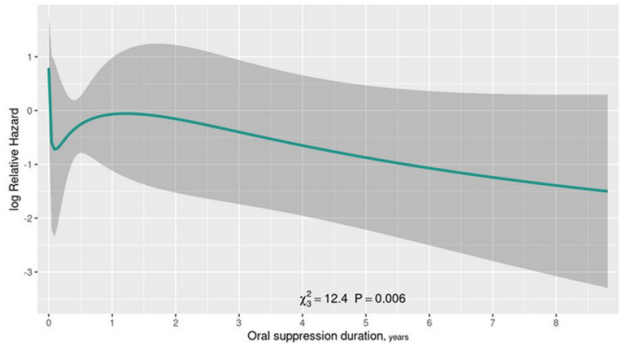
Figure 2. Time-Dependent Analysis of Oral Antibiotic Suppression Duration



Conclusion. After DAIR, efficacy from four weeks of parenteral antibiotics was no different from six weeks when followed by chronic oral antibiotic suppression. Our results could not establish an optimal duration but suggested that continuing suppression portends a lower risk of failure of DAIR.

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112. A Rapid Host-Protein Signature Based on TNF-related Apoptosis-Induced Ligand (TRAIL), Interferon Gamma Induced Protein-10 (IP-10) and C-Reactive Protein (CRP) Accurately Differentiates Between Bacterial and Viral Infection in Febrile Children: Apollo Sub-Study

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Session: O-24. New Developments in Infectious Diseases Diagnostics

Background. Identifying infectious etiology is essential for appropriate patient management, including antibiotic use. A host-protein signature for differentiating bacterial from viral infection has exhibited robust performance (AUC of 0.9, 95% CI 0.86-0.95) in prior studies. Performance data was lacking for a broad pediatric population recruited in emergency departments (EDs) and urgent care centers (UCCs).

Methods. Non-immunocompromised children were recruited prospectively from 5 EDs and 3 UCCs in the U.S. and 1 ED in Israel between May 2019 and August 2020. Eligibility required physician's clinical suspicion of acute infection and reported fever. Reference standard etiology was adjudicated by experts based on clinical, laboratory, radiological, microbiological and follow-up data. For the primary analysis, experts blinded to one another, to the host-signature results and also to procalcitonin and CRP, classified cases as bacterial or viral. For the secondary analysis, experts blinded to one another and the host signature results, were permitted to classify cases as bacterial, viral or indeterminate; indeterminates were removed from the secondary analysis. Host signature (comprising TRAIL, IP-10 and CRP; MeMed BV®) was measured using a rapid platform (MeMed Key®) generating a bacterial likelihood score (0-100) in 15 minutes.

Results. The study cohort comprised 162 children (median age, 5.5 yrs; interquartile range, 8.5), of whom 69 (43%) presented within 2 days of symptom onset and 37 (23%) were hospitalized for a median of 3 days. Respiratory tract infection was the predominant syndrome (11% lower and 44% upper). Host signature attained AUC 0.87 (0.74-1) and 0.92 (0.79-1) in the primary and secondary analysis, respectively. With higher the signature score, there was a significantly higher likelihood of bacterial infection ($p< 0.001$; Table 1). The 3 bacterial infections assigned score < 35 (false negative) would have been identifiable by physical examination (Table 2).

Increasing host signature score is associated with increasing likelihood of bacterial infection across both the primary and secondary cohort

