To Be Cultured or Not To Be

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Introduction

Many of the improvements in the management of surgical infections have come from increasing sophistication in medical microbiology and speciation of infecting organisms. A major advance was seen with the expanded capability two decades ago to isolate and identifiy anaerobic organisms throught the application of special transport media and handling techniques to isolate these most numerous flora of the lower gastrointestinal tract.

Microbiologic identification is of critical importance in identifying an infecting pathogen, particularly those that are fastidious in their growth characteristics and may carry the capacity for resistance to commonly used antimicrobials and the further capability of transferring these "R-factors". Culture and sensitivity testing, however, are especially important in these circumstances of mono-bacterial culture of a virulent infecting pathogen, and these benefits are not necessarily translated through culture identification of all contaminants.

"Surgical Infection" versus "Medical Infection"

An arbitrary distinction can be drawn between "medical infection" and "surgical infection" not based simply on the techniques of treatment (Table 1). Many of the patients may be unaware of which service they are on, let alone the microbes, and it should make no difference to the behavior of either. However, there is a distinctive difference among surgical infections, both with respect to the flora and the pathophysiology they may lead to, and this makes an immediate difference in treatment.

As a rule, a "medical infection" is caused by a virulent pathogen; for example, staphylococcal endocarditis or meningococcal meningitis. Surgical infections are, as a rule, the result of nonpathogenic commensal organisms that are ordinarily resident on epidermal or mucosal surfaces such as the skin, or the alimentary canal. Not only are they not typically harmful, but their presence is beneficial to the hosts they colonize. These organisms by their presence crowd out pathogenic microbes, and in some instances contribute more than the neutrality of taking up space. They may in the gastrointestinal tract assist in the metabolism of bile salts, the production of vitamin K, or break down potentially harmful substances into metabolites that may be more innocuous. The objective of antimicrobial therapy is not to sterilize man, since this objective would not necessarily be beneficial even if possible.

A fundamental distinction between infections of the medical versus surgical type is that the former are typically monobacterial, and the latter nearly always polymicrobial. The nature of this polymicrobial inoculum comes from the method whereby surgical contaminants gain access to the interior milieu: the mixed species resident on these surfaces or contained within the viscera gain access following a barrier breach. This failure of containment can be obvious with such examples as a knife penetrating the skin and the mixed flora resident upon it, and similarly with opening the viscera containing 6.8 billion organisms per gram of the dry weight of feces. Less obvious, but increasingly important in the recognition of patients undergoing intensive care and often leading to multiple organ failure syndromes, is the phenomenon of "translocation".

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Barrier Breaches That May Cause Failure of Containment of Mixed Flora

The phenomenon of "translocation" has assumed wider acceptance and greater clinical importance, following experimental proof of its potential, with the bacteriologic study of patients who have experienced low flow states. In one such example, the single most important determinant as to whether a patient who had undergone trauma whether blunt or penetrating would demonstrate a positive blood culture was the presence or absence of shock (1). Although counterintuitive, even a penetrating gastrointestinal injury might not necessarily lead to a positive blood culture in a patient with no significant shock, and even blunt injury or no trauma at all in the presence of shock gave rise to a much more significant probability of bacteremia. This clinical evidence supports, though it does not prove, that a barrier breach can be a decrease in flow, through whatever means of host impairment secondary to that decreased nutrient flow, and does not require obvious macropenetration.

Since surgical contaminants are polymicrobial and typically commensal rather than the kind of medical infection seen with a single species of virulent pathogenicity, this distinction has important implications both for the practices of culturing such patients and their management.

Culture Protocol and Rationale

It has long been taught that obtaining a culture is an important if not necessary precondition for antimicrobial treatment, following the medical model of monobacterial pathogen identification. When carried over to the surgical patient, this practice may be reduced to absurdity, though it is still present in nursing manuals and common procedure of good clinical practice whereby appropriateness of therapy is checked in quality control. This "protocol response" is the reason behind most routine "bile cultures" at the time of cholecystectomy, and gross contamination cultures of community-acquired inocula. As an example, when operating with surgical residents on an emergency laparotomy for penetrating gunshot wound of the abdomen, I cannot restrain them from culturing gross fecal soilage of the peritoneum. I believe three questions are appropriate in reviewing this practice persists: [1] Did you expect this material to be sterile? [2] When do you think the laboratory will quit in speciating the flora present, and with what report will you be content ? [3] How will this information in any way change your management?

