



Microbiology Newsletter

Sir Ganga Ram Hospital

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Invasive Aspergillosis : A Diagnostic Challenge

Case Study:

A 3 years old male child, known case of aplastic anemia was admitted at Sir Ganga Ram Hospital for routine course of therapy. Patient also had low grade fever for the past 1 month associated with intermittent cough for which he was treated with antibiotics and antifungals off and on. Vital parameters were normal except for mild fever of 100°F. Cardiovascular and central nervous system did not reveal any abnormality. Lungs showed signs of bilateral upper lobe consolidation and patient was given antibiotics and Voriconazole prophylactically. He was also given high dose of Antithymocyte immunoglobulin therapy for 5 days. Two days later patient developed slight abdominal distention and swelling of the right eye along with persistent cough.

Investigations showed a hemoglobin of 8.5 gm/dl, TLC count of 2400/mm³, platelet counts of 10,000/mm³ and raised BUN level of 18.4 mg/dl. Blood and urine cultures were sterile. Computed tomographic scans of thorax, brain and paranasal sinuses revealed infiltrates in bilateral lung fields, right sided maxillary and ethmoidal sinusitis, with total opacification of right ethmoidal air cells and right maxillary antrum. There was also mucosal discharge in right sided nasal cavity engulfing right middle and inferior turbinate. Serum for Galactomannan antigen was tested and it was positive with an index value of 2.16. Amphotericin B was added to his antifungal regimen.

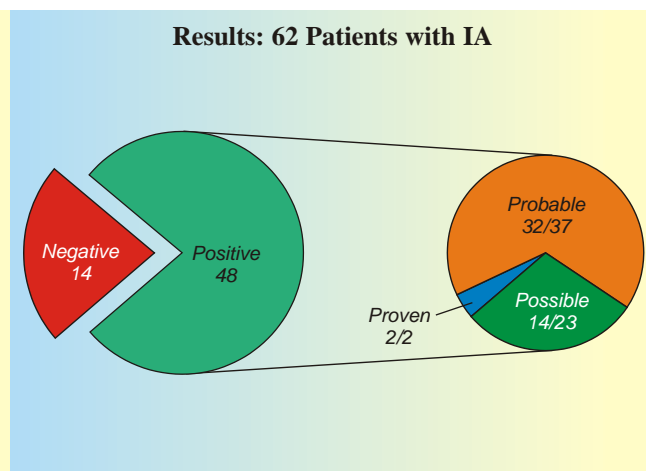
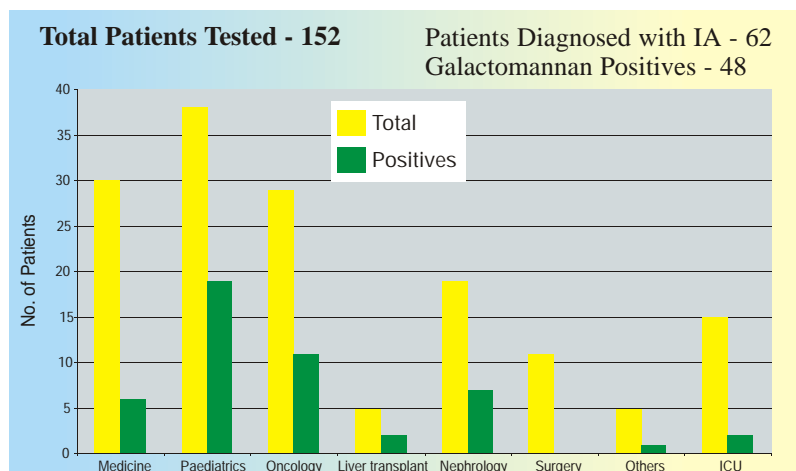
In spite of high dose antifungals being given to the patient, there was increasing pain in the eye with increased breathlessness for which he required ventilatory support and despite all measures died of cardio respiratory arrest on the 10th day of admission.