	Host signature score bin	n patients	% patients	n Bacterial reference standard patients	% Bacterial reference standard patients = PPV	n Viral* reference standard patients	% Viral* reference standard patients = NPV	Likelihood ratio (95% CI)
Primary cohort	90 ≤ score ≤100	7	4.3%	6	85.7%	1	14.3%	75.0 (9.8-573.2)
	65 < score <90	12	7.4%	2	16.7%	10	83.3%	2.5 (0.6-10.1)
	35 ≤ score ≤ 65	13	8.0%	1	7.7%	12	92.3%	1.0 (0.1-7.3)
	10 < score <35	19	11.7%	0	0.0%	19	100.0%	0.00
	0 ≤ score ≤10	111	68.5%	3	2.7%	108	97.3%	0.4 (0.1-0.9)
	Total	162	100.0%	12		150		
Secondary cohort	90 ≤ score ≤100	6	4.1%	5	83.3%	1	16.7%	87.5 (11.5-663.2)
	65 < score <90	10	6.8%	1	10.0%	9	90.0%	1.9 (0.3-13.5)
	35 ≤ score ≤ 65	9	6.1%	0	0.0%	9	100.0%	0.00
	10 < score <35	18	12.2%	0	0.0%	18	100.0%	0.00
	0 ≤ score ≤10	105	71.0%	2	1.9%	103	98.1%	0.3 (0.1-1.1)
	Total	148	100.0%	8		140		

The performance of the host signature score in differentiating between bacterial and viral infection was evaluated by allocating children to one of five score bins and within each bin according to their adjudication label and determining if there is a meaningful increase in the relative likelihood of bacterial infection across the bins based on the Cochrane-Armitage test of trend. PPV, positive predictive value. NPV, negative predictive value. *Includes patients adjudicated as non-infectious

Three children assigned a bacterial adjudication label and a score of 35 or less (false negatives) have bacterial infections identifiable in physical exam

Patient ID	BV Score	PCT (ng/ml)	Age (yr)	Max Temp (C)	Time from symptom onset (days)	Hospitalized	Microbiology	Comorbidity	Discharge Diagnosis	Current illness and Follow Up
1	5	0.07	8.6	40.0	2	No	Strep A	Type 1 Diabetes	Upper respiratory tract infection /strep throat	Presented with 1 day of measured temperature 104.0F, 2 days of sore throat, headache and abdominal pain. Physical examination significant for pharyngeal erythema. Rapid strep test was positive for Strep A. Prescribed amoxicillin. No follow up available.
2	2	0.16	3.1	38.9	2	No	Human-Rhinovirus/Enterovirus , Respiratory-Syncytial Virus		Upper respiratory tract infection /acute otitis media + reactive arthritis	Presented with 2 days measured temperature 102.0F. Physical examination significant for right tympanic membrane erythematous with fluid. Suspected of Lyme, had a positive ELISA but a Western immunoblot was not available at time of discharge. Was prescribed 28 days of cefdinir to cover the potential Lyme disease and concurrent otitis media. Symptoms subsided within 10 days.
3	9	0.05	2	38.0	5	Yes	Influenza A sub H1-2009		Periorbital cellulitis	Presented with 5 days of measured temperature 38.0C , cough and 2 days of closed and swollen left eye. Physical examination significant for left eyelid swollen shut without discharge and mild oropharyngeal erythema. Admitted for 6 days. Discharged with a 5-day course of cefuroxime, symptoms resolved within 7 days.

Conclusion. The host-protein signature measured using a rapid platform attained robust performance in differentiating bacterial vs viral infection in children with acute febrile illness, supporting its potential to enhance rational use of antibiotics in the ED and UCC.

