white cell count (over 100 cells/μl). A rapid point-of-care diagnostic test would accelerate diagnosis and potentially improve outcomes from infection. Here, in a clinical audit project, we used PERiPLEX®, a point-of-care device which detects when levels of matrix metalloproteinase-8 and interleukin-6 are elevated above a threshold within minutes in dialysis effluent, to assess whether it could confirm or exclude peritonitis in 107 patients undergoing peritoneal dialysis. Mean patient age was 64.6 years with a median duration of peritoneal dialysis of 3.5 months (interquartile range 6.4 – 31.5 months). Presence of peritonitis was confirmed by clinical criteria. There were 49 positive tests of which 41 patients had peritonitis, three had other causes of intra-peritoneal inflammation, three had severe urosepsis and two patients required no treatment. Fifty eight tests were negative with one patient having a false negative result. The positive predictive value of the test was 83.7% (95% confidence interval 72.8 – 90.8) and the negative predictive value was 98.3% (89.1 – 99.8). Sensitivity and specificity were 97.6% (87.4 – 99.9) and 87.7% (77.2 – 94.5) respectively. Thus, PERiPLEX® could be used as a rapid point-of-care test that can aid the diagnosis or exclusion of peritonitis with a high negative predictive value.

Keywords

Peritoneal dialysis, peritonitis, biomarkers, infection diagnosis, Point-of-care (POC), PERiPLEX®

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Introduction

Peritonitis remains the major cause of peritoneal dialysis (PD) technique failure and transfer to haemodialysis[1] or adverse outcomes[2]. When PD peritonitis is suspected, making the correct diagnosis quickly is important to permit rapid initiation of appropriate antibiotic treatment and improve outcomes[3]. Some patients present with clinically obvious features such as cloudy effluent dialysate and abdominal pain[4] but the diagnosis of infection is not always immediately clear. Some patients present with a cloudy bag and minimal symptoms, and there are causes other than infection for hazy fluid. Patients using automated PD (APD) may have their dialysis effluent drained directly, so be unaware of its appearance. Often, a standard two or four-hour dwell of PD dialysate is required[5]. The drained dialysate is sent for formal cell count to confirm or exclude peritonitis[4]. Excluding peritonitis rapidly in patients with a cloudy bag who are clinically well would allow these patients to be reassured and discharged home. Other PD patients present feeling generally unwell and their dialysis effluent is analysed as part of a wider diagnostic screen. A secure diagnosis of peritonitis in this group would allow the earlier initiation of intra-peritoneal antibiotics, while rapid exclusion of peritonitis would focus management on obtaining an alternative diagnosis.

The PERiPLEX® device was developed by Mologic Inc. (Thurleigh, Bedfordshire, UK) as part of a National Institute for Health Research (NIHR) Invention for Innovation (i4i) grant, in collaboration with Cardiff University. It uses the unique specificity of the immune response to detect infection[6]. PERiPLEX® is a CE marked, single use, point of care (POC) device designed to be used by health professionals or patients. PERiPLEX® detects matrix metalloproteinase-8 (MMP-8) and interleukin 6 (IL-6) using lateral flow technology. MMP-8 is produced by activated neutrophils during acute inflammation and facilitates recruitment and trafficking of inflammatory cells[7]. MMP-8 detection during acute inflammation has been explored in peri-implant infections[8], periodontal inflammation[9] and intra-peritoneal bacterial infection[10]. IL-6 is present in the effluent dialysate of PD patients[11] and is a key regulator of acute peritoneal inflammation in response to infection[12]. Although IL-6 is detectable in the effluent dialysate of healthy PD patients, concentrations are significantly elevated early during an episode of peritonitis[13].

This clinical audit project assessed PERiPLEX® as a means of rapidly detecting/excluding infection in a “real-world” clinical environment using 107 dialysis effluent samples collected in satellite unit PD clinics, the emergency department and the inpatient wards.

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Results

A single fresh dialysis effluent sample was collected from 107 different PD patients between November 2017 and October 2019. Patients presented directly to the PD nurses or were referred with suspected PD peritonitis, or to exclude PD peritonitis. Mean patient age was 64.6 (SD 15.3) years, median duration of PD was 13.3 (inter-quartile range 6.3 – 33.5) months. 53% of patients were male and 34% diabetic. All patients used standard lactate-containing dextrose dialysis solutions (Baxter Healthcare, Deerfield, USA). Icodextrin (7.5%) (Baxter Healthcare, Deerfield, USA) was used in 75% of the patients. Table 1 reports the clinical characteristics of the patients tested.

Table 1: Clinical characteristics of patients at presentation

	n	**%**
Abdominal pain:		
Severe abdominal pain	6	6
Moderate abdominal pain	26	24
Mild abdominal pain	29	27
No abdominal pain	46	43
Clinical suspicion of peritonitis:		
High	31	29
Moderate	24	22
Low	52	49
Main indication for testing:		
Cloudy dialysate bag	40	37
Septic screen	32	30
Abdominal pain	20	19
Line contamination / exit site infection	6	6
Other / indication not recorded	9	8
Sample obtained from a dwell of 4 hours	92	86

The results are summarised in Figure 1.

Microbiology results from 42 patients treated for peritonitis are shown in Table 2:

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Table 2: Microbiology culture results from patients treated for peritonitis

Organism	Number of cases
Staphylococcus epidermidis	6
Other coagulase negative staphylococci	7
Staphylococcus aureus	2
Klebsiella species	2
Pseudomonas species	4
Enterococcus species	1
Enterobacter species	1
Escherichia coli	1
Stenotrophomonas maltophilia	1
Ochrobactrum anthropi	1
Actinomyces naeslundii	1
Corynebacterium species	3
Streptococcus oralis	1
Gordonia species	1
Culture negative	10

Although 46 patients met the International Society of Peritoneal Dialysis (ISPD) definition of PD peritonitis on laboratory grounds (dialysate white cell count (WCC) >100 cells/µL), 5 patients did not clinically have peritonitis, were not prescribed antibiotics and did not subsequently develop peritonitis or have positive microbiology cultures. In 3 of these 5 patients the PERiPLEX® was correctly negative: one patient had not performed PD for some days (WCC 405 cells/µL), one had a chyle leak (WCC 470 cells/µL) and the third had a WCC of 210 cells/µL without clinical peritonitis. In 2 of these 5 patients the PERiPLEX® was falsely positive; one had an infected lymphocele and the other urosepsis.