Discussion:

Invasive aspergillosis (IA) is one such major emerging opportunistic infection, among various categories of immunocompromised patients.¹ It occurs in 8%-15% of patients undergoing allogeneic stem cell transplantation,² and in 1%-15% of patients undergoing solid-organ transplantation.³ There is a 5-25% risk for development of Invasive Aspergillosis in patients of profound neutropenia due to a hematologic malignancy or aplastic anemia.^{4,5} Despite advances in therapy, IA is associated with considerable morbidity and mortality, ranging from 30% to 70% in transplant recipients.

Serological tests being non-invasive are a promising approach to an early diagnosis of IA. Those based on detection of anti-aspergillus antibodies have proved to be best non-invasive means of establishing the diagnosis of sub-acute invasive aspergillosis in non-neutropenic patients,⁶ but are unreliable in transplant recipients receiving immunosuppressive drugs. However, immunocompromised patients at risk of IA are not able to mount an antibody response against Aspergillus.

Detection of 1,3- β -D-glucan, present in cell wall of most fungi except cryptococcus and Zygomycetes has also been used as a

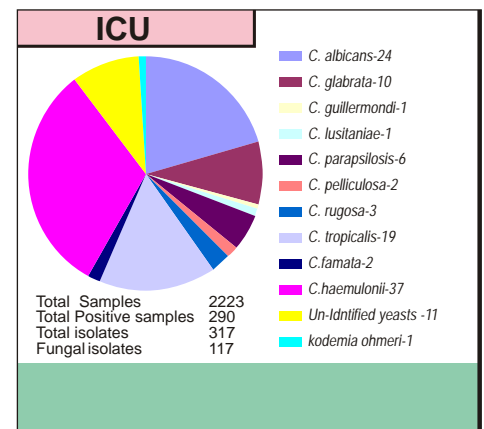
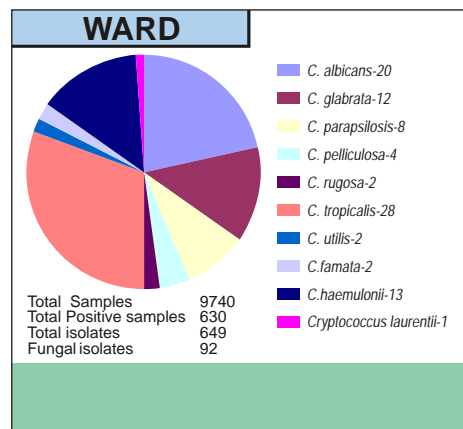
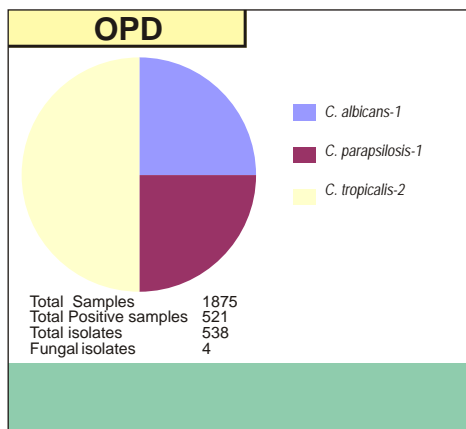


A nasal secretion sent for fungal examination revealed few septate branching hyaline fungal hyphae. Culture for fungi was also put up. A repeat Galactomannan antigen test done a week later was again positive with an index value of 1.64

The patient by this time developed breathlessness and a bronchoscopy was performed. BAL sample also showed the presence of moderate number of septate hyaline fungal hyphae. Biopsy of the tissue sample from right maxillary sinus revealed similar looking hyphae. Fungal cultures of all samples grew *Aspergillus fumigatus*.