Disclosures. **Sheldon L. Kaplan, MD**, **Pfizer** (Research Grant or Support) **Mark Kellogg, PhD**, **MeMed** (Scientific Research Study Investigator) **Andrea T. Cruz, MD, MPH**, American Academy of Pediatrics (Individual(s) Involved: Self): editorial board member **Kristina G. Hulten, PhD**, **Pfizer** (Research Grant or Support) **Cesar A. Arias, M.D., MSc, Ph.D., FIDSA**, **Entasis Therapeutics** (Grant/Research Support)**MeMed Diagnostics** (Grant/Research Support)**Merk** (Grant/Research Support) **Richard Gordon, MD**, **MeMed** (Scientific Research Study Investigator) **Sergey Motov, MD**, **MeMed** (Scientific Research Study Investigator) **Theresa Jacob, PHD MPH**, **MeMed** (Scientific Research Study Investigator) **Natasha Ballard, MD**, **MeMed** (Scientific Research Study Investigator) **George Suits, MD**, **MeMed** (Scientific Research Study Investigator) **Jeffrey Harris, MD**, **MeMed** (Scientific Research Study Investigator) **Maanit Shapira, Ph.D**, **MeMed** (Scientific Research Study Investigator) **Richard E. Rothman, PhD, MD**, **Chem bio** (Grant/Research Support) **Karen C. Carroll, MD**, **MeMed** (Scientific Research Study Investigator)**Meridian Diagnostics, Inc.** (Grant/Research Support)**Pattern Diagnostics** (Advisor or Review Panel member)**Scanogen, Inc.** (Advisor or Review Panel member) **Karen C. Carroll, MD**, Pattern Diagnostics, Inc. (Individual(s) Involved: Self): Grant/Research Support; Scanogen, Inc. (Individual(s) Involved: Self): Consultant **Leticia M. Ryan, MD MPH**, **MeMed** (Scientific Research Study Investigator) **Richard Bachur, MD**, **MeMed** (Scientific Research Study Investigator)

113. Reliability of Nasopharyngeal PCR for the Detection of Otopathogens in Children with Uncomplicated Acute Otitis Media

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Session: O-24. New Developments in Infectious Diseases Diagnostics

Background. Among children with acute otitis media (AOM) *S.pneumoniae*, *H.influenzae*, and *M.catarrhalis* are the predominant bacterial otopathogens. There is a high correlation between nasopharyngeal (NP) and middle ear fluid (MEF) organisms during AOM. Thus, NP samples could serve as a surrogate for detection of otopathogens and are more easily collected in a typical practice environment than MEF. Though culture is considered the gold standard for detection, it is time-consuming, which can limit its diagnostic utility to guide clinical care. We aimed to determine the sensitivity, specificity, positive (PPV) and negative predictive value (NPV) for NP qualitative PCR for bacterial otopathogens compared to NP culture.

Methods. Patients age 6-35 months with uncomplicated AOM who were prospectively enrolled in an AOM study in Denver, CO from Jan 2019-Dec 2020 were included. All patients had an NP flocked swab (Eswab®, Copan Diagnostics) at enrollment. Otopathogen culture was completed using standard techniques. Nucleic acids were extracted using the NucliSENS® easyMAG® system (Quidel, San Diego, CA) per manufacturer's instructions. Multiplex RT-PCR for *S.pneumoniae, H.influenzae,* and *M.catarrhalis* was completed using Lyra® (Quidel, San Diego, CA) and AnDiaTec® assay kits (Quidel Germany GmbH, Kornwestheim, Germany). Nucleic acid amplification and detection was completed on the Applied Biosystems® (ABI) 7500 Fast Dx Real-Time PCR Instrument.

Results. Of the 80 children included, 18 (22.5%) had no organism detected on culture, 31 (38.8%) had one and 31 (38.8%) had multiple organisms detected. The most commonly identified organisms on culture were *M.catarrhalis* (42, 52.5%), followed by *S.pneumoniae* (30, 37.5%), and *H.influenzae* (17, 21.3%). Of *H.influenzae* isolates 8 (47.1%) produced beta-lactamase. The sensitivity of PCR was high (>94%) for all organisms whereas the specificity was lower (50.0-77.8%) and varied by organism (Table). NPV were high (>96%) for all otopathogens, whereas, PPV ranged from 53.3 to 68.9%. PCR detected 1.6 times more organisms than culture (149 vs. 96).

Sensitivity, specificity, positive and negative predictive value of PCR compared to culture for otopathogens.