If the majority of the material in the colon it is actually bacterial by mass and weight, it is highly unlikely that a negative culture will result from even inappropriate handling of such a specimen. If the purpose is to test the laboratory as quality control, this is a different objective than clinical care. However, would a clinician be satisfied with the report that *Escherichia coli* and *Bacteroides* species are present?

In a compulsive analysis of fecal flora (Table 2), well over 500 species can be isolated, 80% of which are anaerobic, so even a well-performed culture transported appropriately and immediately for analysis is less than edifying. More importantly, since we already know what species will be present, the burden on the clinician is to manage the significant pathophysiologic risks that come from these mixed flora inocula, and not necessarily the speciation of this primary contaminant.

Table 1. Infection

Medical	Rx	Surgical
Pathogenic Organism	Pathogenesis	Commensal flora invade
Monobacterial	Number of organisms	Polymicrobial
Organisms known	Culture	Organism unknown
Sensitivity-guided	Therapy	Empirically initiated
Principal therapy	Purpose of Rx	Adjunctive only
Monotherapy (the rule)	Number of Rx	Combination therapy
Drug	Primary treatment	Operation
Superinfection	Redox potential	Synergistic

Cultural Nihilism in Primary Mixed Inocula

Although it may seem like heresy in the management of surgical infection, a substantiated case can be made that there is no purpose to the culture of primary community-acquired mixed surgical inocula. Each of these qualifiers are important, since the selection of resistant organisms in an inpatient setting, or those that follow after prophylaxis with surgical decontamination preps or systemic antimicrobials, or those organisms that emerge through the pressures of antibiotic therapy are all critically important elements of managing infection that require cultures. But, we should distinguish infection (and superinfection, especially) from contamination with the colonization one would expect of resident flora given the clinical circumstances. This nihilism with respect to primary culture should not be interpreted as holding for "medical infections" based in pathogens (Table 1) or hospital-acquired contaminants such as aspiration pneumonia. However, gross contaminant cultures, even though routinely positive, are not informative, may be misleading, and those dollars spent were better redirected toward other surveillance than identification of community flora.

Extending this beyond a suggestion that it is defensible not to culture gross contamination, I would suggest that it is inappropriate to do so and constitutes at least a waste of funds in obtaining worthless information and at worst misleading direction if therapy is in anyway changed by the report of this information.

Presumptive Management of Mixed Flora Contaminants

There are three principal flora in mixed surgical infections that are present because of the nature of their resident status on epidermal and mucosal body surfaces (Table 3). Whether or not isolated and identified by culture, their presence is presumed and covered, principally because of the pathophysiologic risk they represent to the patient. The Gram-positive aerobe can give rise to cellulitis or superficial abscesses and besides febrile morbidity, this can lead to seeding of deeper structures and organs, and is therefore covered in any barrier breach. Particularly with penetrating trauma, presumptive therapy has as a major concern the coverage of these Gram-positive aerobic skin flora, and often a beta-lactam antibiotic is chosen for appropriate coverage of these organisms, isolated not so much by their speciation as by this distinctive pathophysiologic risk.

A second major flora, particularly of concern in upper gastrointestinal and genitourinary tracts is the Gram-negative aerobe. These coliform organisms have a common pathophysiology in that they readily invade the blood stream and there elaborate endotoxin which gives rise to circulatory instability, recognized by physicians as endotoxic shock. The early mortality that is exhibited in polymicrobial sepsis is due to this coliform toxicity mediated by endotoxin and the host responses initiated by its release. Clinicians have recognized this risk and have sought therapy to cover these organisms whether or not identified by administering an agent such an aminoglycoside.