diagnostic modality for fungal infections. But due to its presence in fungi other than Aspergillus, eg. Candida, its role in establishing a specific diagnosis of IA is limited.³ Aspergillus sp. produces D-mannitol which also has a potential to serve as a diagnostic marker for IA. But its use is limited because of the complexities of the measurements using gas liquid chromatography and mass spectroscopy. PCR-based molecular diagnostic tests have shown a low positive but high negative predictive value in diagnosis of IA. However, the lack of standardization of technical issues is a major

contd. on page 12



% Sensitivity in Yeasts Fungi* (Blood)

Species	Amphotericin B	Flucytosine	Fluconazole	Itraconazole	Voriconazole
<i>C albicans</i> (28)	100	100	100	89	100
<i>C tropicalis</i> (39)	100	100	90	49	97
<i>C parapsilosis</i> (6)	100	100	83.3	83.3	83.3
<i>C glabrata</i> (17)	100	100	59	31	100
<i>C.haemulonii</i> (24)	17	100	0	0	38
<i>Crypto. laurentii</i> (1)	100	100	100	89	ND**
<i>C. pelliculosa</i> (5)	100	33	60	0	100
<i>C. utilis</i> (3)	100	50	100	50	100
<i>Kodomea ohmeri</i> (1)	100	100	100	100	100
<i>C guillermondi</i> (1)	100	100	0	0	0
<i>C rugosa</i> (2)	100	100	100	100	100
<i>Un-Identified yeasts</i> (20)	95	85	40	30	70

Figures in parenthesis indicate the number of isolates tested.

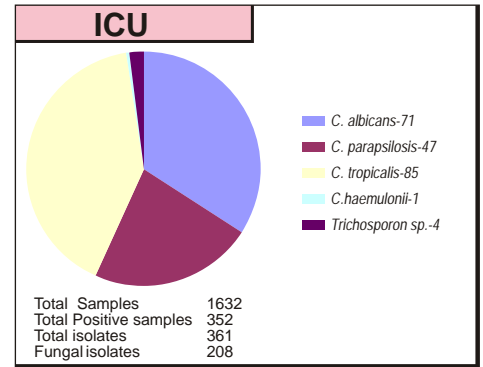
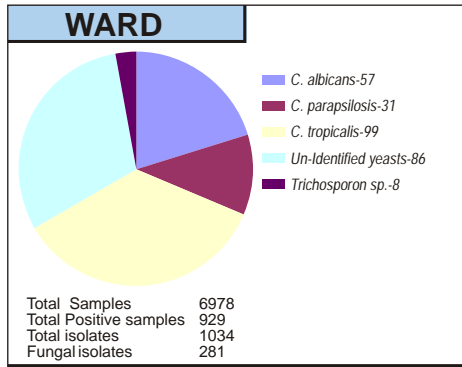
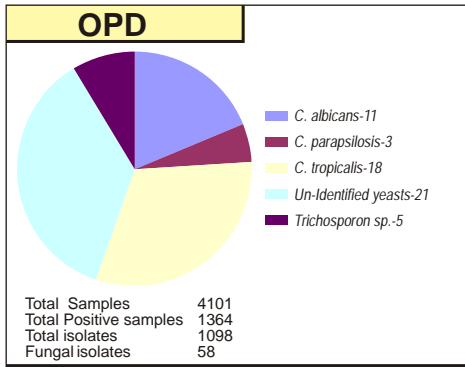
Note: 3 Isolates of *Cryptococcus neoformans* were isolated from CSF samples and all were sensitive to the above drugs tested.

*ATB fungus 3 (bioMerieux, France), E Test (Rpt. isolates excluded), CLSI M-39A Vol. 22, No. 8; 2002 (global consensus guidelines).