One further patient with a WCC of 54 cells/µL had a clinical diagnosis of peritonitis (and was PERiPLEX® positive).

The relationship between effluent WCC (cells/µL) and PERiPLEX® results is shown in Figure 2 and Figure 3 examines the relationship between the microbiology culture and PERiPLEX® results. As expected, some patients with clinical PD peritonitis were culture

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negative (the ISPD standard is < 20% of cases)[4]. Both PD WCC and PERiPLEX® misclassified some cases; a PD WCC of >100 cells/µL had a lower rate of false positive results, although the PERiPLEX® has the significant advantage of providing information more rapidly.

Table 3 summarises patients in whom the PERiPLEX® result was non-concordant with the ultimate clinical diagnosis:

Table 3: Characteristics of the patients with non-concordant PERiPLEX® results

False positive results:			
Clinical Diagnosis	**Dialysate WCC (cells/µL)**	**Cytology**	**Possible explanation**
Urosepsis	104	Macrophages and mesothelial cells	Systemic sepsis with systemically generated mediators of inflammation crossing the peritoneum
Urosepsis	86	N/A	
Urosepsis	36	Numerous leukocytes	
Gallstone ileus	56	Numerous leukocytes	Local, intra-peritoneal inflammation with local generation of mediators of inflammation
C. difficile diarrhoea	25	Predominantly leukocytes	
Infected lymphocele (on CT and at later surgery)	690	N/A	
Tunnel infection with abscess	44	Predominantly leukocytes	Intra-peritoneal inflammatory response
Streptococcus oralis cultured but no clinical symptoms of peritonitis	15	Mixture of leukocytes and macrophages	Transient dialysate bacteria?
False negative results:			
Clinical Diagnosis	**Dialysate WCC (cells/µL)**	**Cytology**	**Possible explanation**

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Previously treated episode of PD peritonitis	310	Predominant lymphocytosis; microbiology cultures and 16S rDNA PCR negative	Leukocytes present after treatment did not produce the mediators required to generate a positive result

Compared to the combination of abdominal pain or cloudy bag (presenting symptoms specified in ISPD guidelines as suggestive of peritonitis[4]), PERiPLEX® has substantially better test performance (Table 4). Of 28 patients with abdominal pain or a cloudy bag who were PERiPLEX® negative, only one had PD peritonitis as the final diagnosis (Figure 4).

Clinical judgement also determines initial management of patients with suspected peritonitis. Importantly, PERiPLEX® was positive and correctly diagnosed peritonitis in 5 of 50 (10%) patients where the clinicians had thought peritonitis unlikely, and excluded peritonitis in 13 of 57 (22.8%) patients where clinical suspicion had been moderate or high. The use of PERiPLEX® might therefore have changed management in at least 18 of the 107 presentations (16.8%), giving a "number needed to test" of six.

The PERiPLEX® had high negative and positive predictive values (Table 4). The likelihood ratios indicate that a positive test has a strong probability of indicating PD peritonitis. Equally, a negative test has a very high probability of excluding PD peritonitis, resulting in a very strongly positive diagnostic odds ratio of 292.

Table 4: Summary of test characteristics

	PERiPLEX % (95% confidence intervals)	Abdominal pain or cloudy bag % (95% confidence intervals)	PD WCC > 100 cells/µL % (95% confidence intervals)	Positive microbiology culture % (95% confidence intervals)
Positive predictive value	83.7 (72.8 – 90.8)	55.1 (49.3 – 61.3)	91.3 (80.2 – 96.5)	97 (82 – 99.6)
Negative predictive value	98.3 (89.1 – 99.8)	97 (82 – 100)	93.8 (84.7 – 98.3)	86.3 (78.6 – 91.6)

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Sensitivity	97.6 (87.4 – 99.9)	97.6 (97.4 – 99.9)	97.6 (87.7 – 99.9)	76.2 (60.6 – 88)
Specificity	87.7 (77.2 – 94.5)	49.2 (36.6 – 61.9)	93.8 (84.7 – 98.3)	98.4 (91.6 – 100)
Positive likelihood ratio	7.93 (4.14 – 15.2)	1.92 (1.51 – 2.45)	15.63 (6.04 – 40.4)	48.8 (6.92 – 343.4)
Negative likelihood ratio	0.03 (0 – 0.19)	0.05 (0.01 – 0.34)	0.02 (0 – 0.17)	0.24 (0.14 – 0.42)
Accuracy	91.6 (84.6 – 96.1)	68.2 (58.5 – 76.9)	95.3 (89.4 – 98.5)	89.6 (82.2 – 94.7)

Discussion

Peritonitis is the most important complication of PD therapy and accounts for the majority of technique failures[1,2]. Traditionally, the diagnosis of infection is based on clinical symptoms, a raised PD effluent leukocyte count (cloudy bag) and eventually microbiological culture results. To increase the yield from microbiological cultures ISPD guidelines recommend a minimum 2 hour dwell of fresh dialysate[4]. Many PD patients use APD cyclers with shorter dwell times, and the need for an additional dwell delays diagnosis and management. A simple POC test that can quickly support or refute the diagnosis of PD peritonitis and avoid delay in initiating antibiotic treatment could improve patient outcomes[3].