Pathogen	Prevalence in Nasopharynx[a] N (%) N=80	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV[b] % (95% CI)	NPV[c] % (95% CI)
S.pneumoniae	30 (37.5)	96.7 (82.8, 99.9)	62.0 (47.2, 75.4)	60.4 (51.5, 68.6)	96.9 (81.7, 99.5)
H.influenzae	17 (21.3)	94.1 (71.3, 99.9)	77.8 (65.5, 87.3)	53.3 (41.5, 64.8)	98.0 (88.0, 99.7)
M.catarrhalis	42 (52.5)	100.0 (91.6, 100)	50.0 (33.4, 66.6)	68.9 (61.7, 75.2)	100.0 (NA)
S.aureus[d]	7 (8.8)				
Multiple organisms	31 (38.8)				
No organism	18 (22.5)				

[a] As detected by culture [b] Positive predictive value [c] Negative predictive value [d] PCR results not available

Conclusion. NP PCR has a high predictive value for excluding otopathogens and warrants further exploration as a diagnostic tool to evaluate for otopathogens in children.

Disclosures. **Andreas Bress, PhD**, **Quidel Laboratories- Germany** (Employee) **Richard Egan, PhD**, **Quidel Laboratories** (Employee) **Samuel R. Dominguez, MD, PhD**, **BioFire Diagnostics** (Consultant, Research Grant or Support)**DiaSorin Molecular** (Consultant)**Pfizer** (Grant/Research Support) **Samuel R. Dominguez, MD, PhD**, BioFire (Individual(s) Involved: Self): Consultant, Research Grant or Support; DiaSorin Molecular (Individual(s) Involved: Self): Consultant; Pfizer (Individual(s) Involved: Self): Grant/Research Support

114. Prospective Trial of Passive Diversion Device to Reduce Blood Culture Contamination

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Session: O-24. New Developments in Infectious Diseases Diagnostics

Background. Blood culture contaminants can lead to inappropriate antibiotic use, prolonged length of stay, and additional hospital costs. Several devices have been developed to reduce the risk of blood culture contamination by diverting a portion of the initial blood sample from the blood culture bottle. We have assessed the effectiveness of one blood diversion device in a prospective trial performed at the two separate emergency departments (EDs) of a three-campus Academic Medical Center.

Methods. A multi-phase prospective crossover trial was performed with the blood diversion device initially in use at one ED (Memorial) and standard equipment at the other ED (University) for 10 weeks. After a washout phase, a second 10-week study phase used the blood diversion device in the other ED (University) and standard equipment at the first ED (Memorial). Contaminants were identified by the clinical microbiology lab using standard criteria, and further defined by independent retrospective review by 3 infectious disease physicians prior to statistical analysis. An intention-to-treat analysis was performed, and Chi-square tests were used to compare contaminant rates among samples obtained using the blood diversion device versus standard equipment.

Results. 5,675 blood samples were obtained with 5,661 samples analyzed after 14 were deemed inconclusive by the ID physician review. There were 1,719 samples obtained at Memorial ED and 3,942 at University ED, with 2,836 samples collected during diversion device periods and 2,825 during standard equipment periods. Based on the ID physician review, the contaminant rates were 1.9% in diversion device periods versus 2.9% in standard equipment periods (P = 0.018). There was a marked difference in blood culture contamination rates between the two EDs with contaminant rates at the Memorial ED of 1.1% and 1.4% (P=0.57), and at the University ED of 2.3% and 3.5% (P=0.024) for the diversion device and standard equipment periods, respectively.

Conclusion. The blood diversion device was able to significantly lower blood culture contamination rates overall by 1% at the institution's two EDs (34% relative reduction), with a stronger effect noted at the campus with both a level 1 trauma center and transplant programs.

Disclosures. **All Authors**: No reported disclosures

115. The Utility of (1→3)-β-D-glucan Assay in the Diagnosis of Severe Coccidioidomycosis Infections among Immunocompromised Hosts

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Session: O-24. New Developments in Infectious Diseases Diagnostics

Background. Coccidioidomycosis is associated with increased morbidity and mortality in immunocompromised (IC) patients. The diagnosis of invasive fungal infections can be challenging in IC hosts. Culture results may take time to identify *Coccidioides* species, and serologic based tests are less sensitive in IC patients. (1-3)-β-d-glucan (BDG) has been reported to be detected in patients with coccidioidomycosis. We hypothesized that BDG in combination with serology may assist in the early detection of coccidioidomycosis in IC patients.