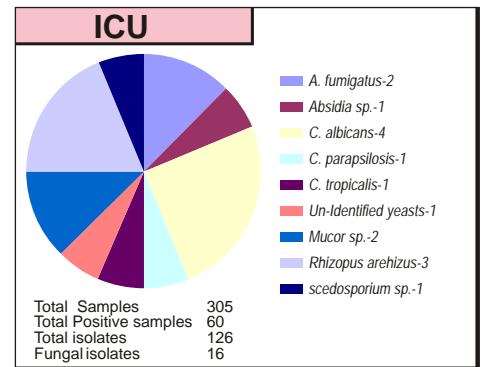
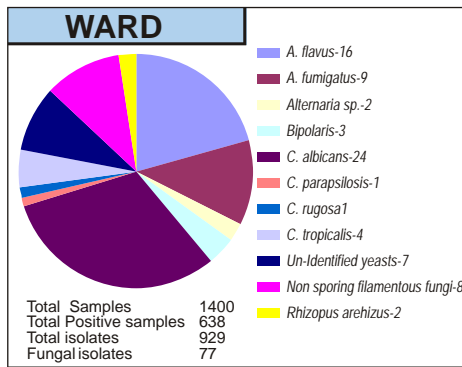
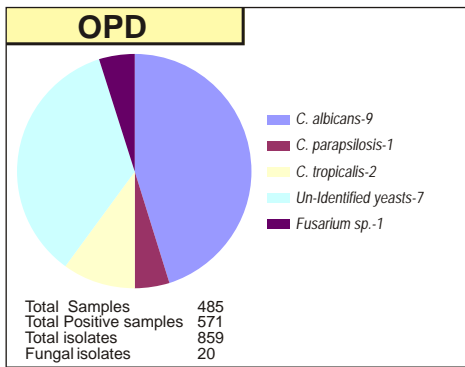
** Not done.

78.8% yeast isolates were *Candida* non-*albicans*, almost similar to that of test previous year (82.5%) *C. tropicalis* was the most common species isolated from patients in admitted in wards whereas *C. haemulonii* emerged as the leading isolate in ICU settings.

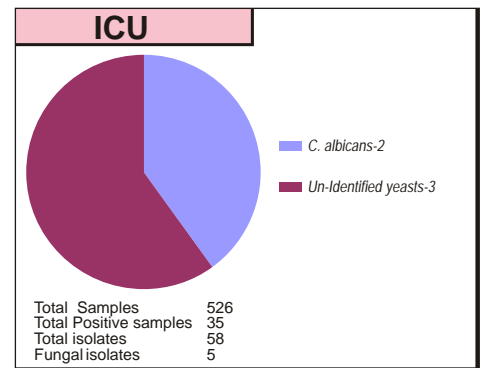
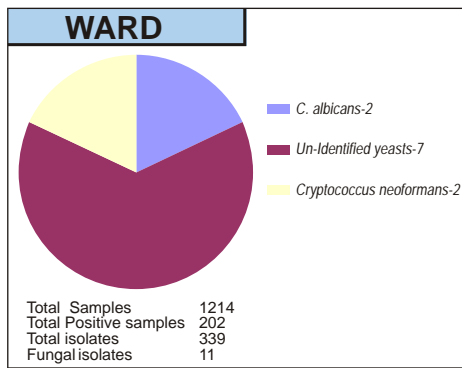
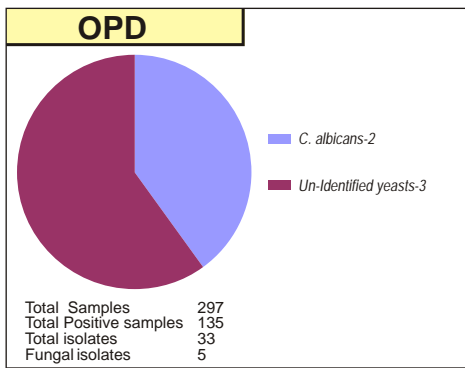
Urine