Tests used to diagnose serious conditions like peritonitis must have favourable test characteristics. We found a sensitivity of 97.6% and specificity of 87.7%, with a diagnostic accuracy of 92%. PERiPLEX® had high positive and negative predictive values. These tests may be adjusted to a prevalence of 50%[14]; in our study 46% of tests were positive with a peritonitis prevalence of 39%. The level of clinical suspicion (pre-test probability) was evenly distributed and represents a “real-life” sample of patients. In clinical practice PD effluent is often tested to exclude peritonitis when the cause of inflammation is suspected to lie elsewhere; similarly, some patients with hazy fluid alone appear at low risk of peritonitis, but clinicians do not wish to miss this diagnosis. Given the high negative predictive value of 98.3% and negative likelihood ratio of 0.03[15], if the test is negative clinically well patients can be reassured and discharged. In a symptomatic PD patient, a negative PERiPLEX® result should prompt investigation for an alternative diagnosis.

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False positive results

There were 8 positive tests in patients without PD peritonitis. A false positive PERiPLEX® result arises from an alternative cause of inflammatory mediators in the dialysate. MMP-8 is a mediator of the response to intra-abdominal sepsis[10]. Plasma IL-6 rises with systemic inflammation and IL-6 transfers across the peritoneal membrane into the dialysate[16,17]. Patients with false positive PERiPLEX® results and systemic sepsis are likely to have transfer of inflammatory mediators from the circulation and those with intra-abdominal inflammation may have locally generated mediators. Additional markers in future POC devices might increase specificity and positive predictive value by detecting the consequences of more complex systemic activation.

A false positive PERiPLEX® result could lead to the inappropriate institution of antibiotics; however, in 5 of the 8 patients with false positive results antibiotic therapy was warranted to treat other infectious conditions. Further testing can be undertaken and antibiotic treatment refined or stopped as clinically appropriate.

False negative results

The only false negative case followed recent treatment of PD peritonitis. The elevated PD WCC (310 cells/µL) was predominantly a lymphocytosis. The PERiPLEX® is designed to detect the products of activated neutrophils and a lymphocytic infiltrate may not generate the necessary biomarker profile (particularly MMP-8).

Could the PERiPLEX® change clinical management?

Seventy four patients presented with abdominal pain and/or a cloudy bag. Of these, PERiPLEX® was appropriately negative in 27 patients, with one false negative result. Management in these 27 patients could have concentrated on finding alternative diagnoses.

While experienced clinicians synthesise more factors than the presence / absence of abdominal pain or cloudy fluid when deciding initial management, using PERiPLEX® could still improve patient care. Eight patients with low initial clinical suspicion for PD peritonitis had a positive PERiPLEX®; 5 were subsequently treated for peritonitis. PERiPLEX® could modify the index of clinical suspicion resulting in earlier antibiotic initiation.

Where clinical suspicion was moderate or high, 13 patients had a negative PERiPLEX® result, none of whom subsequently had evidence of peritonitis. These patients could have been discharged home more quickly, on the basis of the PERiPLEX® result alone. Intra-peritoneal antibiotics would be avoided and good antibiotic stewardship facilitated.

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Three patients with a negative PERiPLEX® and negative fluid cultures had a dialysate WCC > 100 cells/μL. None of these patients required treatment for peritonitis. A negative PERiPLEX® would provide evidence that antibiotics are not immediately required, pending results of microbiological cultures.

Recent survey data indicates that peritonitis remains the major concern and feared complication for patients using PD therapy[18]. A test which permits rapid reassurance that peritonitis is very unlikely has the potential to reduce this significant patient anxiety.

Areas for further investigation

IL-6 concentrations in dialysate remain high for weeks after PD peritonitis[19], and recurrent episodes of peritonitis disrupt normal peritoneal cytokine patterns over a prolonged period[20]. Further studies are required to determine whether the IL-6 component of PERiPLEX® is a reliable marker for detecting recurrent peritonitis.

Studies suggest that peritoneal IL-6 does not differ between those using dual chamber PD dialysates compared to conventional dialysates[21], although IL-6 may be greater in those prescribed Icodextrin[22]. However, as 75% (80) of our samples were taken from patients who used Icodextrin it does not appear that this adversely affects the utility of PERiPLEX® testing. The number of positive tests in Icodextrin users was 39 (including 4 false positives) with 41 negative tests and results in this group reflect those in the cohort as a whole.

There are a number of IL-6 phenotypes[23]. We did not characterise our patients as high or low IL-6 producers, and are unable to comment on whether IL-6 phenotypes may affect test performance[23]. MMP-8 should in theory only be produced in early inflammation by activated PMN and might be a superior indicator of the presence or absence of recurrent infection[6,24,25], but further work is needed to explore results of testing with PERiPLEX® in this clinical situation.

The number of markers used in a test designed to provide a “yes/no” answer is limited by the need for a simple, cost-effective device. Additional markers might provide a clinically relevant improvement in test characteristics, or might categorise the peritoneal inflammatory response as due to, for example, a Gram negative organism,[26] but at the expense of increased cost.

Follow up studies should include regular PERiPLEX® testing to examine its day-to-day utility in detecting infection, its relationship to symptoms and its usefulness in predicting recovery, response to antibiotic therapy or relapse.

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Summary

In 107 samples from PD patients who had suspected PD peritonitis, or in whom the diagnosis of PD peritonitis needed to be excluded, the PERiPLEX® had a positive predictive value of 84% and a negative predictive value of 98% for PD peritonitis, diagnosed clinically on the basis of PD WCC >100 cells/μL, presenting symptoms, microbiology results and evolution of the clinical episode. PERiPLEX® testing provides immediate information at initial assessment and correctly excluded peritonitis in 27 of 74 patients presenting with either abdominal pain or a cloudy bag. When assessed against the initial level of clinical suspicion for peritonitis, the test might have improved the management of 18 of 107 patients, with a number needed to test of six. Responding to the PERiPLEX® result rather than waiting for confirmatory results from a four-hour dwell would have expedited care. We therefore suggest the PERiPLEX® may have significant clinical utility, with the caveat that as with any test the results must be interpreted in the context of the clinical presentation and appropriate follow up instituted.

