

The Hard Cases Expose the Method

Five studies showing how specimen choice, ambiguous growth, rare enzymes, structural variants, and special stains define diagnostic boundaries.

Wednesday, September 30, 2026

Colonization screening | Cefiderocol AST | Carbapenemases |
Long-read sequencing | Special stains

FIVE SIGNALS WORTH YOUR BENCH TIME

01 / MICROBIOLOGY / SPECIMEN STRATEGY

Broth enrichment changed which resistant colonizers were found

Finding. Fluoroquinolone-resistant viridans streptococci were detected in 62 of 69 HCT candidates. Buccal and oropharyngeal broth enrichment each reached 97% positive agreement for resistant VGS; combining direct plating and enrichment of buccal swabs reached 96% for resistant *S. mitis* group.

Why it matters. Specimen site and enrichment are part of the test definition. A practical screen must identify the organism group of interest without adding a workflow that cannot meet the prophylaxis decision window.

Limits. The comparator was detection by any tested site or method, not later bloodstream infection. The small cohort had 90% colonization, so clinical predictive value and benefit of acting on screening remain unknown.

Evidence label: Peer-reviewed prospective specimen-and-culture comparison; open-access publisher record verified.

02 / ANTIMICROBIAL SUSCEPTIBILITY / ENDPOINTS

Unclear cefiderocol endpoints were common and biologically active

Finding. About 60% of 455 *Acinetobacter* isolates showed trailing, regrowth, or hazy cefiderocol broth-microdilution endpoints. Microscopy found disrupted cell forms, yet plating showed substantial viable growth in most wells above the apparent MIC.

Why it matters. An ambiguous endpoint is not visual noise. Laboratories need reading rules, competency examples, repeat or referral criteria, and result comments that preserve uncertainty near a clinical breakpoint.

Limits. The surveillance collection came from Europe and the United States. The study did not establish how each pattern predicts patient response, optimal reporting, or agreement across routine commercial AST systems.

Evidence label: Peer-reviewed analytical and surveillance study; open-access publisher record verified.

03 / ANTIMICROBIAL RESISTANCE / CARBAPENEMASES

One phenotypic carbapenemase method did not fit every organism

Finding. Across 228 GES-producing isolates, mCIM sensitivity in Enterobacterales was 63.6% versus 40.0% for CIM. CIM-Tris reached 100% sensitivity in carbapenemase-producing *P. aeruginosa*, but was falsely positive in half of non-carbapenemase GES isolates.

Why it matters. Assay performance followed species and enzyme behavior, not the generic label 'GES.' A species-aware algorithm can route discordant or low-MIC isolates to molecular confirmation.

Limits. The collection was enriched for GES producers from selected hospitals and included only 10 *A. baumannii* isolates. Routine predictive values will depend on local prevalence, variants, and comparator access.

Evidence label: Peer-reviewed multicenter isolate study with whole-genome characterization; open access at verification.

Long reads joined structure, haplotype, and methylation in one assay

Finding. An adaptive-sampling protocol optimized for non-high-molecular-weight DNA detected every previously reported X-linked variant in 20 families. It added findings in 7 families and changed variant classification in 3 through breakpoint and methylation information.

Why it matters. Some diagnostic questions require more than variant detection. Linking structural breakpoints with haplotype and allele-specific methylation may resolve phenotype, inheritance, and classification in a single investigation.

Limits. Families were preselected for known X-linked defects, and the cohort was small. The study did not establish first-line sensitivity, reproducibility across laboratories, turnaround, cost, or yield in unsolved cases.

Evidence label: Peer-reviewed targeted sequencing validation in 20 families; full text may require subscription.

The elastin stain changed venous-invasion detection

Finding. In 78 colorectal-cancer resections and 155 evaluable slide sets, EVG missed 21% of venous-invasion foci identified by orcein. Orcein showed circumferential vessel-wall staining in 78% of sets versus 43% with EVG.

Why it matters. A named special stain is not an interchangeable commodity. Stain selection, section depth, tissue controls, background contrast, and reviewer criteria can change whether a prognostic feature is reported.

Limits. Orcein plus H&E served as the reference rather than an independent ground truth. Deeper-level loss excluded some sets, and performance requires confirmation with local protocols, reagents, and readers.

Evidence label: Peer-reviewed comparative stain study; official Crossref record verified September 18, 2026.

Verified source trail

1. Subramanya, Gottesdiener, Marino, et al. Optimizing methods to detect colonization with fluoroquinolone-resistant viridans group streptococci prior to hematopoietic cell transplantation. Journal of Clinical Microbiology. 2026. DOI: 10.1128/jcm.00687-26.

2. Castanheira, Maher, Kimbrough, et al. Evaluation of cefiderocol trailing and other unclear susceptibility testing endpoints for Acinetobacter spp.. Journal of Clinical Microbiology. 2026. DOI: 10.1128/jcm.00186-26.

3. García-García, Rodríguez-Grande, Siller-Ruíz, et al. Evaluation of carbapenem inactivation method-based phenotypic assays for the detection of GES-type carbapenemases in Enterobacterales, Pseudomonas aeruginosa , and Acinetobacter baumannii. Journal of Clinical Microbiology. 2026. DOI: 10.1128/jcm.00737-26.

4. Zheng, Li, Han, et al. Genetic Investigation of X-Linked Defects with Optimized Targeted Long-Read Sequencing. Clinical Chemistry. 2026. DOI: 10.1093/clinchem/hvag088.

5. Law, Choi, Umetsu, et al. Orcein is a more sensitive stain than EVG for detecting large vessel (venous) invasion in colorectal cancer. Histopathology. 2026. DOI: 10.1111/his.70282.

VERIFICATION	DISCLOSURE & USE
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