

Contaminated Samples

What it means and a short summary of key issues.

The issue

The serious clinical consequences of a contaminated sample (in this case a urine sample) and the need to avoid contamination of samples is an absolute requirement for all clinicians. Every professional body (pathologist, microbiologist, Doctor etc) guidance on standard procedures of operations (SOP's) recommends or mandates avoiding contamination. Before dealing with what the clinician does with a report back from the lab which indicates contamination i.e. a non-pathology reading i.e. a contaminated sample result, the clinician should have ensured that certain requirements regarding its collection are met. Or if not having dealt with the contaminated sample raise the issues to try and ensure a reduction in contamination. So it's important as a 'prep' to examine these issues?

Common mandatory issues

Two key mandatory issues are common: Use of appropriate equipment into which the sample is collected and its sterility assurance and secondly the method of collection and transportation.

EU: This is seen for example in the EU, in the overarching regulation on all IVD (in-vitro diagnostic devices) Directive 98/79/EC (IVD), under which sample bottles fall, requires (Annex I B 2.1 which regulates "Infection and microbial contamination") that "The devices and their manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the user or other persons. The design must allow easy handling and, where necessary, reduce as far as possible contamination of and leakage from, the device during use and, in the case of specimen receptacles, the risk

USA: In the USA aside from Federal and state laws, The College of American Pathologists 'Laboratory General Checklist' sets out standard compliance requirements for accreditation. GEN. 40942 Phase I states: "...the Laboratory should evaluate its specimen containers to ensure that they do not contribute to analytic interference in the assays to be performed." Any device (such as the Whiz Cleancatch) that reduces contamination is therefore to be used over those that have high contamination rates. *GEN.20348 Phase II* states that *Preanalytic (i.e., pre-examination) variables include all steps in the process prior to the analytic phase of testing, starting with the physician's order must be monitored and the variables chosen should be appropriate to the laboratory's scope of care. Any device (like the Whiz Cleancatch) that significantly improves the quality of the sample sent to the lab and reduces preanalytic variables is therefore to be preferred. GEN.40125 Phase II* states that the referring laboratory must follow properly all requisition,

collection and handling specifications and that *Preanalytic variables must be closely controlled to maintain specimen integrity*. GEN.71000 Phase II requires documented procedures detailing procurement, transportation, and handling of patient specimens and that all specimens are submitted in an appropriately labeled and well-constructed container with a secure lid to prevent leakage during transport? In the EU Section 5.5.1 and 5.5.2 of the mandatory EN ISO: 15189:2003 relate to Medical Laboratories and require that: "The laboratory shall use only validated procedures to confirm that the examination procedure is suitable for the intended use. The validation shall be as extensive and as necessary as possible to meet the needs in the given application or field of application. The laboratory shall record the results obtained and the procedures used for validation."

The issue of Sterility: EU and FDA regulations define "Sterility", how it is achieved, and what can be labeled "Sterile". In particular EU Directives 98/79/EC Annex I B 2.1 which regulates "Infection and microbial contamination" states that: "Devices labeled either as 'STERILE' or as having a special microbiological state must be designed, manufactured and packed in an appropriate pack, according to procedures suitable for ensuring that they remain in the appropriate microbiological state indicated on the label when placed on the market, under the storage and transport conditions specified by the manufacturer, until the protective packaging is damaged or opened" and that "Devices labeled either as 'STERILE' or as having a special microbiological state must have been processed by an appropriate, validated method." EU Regulations require a MSU collection device to be sterile. Sterile is defined as "...a validated process used to render a product free from viable micro-organisms. It achieves the complete killing or removal of all types of micro-organisms, including the spores of tetanus and gas-gangrene bacilli..." Ayliffe GAJ, Fraise AP, Geddes AM, Mitchell K (2000) Control of hospital infection - practical handbook 4th edition Arnold. Manufacture by an "aseptic" process is not only not sterile but many USA papers on this subject point out that even if the container is aseptically produced, unlike sterility there is no assurance or quality control method that this was done and no guarantee at all that it is maintained.