Methods

Study participants and eligibility:

All PD patients with a cloudy PD effluent dialysate or abdominal symptoms, or in whom the attending clinicians suspected peritonitis or wished to exclude peritonitis, were tested. There were no exclusion criteria, but as PD nurses performed all PERiPLEX® tests, patients presenting out of hours were not included and the tested group is a convenience sample. Patients could present to our main hospital or any of our satellite PD clinics. We did not specify duration of sample dwell, in order to include shorter – dwell samples from patients using APD (as biomarker levels might be expected to be lower in this group[27]). In total 107 tests were performed on 107 patients. Dialysate was tested as soon as it was drained – before cell counts or culture results were available.

Data collection:

Data were collected between November 2017 and October 2019. We recorded the clinical indication for testing, the presence or absence of abdominal pain, pyrexia and cloudy dialysate. The PD nurses documented their pre-test clinical suspicion of PD peritonitis. Data were recorded on the dialysate WCC and the final microbiological culture results.

PERiPLEX®:

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The PERiPLEX® device detects MMP-8 and IL-6 using lateral flow technology; for guidance on use see https://mologic.co.uk/our-core-markets/infection-and-infectious-disease/periplex. The wick is dipped into a sample of dialysate. After five minutes, a control line in the 'read' window indicates the test has worked correctly. If either result line is visible the test is positive (Figure 5). The test reader was the PD nurse and was aware of patient's clinical condition; the test was read prior to availability of dialysate WCC and culture results.

The PERiPLEX® device was developed through a NIHR i4i collaboration between Mologic Inc. and Cardiff University, registered on the UK Clinical Research Network Study Portfolio (reference number #11838 "Patient immune responses to infection in PD (PERIT-PD)") and approved by the South East Wales Local Ethics Committee (04WSE04/27). Briefly, samples from 66 peritonitis patients and 55 stable patients were obtained from the Cardiff PD patient cohort and via the Tropical Pathology and Infectious Disease Association (study ethics approved by the TPaIDA-IPTEI Institutional Ethics Committee). IL-6 levels in cell-free peritoneal effluent were analyzed on a SECTOR Imager 6000 (Meso Scale Discovery) and with a conventional ELISA kit (Catalogue Number DY206, R&D Systems). MMP-8 was measured using a conventional ELISA kit (Catalogue Number DY908, R&D Systems). The samples were then tested with the PERiPLEX® lateral flow assay and the output quantified using the Cube-Reader (opTricon, Germany); levels were in concordance with those obtained using the reference assays. Biomarker levels in patients with and without peritonitis differed significantly ($p < 0.0001$, Mann-Whitney test). Visible result lines in the PERiPLEX® are generated only when levels of MMP-8 and IL-6 are above those in the stable population, with cut-off points of 0.126 ng/mL for IL-6 and 1.183 ng/mL for MMP-8. The area under the ROC curve was 0.966 (0.928 – 1.000) for IL-6 and 0.988 (0.974 – 1.000) for MMP-8 (determined using GraphPad Prism 6). Figure 6 shows the distribution of IL-6 and MMP-8 levels with the PERiPLEX® threshold values marked.

Further Diagnostics:

Dialysate was sent for Gram stain, WCC and microbiological culture using both blood agar plates and BD BACTEC™ (Becton Dickinson Diagnostic Instrument Systems, Sparks, USA). Dialysate was also sent with EDTA to maximise the percentage of samples suitable for cell count. The majority of samples were also sent for cytology cytospin analysis. Recognising that none of these tests alone are sufficient to make or refute a diagnosis of PD peritonitis, the reference standard therefore was whether the clinical team determined the

patient had peritonitis, based on the cell count, cultures, clinical findings and evolution of disease.

Governance:

This was a clinical service evaluation. PERiPLEX® testing was introduced into routine practice, with PERiPLEX® devices placed with peritonitis packs on the wards and in each satellite unit PD clinic. Clinicians were instructed not to alter clinical management based on PERiPLEX® result. Our service development audit complied with the United Kingdom (UK) National Health Service Health Research Authority guidelines for clinical audit and service development (https://www.hra.nhs.uk), and was registered with the UCL Department of Nephrology, Royal Free Hospital. All patient data were anonymised. The audit complied with UK National Institute for Clinical Excellence (NICE) best practices; www.nice.org.uk/media/796/23/bestpracticeclinicalaudit.pdf.

Statistical analysis:

This clinical audit project was the first use of the PERiPLEX® in the clinical environment. The data therefore represent a convenience sample with no prior calculation of sample size.

Data to be collected were determined prior to initiating the study. There were no missing PERiPLEX® results. All but one patient had results of microbiology cultures and all had a PD WCC result. We calculated the test sensitivity, specificity, positive and negative predictive values and the test likelihood ratios.

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Disclosures

AD, CG, SM, SS, ME and SG – no conflicts of interest

GP is employed by and NT receives honoraria from Mologic Inc

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PERiPLEX® kits were supplied by Mologic free of charge.

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Figure Legends

Figure 1: STARD diagram of patient results

Figure 2: PERiPLEX® results and PD WCC

Figure 3: PERiPLEX® results and microbiology culture results

Figure 4: PERiPLEX® results and peritonitis symptoms

Figure 5: Picture of PERiPLEX® test

Figure 6: Levels of IL-6 and MMP-8 in PD patients with acute peritonitis and control patients determined using PERiPLEX® and quantified using the Cube-Reader (opTricon, Germany). Each data point represents a patient; solid lines with error bars indicate geometric means and 95% confidence intervals. Dashed lines depict PERiPLEX® cut-off values of 0.126 ng/ml for IL-6 and 1.183 ng/ml for MMP-8