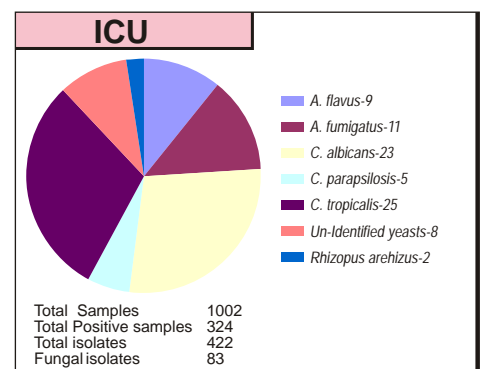
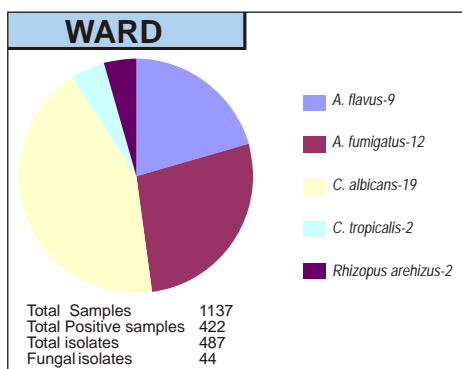
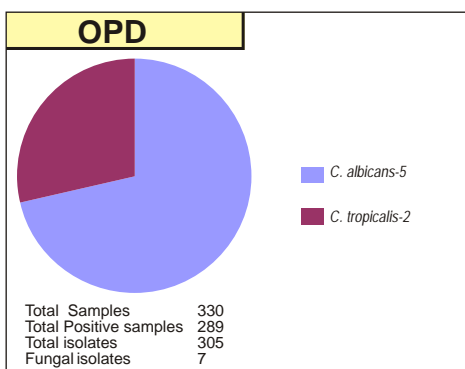
Pus & Tissue



Body Fluids

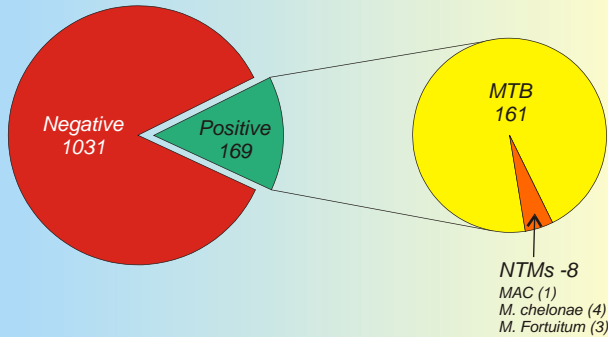


Respiratory Isolates

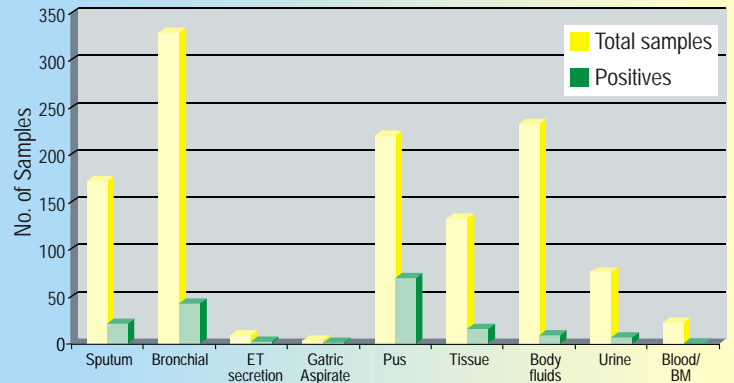


AFB CULTURE

Total Samples Tested: 1200



Culture Positives



BacT/ALERT-3D v/s LJ Medium

Total Samples Cultured (both media): 434
Total isolates: 68

Mycobacterial sps (n)*	Positive specimens detected by	
	BacT/ALERT 3D	LJ
<i>M. tuberculosis complex</i> (64)	64 (100)	48 (75)
Smear Positive (37)	37	32
Smear Negative (26)	27	16
NTM (4)	4 (100)	4 (100)
<i>M. avium-intracellulare</i> (1)	1	1
<i>M. chelonae</i> (2)	1	1
<i>M. fortuitum</i> (1)	1	1
Total (68)	68 (100)	52 (76.4)