Issue of Spillage: Within the process of collection and transference of the sample is the requirement to reduce spillage even at common law. Although urine is sterile on leaving the body, it is classified as a hazardous substance due to its potential to carry HIV etc. In the EU health and safety regulations exist to protect healthcare workers and the public. Under UK COSHH (Control of Substances Hazardous to Health) regulations employers must give the best system of safety to minimise the risk and "to provide suitable work equipment and materials e.g. use processes which minimises the amount of material used or produced or

equipment which totally enclose the process". The term 'enclosed' is to reduce spillage i.e. exposure to the hazardous substance. Regulation 7(1) as defined by the Appeal Court (Dugmore v Swansea NHS Trust, 2002). Similar provisions exist throughout the world and in effect mean that exposure to substances hazardous to health by any route should be "prevented, unless this is not reasonably practicable, in which case it should be adequately controlled."

Pre-wipes: It is perhaps worth mentioning here that the practice of giving wipes or pre-wipes to patients to use prior to giving the sample has in many clinical papers (e.g. Lifshitz et al) shown to have no effect on the result and in case with women worse results than not using a wipe where they wipe back to front. Again a number of clinical trials (e.g. Jackson et al) show that in the privacy of the WC patients seldom use the pre-wipes leaving them unopened. This may be a result of the fact that the existing methods of urine collection cause patients embarrassment and distress - often with hands, clothing and feet contaminated with their own and others' urine and the pre-wipe just adds to this concern. For women too it is a fact that there are no effective barrier protections for women for the spillage of urine when giving a sample. Urine may contain infections such as Chlamydia, Gonorrhoea, Hepatitis B and C, HIV and MRSA, and UTI.

Method of Midstream Collection: On the Method of collection the midstream CleanCatch is preferred. The UK British Standard Operating Procedure, BSOP 41 v, 2006 is the regulatory "Investigation of Urine" document, issued by the UK Regulatory Body (Health and Safety Executive) after consultation with professional bodies. BSOP41 states a mid stream urine samples is to be collected "without interrupting the flow". WHO (World Health Organisation) regulations stipulate the MSU sample must be given 'Without Interrupting the Flow" and similar regulatory operating procedure directives. The reason is the contamination lies in the first stream. A stop start process of collection will increase contamination.

What is a contaminated sample: Below is a table that provides a general guideline to the clinician – a heavy mixed growth is clear contamination, and requires a retest but a equivocal growth of 2 or more organisms is a probable contamination or possible early UTI. These guidelines all suggest a retest to be certain but this is the discretion of the clinician OR if the patient is fully informed of the issues of retest, contamination and risks, a decision of the patient. Cases of wrong diagnosis when a retest was not done have certainly led to legal action

and payout in damages. Furthermore this guideline may be conservatively set for children and for symptomatic patients. There are suggestions that repeats should be carried out if there is either one strain of isolate or if there is one predominant strain at a level with a total of 107 to 108 cfu/L. Such a guideline would encourage more retests that the parameters set in the table below.

TABLE 1 Interpretation of and clinical response for semiquantitative MSU culture

| Growth, CFU/mL | N different organisms | Clinical interpretation | Action |
|----------------|-----------------------|---|-----------------------------------|
| <10 000 | Any number | Not significant | No further action if asymptomatic |
| 10 000–100 000 | 1–2 | Equivocal growth Possible early infection or contamination | Retest |
| 10 000–100 000 | >2 | Equivocal growth. Probable contamination | Retest |
| >100 000 | >2 | Heavy mixed growth. Frankly contaminated | Retest |
| >100 000 | 1–2 | Significant growth indicating UTI | Treat if clinically indicated |

CFU, colony-forming units.

Table 1: Jackson et al, 2005 extract.

Why is it important to get a quality result first time or to retest a contaminated sample?

The patient (and clinician) wants to get/give the best possible healthcare and this can only be done when based on an accurate pathology report. Furthermore many clinical papers and Government reports show that accurate sample reading can reduce preterm birth and neo natal death or renal failure and blindness. This is discussed in more detail under false positives and false negatives which are possible clinical results of the wrong call by a clinician when receiving a result of a contaminated sample.

Consequences for a clinician of a mixed growth or contaminated sample:

The clinician receiving a result which states mixed growth has to make a clinical decision. Generally he/she has three choices when the sample is not from Obstetrics and Gynecology and or involving children.