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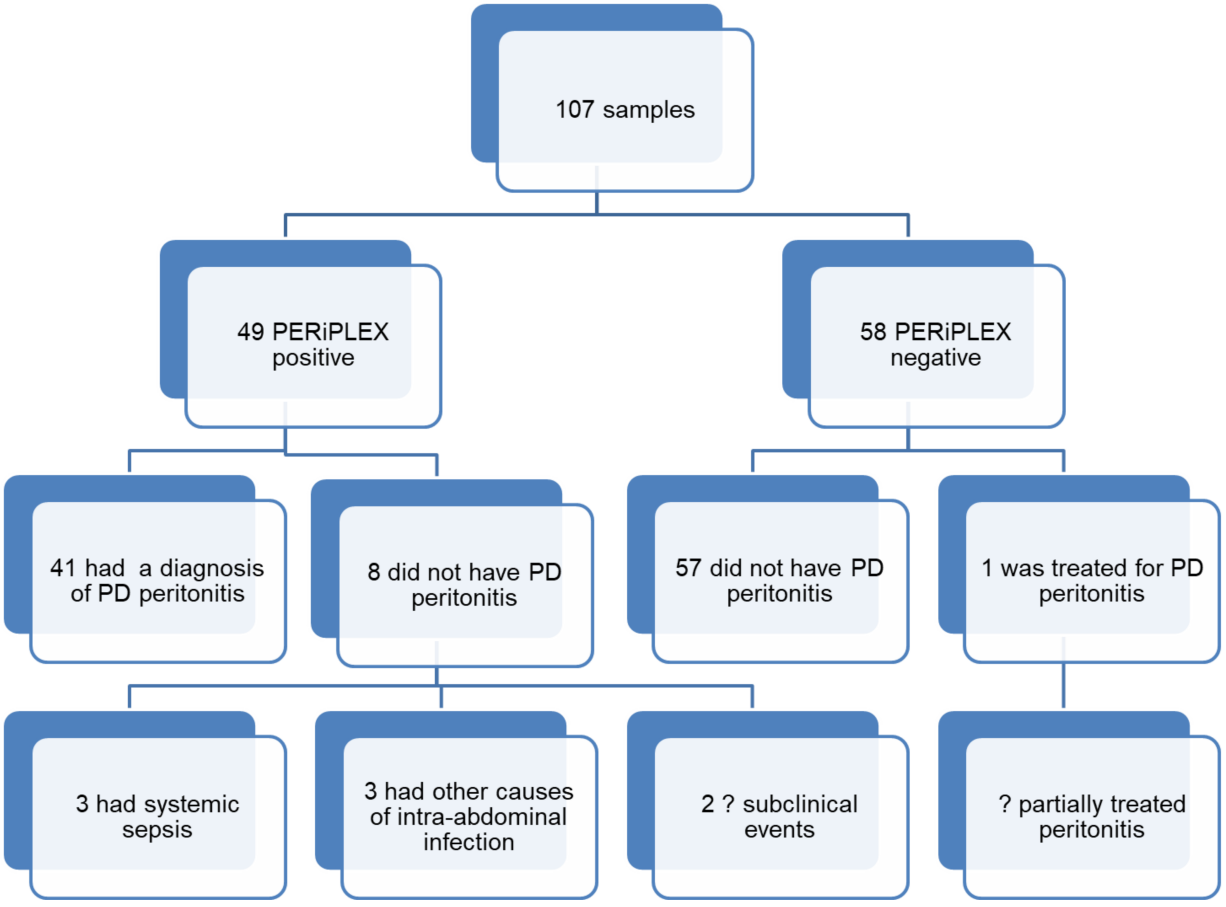
107 samples
49 PERiPLEX positive
58 PERiPLEX negative
41 had a diagnosis of PD peritonitis
8 did not have PD peritonitis
57 did not have PD peritonitis
1 was treated for PD peritonitis
3 had systemic sepsis
3 had other causes of intra-abdominal infection
2 ? subclinical events
? partially treated peritonitis