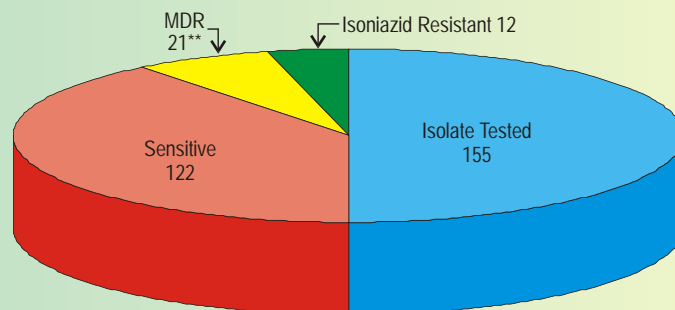
* Using AccuProbe (bioMeurieux, France)

Time to Positivity

Total Isolates Recovered on both Systems: 52

Sample	Smear status	Mean time to positivity (days)	
		BacT/ALERT 3D	LJ
Pulmonary (21)	Positive	13.8	23.62
	Negative	22.8	29.4
Extra Pulmonary (31)	Positive	15.78	25.15
	Negative	24.6	33.58
All Samples (52)	Positive	14.9	24.4
	Negative	24.1	32.35

Sensitivity of *M. tuberculosis**



Mycobacteriology Assays available at SGRH

- AFB smear (ZN/DF).
- AFB culture (BacT/ALERT-3D & LJ).
- Mycobacterial Identification by AccuProbe.
- Genprobe - Direct Nucleic Acid amplification.
- Quantiferon TB Gold Assay.
- Mantoux test.

*1% Proportion Method.

** No clear distinction between primary and acquired resistance was possible to determine, though 4 patients were previously on ATT.

Direct Nucleic Acid Detection for *M. tuberculosis* Amplified Mycobacterium Tuberculosis Direct (AMTD) Test

(Gen-Probe Inc., bioMerieux, France)

Two tests have been cleared by the U.S. Food and Drug Administration (FDA) for direct detection of MTBC in respiratory specimens: Amplified Mycobacterium Tuberculosis Direct Test (MTD) (Gen-Probe Inc., bioMerieux, France) and AMPLICOR *Mycobacterium tuberculosis* Test (Roche Diagnostic Systems, Inc., Indianapolis, IN). Following the initial FDA clearance, Gen-Probe enhanced the MTD, increasing sensitivity and decreasing technical time. In September 1999, the enhanced version of the MTD (AMTD) was approved by the FDA for testing respiratory specimens, regardless of the AFB smear results.

There is considerably less experience with direct detection of MTB in extra-pulmonary specimens. Paradoxically, it is the extrapulmonary situation of TB, for which a rapid and accurate laboratory diagnosis is often sought for, since the traditional techniques of detecting AFB have failed to deliver due to the small amount of bacteria normally present in these type of specimens, thus prompting the adaptation of these techniques to non respiratory specimens. Hence, in-house validation is needed for using these for nonrespiratory specimens.

The enhanced Amplified Mycobacterium Tuberculosis Direct (AMTD) test uses transcription-mediated amplification and hybridization procedures to qualitatively detect *M. tuberculosis* complex (MTBC) rRNA. Compared to culture, the sensitivity of the MTD test ranged from 65 to 97% in different studies, whereas its specificity was always high. It is well recognized that variability in laboratory methods, TB prevalence, and prevalence of other mycobacterial diseases in a specific local area may all have a substantial impact on the predictive values of the AMTD test. Consequently, it is important to collect information on the performance of the AMTD test in local settings and to provide this information to clinicians.