With Obs and Gyn and especially pregnant women the clinician has no choice. They must retest. In the UK this is not only best practice but set out in the NICE mandatory guidelines CG6, 2003 (*Antenatal Care: Routine care for healthy pregnant women*)¹ and CG54, 2007 (*Urinary tract infection in Children*)

Outside this group this is the situation for the clinician:

1. **First** she/he can treat it as symptomatic of a bug, i.e. infection and prescribe antibiotics.

These would have to be broad based as he/she would have no pathology of the growth. If the clinician is wrong then this is called a false positive and not only is this a waste of money of the antibiotics but is, as studies and Government reports have shown, is one of the main causes of HAI such as MRSA, C.difficile and ESBL – the indiscriminate use of broad based antibiotics.

In fact as one senior microbiologist wrote:

“The cost of an incorrect sample in relation to false positives

1. False-positive results will lead to unnecessary treatment for some of the patients [20p for trimethoprim, £10 for cipro]
2. Said treatment will cause side-effects needing further treatment in a proportion of patients: piriton for the rash, fluconazole for thrush, metronidazole for C.diff]
3. If you are really unlucky, the C.diff case will escalate into a full-blown outbreak, with all the associated direct and indirect costs.
4. Then the lawyers get involved, add several zeroes...”

But cost is not the only issue. Ciprofloxacin (Cipro) has a known huge list of persistent? Side effects e.g.:

- Tendonitis, **Tendon Rupture**, Tendon, Ligament, Joint and Muscle Damage Vision Damage, Hearing Loss, Taste Perversion

¹ Section 1.8.1.1 mandates that: “*Pregnant women should be offered routine screening for asymptomatic bacteriuria by midstream urine culture early in pregnancy. Identification and treatment of asymptomatic bacteriuria reduces the risk of preterm birth.*” CG6 recommends 12 urine tests per pregnancy.

- Peripheral Neuropathy (Tingling, burning sensation)
- Insomnia, Nightmares, Anxiety Attacks, Depersonalization, Cognitive Disorders
- Brain, Heart, Liver, Kidney, Pancreas, Blood and Endocrine Disorders
- Severe Psychotic Reactions, Suicidal Thoughts or Actions
- Gastrointestinal Damage
- As well as joint pains, muscle aches, feeling of pressure in ears, foggy brain, an awareness of feeling your heart beat,

There are many website regarding inappropriate drugs, antibiotics and side effects e.g. www.worstpills.org, www.antibiotics.org, www.drugvictims.org

2. **Second** the clinician can treat the mixed growth result as not being a bug and do nothing. If wrong then this is called a false negative i.e. it is an early stage UTI and has major repercussions in ante-natal clinics from renal failure to kidney damage in the unborn child to possible neonatal death and prematurity. In the rest of the population an undetected UTI has a host of complications for the public and the patient.

3. **Third** the clinician can order a retest. This of course is not only time consuming administratively but also a disruption for the patient, costly and delays diagnosis and treatment.

On an ordinary urine test, the most up-to-date cost analysis for general tests in microbiology is Whiting et al [Whiting P, Westwood M, Bojke L et al. *Clinical effectiveness and cost effectiveness of tests for the diagnosis and investigation of urinary tract infection in children: a systematic review and economic model*. Health Technology Assessment 2006; 10 (36)] and NICE guidelines, CG54, 2007. Whiting et al at page 116, places the cost of a urine test from a GP at £25.65 and at £104.85 when from a hospital outpatient. CG54 places lab costs at £16.00 for pyuria/bacteriuria and dipslide and lab culture being £2.60 each and then add nitrite and glucose etc. Emergency microbiology is £12.00 not £8.00 as see in CG54 table 11 page 20.

This does not include the following economic costs which are set out in the NHS Centre for Evidence Based report (CEP07004), 2008

“There might be additional benefits not captured in the cost impact analysis, such as the value of enhanced compliance with best practice and national guidelines, and how this might impact on local risk assessment strategies” and

(2) Also not included are “...resource implications of delayed diagnosis

due to retesting ...”

(3) And not included is that “...*its cost data is limited and does not include cost of post treatment diagnosis...*’ so thus does not include any costs relating to false positives or false negatives which can run to many thousands of pounds.

d) Nor are patient costs included and as Nice CG54, 2007 estimates the cost to a parent of £300 per week for a failed diagnosis and recall

There are specialised urine tests which cost £500 per test.

Avoiding a retest due to a contaminated sample saves a significant amount of money.

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