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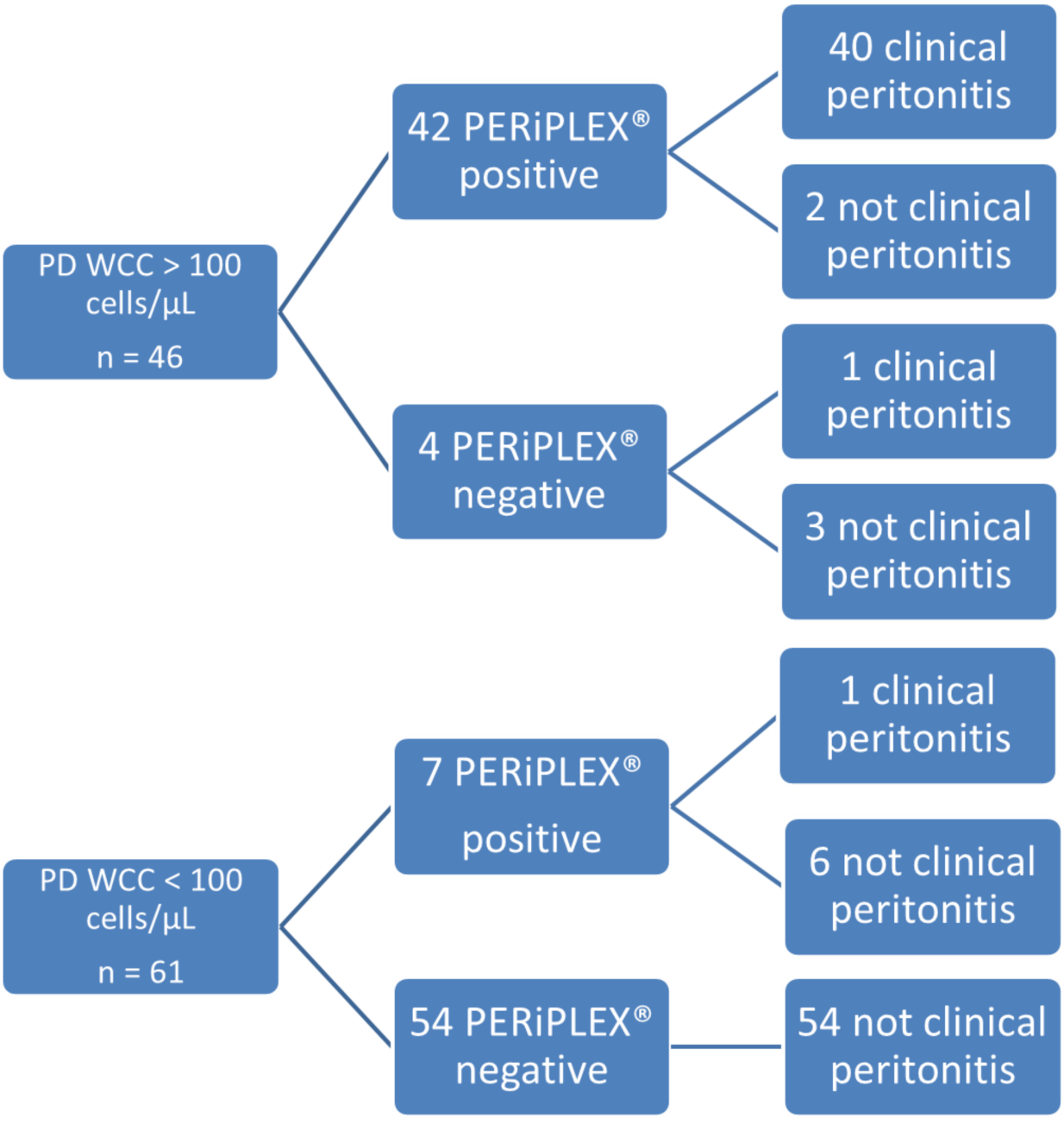
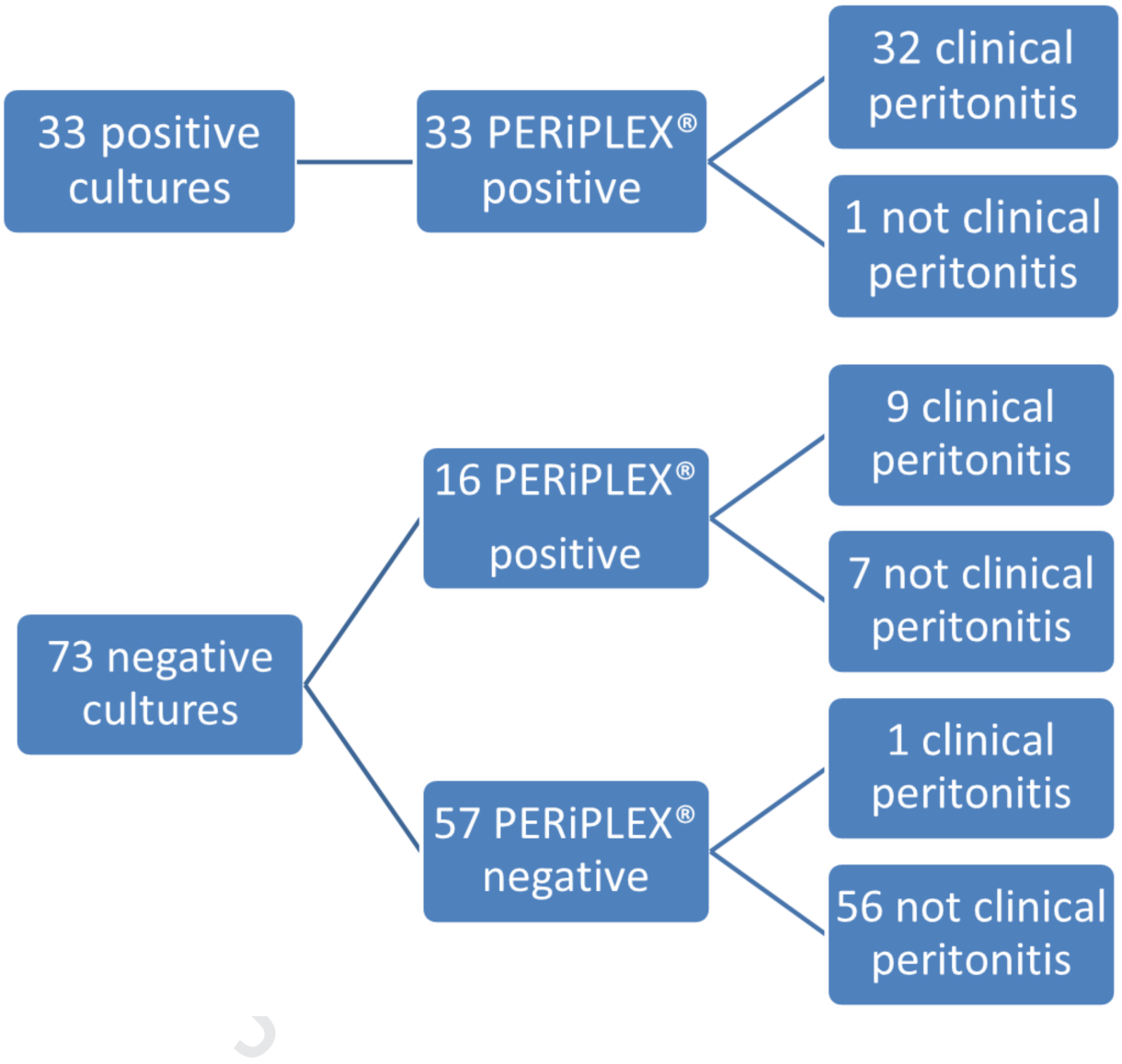