A third class of organism distinguished by their pathophysiology is the Gram-negative anaerobe or a term covered by the representation in their most numerous species, *Bacteroides* species. These Gram-negative anaerobes do not similarly readily invade the blood stream and there elaborate endotoxin, and are not primarily pathogens of themselves, but are evident in surgical failure following control of the coliform and skin flora groups since they are abscessogenic. They are often facultative organisms that until recently have not been identified by culture, but often through their effect, since a mixed flora inoculum has much more virulence than the injection of a single species alone. The *E.coli*, for example, when injected into the blood stream has less virulence than when a mixture of *Bacteroides* and *E.coli* are introduced, since the oxidation-reduction potentials are such that an anaerobe facilitates the growth of the aerobe and conributes to the virulence of the mixed inoculum. Because of this risk, more recently appreciated, of the anaerobic flora, a third class of antimicrobials was added for this third pathophysiologic risk such as chloramphenicol, metronidazole, clindamycin, or other broader coverage agents such as cefoxitin or even some third generation cephalosporins.

Through the recognition of these distinguishable pathophysiologic risk, and the differences in antimicrobial inoculum was introduced, particularly when compounded with the host defense impairment that followed shock. Furthermone, failures that slipped through this coverage were seen in protracted organ failure states. When local inflammation around the site of an inoculum, for example in the peritoneum, occurred with an imferred "containment" of the inoculum, this local reaction was beneficial, but the systemic inflammatory response mediated by cytokine activation and multiple cascades in complement, clotting, eicosanoid elaboration led to sequential organ failure through permeabilities in alveolar capillary membrane, renal tubular damage, and homeostatic mechanisms derangements such as liver protein synthesis failures. As the local inflammation achieved "re-containment" of the inoculum, the systemic price was paid in inflammatory processes in multiple organ failure.

Monotherapy as a Replacement for Combination Antimicrobials

Still recognizing this "triple risk" some antimicrobials were selected because they might cover more than one risk. For example, clindamycin would cover the Gram-positive anaerobic risk from skin flora as well as the *Bacteroides* potential, and then when combined with aminoglycoside would do effectively what triple therapy had been designed to do. If there were concern about aminoglycoside toxicity despite its demonstrable effectiveness, either substitution of the aminoglycoside for a drug of comparable efficacy but without the toxicity could be attempted or a more rational approach would be to attempt monotherapy of all three risk. The carbapenem class of antimicrobials emerged in time to be

Table 2. Fecal Flora

1 gram has 10^{12} organisms
25% of weight is bacteria
400 anaerobes
100 aerobes (or facultative)

Table 3. Polymicrobial Flora and Pathophysiologic Risks in Intra-abdominal Sepsis

Mixed Flora	Representatives	Pathophysiologic Effect
Gram-positive aerobes	Skin flora	Cellulitis, superficial abscess
Gram-negative aerobes	Coliforms	Endotoxic shock
Gram-negative anaerobes	*Bacteroides*	Abscessogenic ➡ MOF

proposed as effective monotherapy for all three pathophysiologic risks with at least equivalent, and later demonstrably superior (2), effectiveness without toxicity of some elements in combination therapy.

Prophylaxis, Presumptive, and Precise Therapy

By definition, there will never be a culture of the contaminating organisms to direct a specific case in prophylaxis, since, the definition of prophylaxis includes a circulating presence of the antimicrobial before the inoculum. When the inoculum is already present and presumptive treatment is initiated, but that identification is not known, and for primary surgical contamination, I submit, should *not* be known, but presumed, whether or not it were possible to identify by isolation. Precise therapy is predicated upon culture and sensitivity, since precise therapy is the targeting of an identified pathogen with the most appropriate antimicrobial selected by its laboratory-demonstrated sensitivity to the agent, among other mitigating factors such as toxicity and costs or patient hypersensitivity.

For prophylaxis, culture is impossible. For presumptive treatment, it is unnecessary, and if done, inadequate and not normative. For precise therapy culture and sensitivity identification are critical.

Conclusion

Much has been learned in microbiologic sophistication that has been helpful in medical infections often relying upon precise therapy. For most surgical infections, mixed flora of community origin resident surface flora are presumed, whether or not identified, and treated even if not isolated. The treatment of choice for a mixed surgical infection is an operation with an adjunctive presumptive monotherapy. Culture practices have improved management of superinfection and precise treatment of emerging pathogens. Culture protocols have not helped or have actually interferred with management of surgical risks which must be treated presumptively. Funds expended in culture identification of contamination microbes would better be spent precisely.

References

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