Methods. After the institutional review board approved the study, we conducted a retrospective chart review from 10/1/2017 through 09/15/2020, including ≥18 years old IC patients with a confirmed diagnosis of coccidioidomycosis by culture. Information regarding demographics, comorbidities, immunosuppression, medications, BDG, serology, and clinical presentation was collected. Patients with infusions that can result in possible false-positive BDG were excluded. Patients with other fungal infections were also excluded. Chi-square test was used to compare categorical variables, Wilcoxon rank-sum and Kruskal-Wallis tests were used to compare non-parametric variables, accordingly.

Results. Over the study period, 269 encounters with positive *Coccidioides spp.* cultures were identified, 78/269 of patients were IC patients, 55/78 were excluded, and 23 cases were included in the final analysis. Among the 23 IC patients, the median age was 64, 43% were female, 74% were White. There were 8 post solid organ transplantation, 7 with a hematological malignancy, and 8 with other types of IC conditions. 19/23 had a pulmonary infection. 4/23 patients died within one month of their encounter. There was no statistical significance difference between positive BDG and serology tests, with 12/23 had positive BDG, and another 12/23 had positive serology. Combined serology and BDG detected 18/23 of the Coccidioidomycosis cases. 17% of the cohort died within the one-month follow-up.

Conclusion. The combined use of BDG assay and *Coccidioides* serology increases the sensitivity of coccidioidomycosis diagnosis to 78% in IC patients. Future prospective studies are needed to further evaluate the utility of serum BDG in diagnosing coccidioidomycosis in IC patients.

Disclosures. **Mohanad Al Obaidi, MD**, **Shionogi Inc.** (Advisor or Review Panel member)

116. Characterization of small colony variants from a patient with bloodstream infection of Candida glabrata

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Session: O-24. New Developments in Infectious Diseases Diagnostics

Background. Bacterial small colony variants (SCVs) that are tolerant to commonly used antibiotics are well recognized. Clinical SCV *Candida* have been rarely reported. We describe SCV *C. glabrata* (CG) strains recovered from within a population causing bloodstream infection (BSI) in a patient (pt), which were not recognized by the micro lab. Pt J developed CG BSI shortly after liver transplant (OLTX), which was treated with voriconazole (VOR). VOR was also used for post-OLTX mold prophylaxis. 67 d after BSI, he developed intra-abdominal infection due to VOR-resistant CG. We hypothesized that BSI might be caused by an unrecognized mixed population of azole-susceptible and –resistant strains.

Methods. Ten colonies from small (SCV) and large colonies (LC) from blood culture (BC) agar plates underwent Illumina NextSeq WGS and phenotype testing.

Results. BCs from pt J harbored a diverse population of genetically distinct CG strains, differing by unique SNPs and indels [Fig. 1]. Gene variants identified were enriched for biological processes involved in mitochondrial processes (2.5e-9), cell adhesion (3.3e-5), and respiration (3.5e-4). Unlike LC, SCVs were fluconazole (FLU) resistant (MIC: 128 μg/mL), and exhibited enhanced *CDR1* and *PDR1* expression (257 ± 11, 15 ± 4, respectively). Compared to LCs, SCVs grew slowly in YPD, did not grow on media containing glycerol as sole carbon source, and were less adherent to agar. SCVs stained poorly with rhodamine 123 by fluorescence flow cytometry and had fewer mitochrondria by transmission electron microscopy, consistent with WGS findings and respiratory deficiency. SCVs were less susceptible to macrophage (J774) phagocytosis, and they were significantly outgrown by other strains in competitive infections *in vitro* and during disseminated candidiasis in mice. LCs incubated with FLU *in vitro* yielded SCVs in concentration-dependent manner. Likewise, LCVs passed through spleens of mice following IV inoculation yielded SCVs in both presence and absence of FLU.