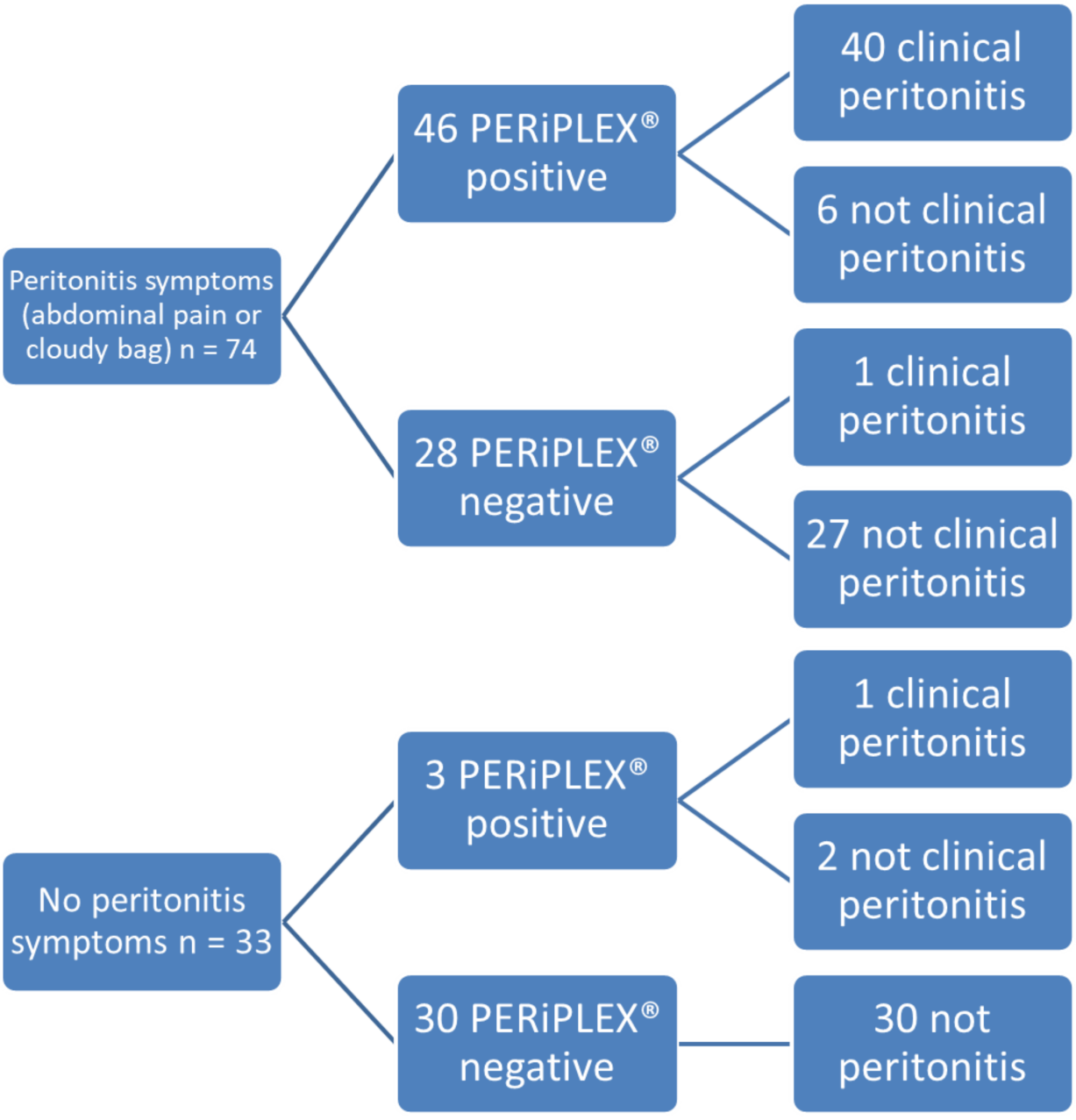
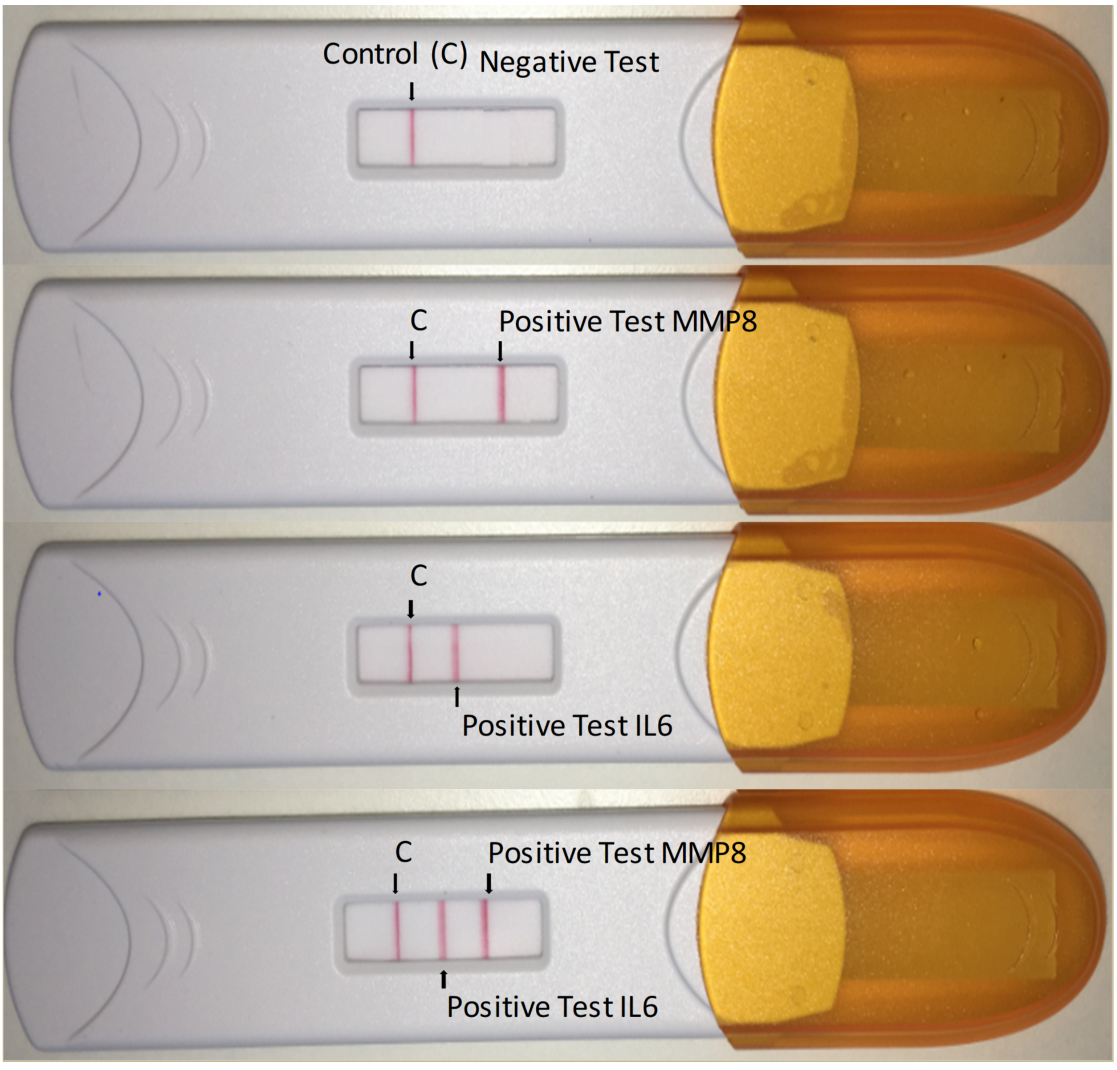
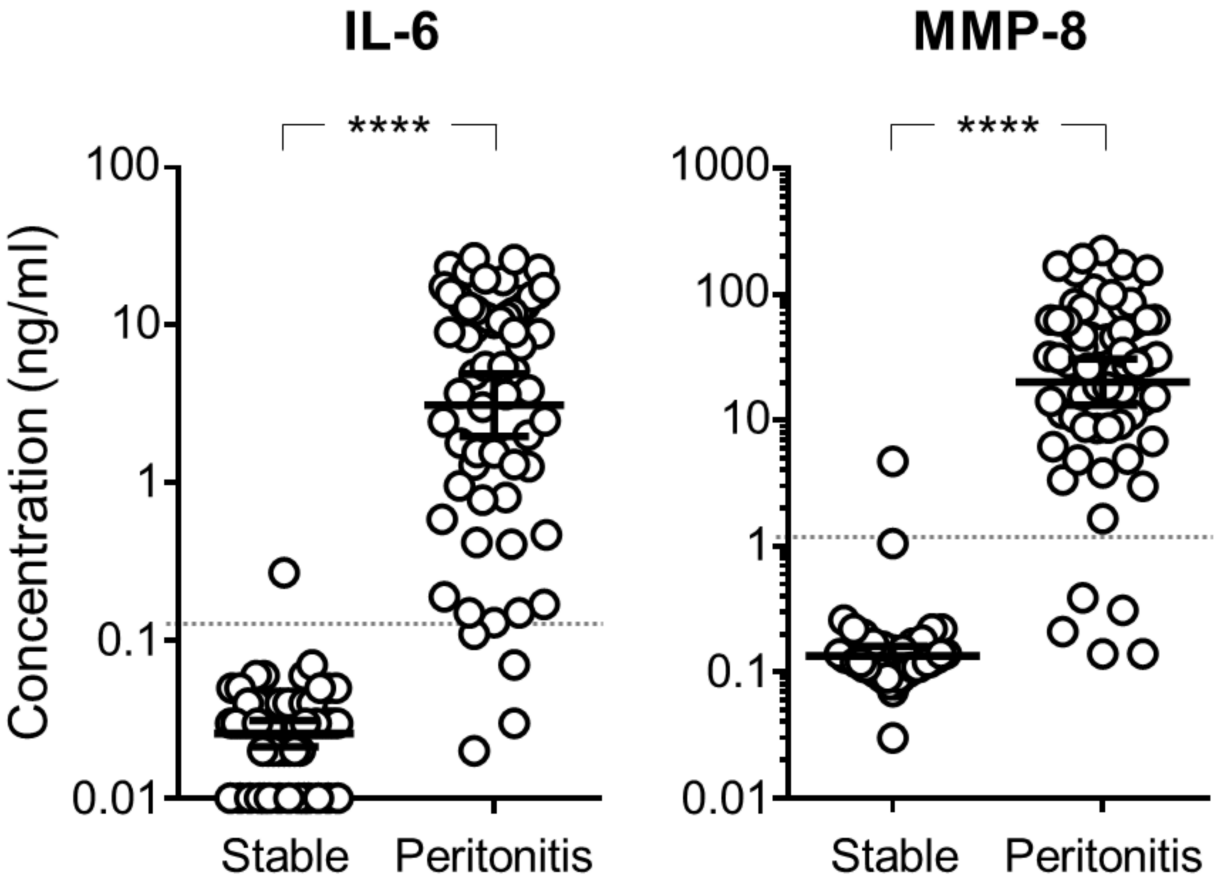

PD WCC > 100 cells/µL
n = 46
42 PERiPLEX® positive
40 clinical peritonitis
2 not clinical peritonitis
4 PERiPLEX® negative
1 clinical peritonitis
3 not clinical peritonitis
PD WCC < 100 cells/µL
n = 61
7 PERiPLEX® positive
1 clinical peritonitis
6 not clinical peritonitis
54 PERiPLEX® negative
54 not clinical peritonitis


33 positive cultures
33 PERiPLEX® positive
32 clinical peritonitis
1 not clinical peritonitis
73 negative cultures
16 PERiPLEX® positive
9 clinical peritonitis
7 not clinical peritonitis
57 PERiPLEX® negative
1 clinical peritonitis
56 not clinical peritonitis


Peritonitis symptoms (abdominal pain or cloudy bag) n = 74
46 PERiPLEX® positive
40 clinical peritonitis
6 not clinical peritonitis
28 PERiPLEX® negative
1 clinical peritonitis
27 not clinical peritonitis
No peritonitis symptoms n = 33
3 PERiPLEX® positive
1 clinical peritonitis
2 not clinical peritonitis
30 PERiPLEX® negative
30 not peritonitis


Control (C) Negative Test
C
Positive Test MMP8
C
Positive Test IL6
C
Positive Test MMP8
Positive Test IL6


IL-6
MMP-8
****
****
Concentration (ng/ml)
100
10
1
0.1
0.01
1000
100
10
1
0.1
0.01
Stable
Peritonitis
Stable
Peritonitis

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