AMTD (GenProbe) for Tuberculosis

(Jan. 2006 - Dec. 2007)[#]

Sample	Smear Status	No. of Samples	Positives	Indeterminate	Negative
Pulmonary (39)	Positive	20	16	0	4*
	Negative	19	4	0	15
Extra Pulmonary (202)	Positive	26	24	0	2**
	Negative	176	28	7	141

Sensitivity: 93.4%

Sensitivity: 82.9%

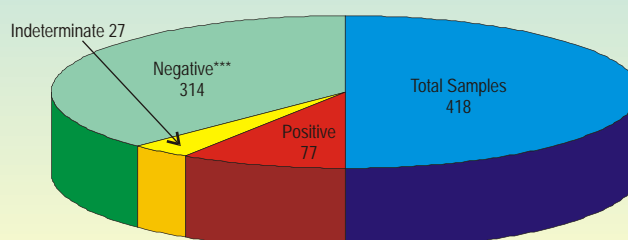
*Three samples grew NTM

**One sample from a patient on ATT

QuantiFERON - TB Gold In-Tube Assay

QuantiFERON - TB Gold in-tube test, a FDA approved indirect test is used as an aid in diagnosing *M. tuberculosis* infection, including latent and active tuberculosis. This test detects the release of interferon-gamma (IFN- γ) in fresh heparinized whole blood from sensitized persons when it is incubated with mixtures of synthetic peptides representing three proteins present in *M. tuberculosis*: early secretory antigenic target-6 (ESAT-6), culture filtrate protein-10 (CFP-10) and TB7.7 (p4) proteins. Because these proteins are absent from the BCG vaccine strains and from commonly encountered nontuberculous mycobacteria, except *Mycobacterium kansasii*, *Mycobacterium szulgai*, and *Mycobacterium marinum*, QFT-G is expected to be more specific for *M. tuberculosis* than tests using tuberculin PPD as the antigen. However, it does not differentiate between latent and active TB disease. A positive result should not be interpreted in isolation. A negative result does not preclude the possibility of *M. tuberculosis* infection or disease. An Indeterminate result suggests that the test results cannot be interpreted as a result of low mitogen response, possibly due to poor CMI or high background due to excessive levels of circulating non-specific gamma interferon.

QuantiFERON - TB Gold (Oct. 2006 - Dec. 2007)[#]



Total samples	418
Positive	77
Indeterminate	27
Negative	314

[#]Microbiology Newsletter SGRH (Vol. 13:No.1), 2007

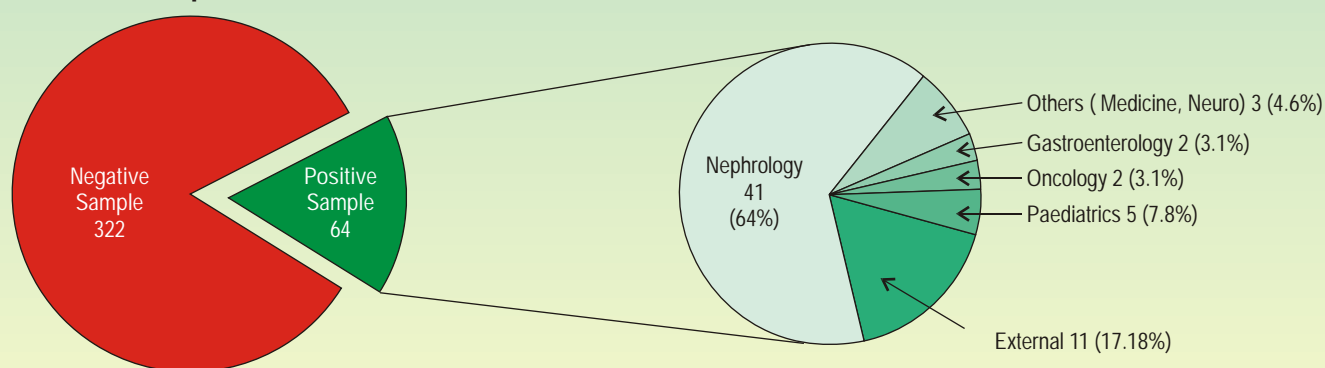
*** True negatives are ascertained by using a mitogen tube for every sample.

NASBA

NucliSENS CMV pp67 measures replication of CMV in blood and body fluids. Using the well-established NASBA RNA amplification technology, this assay detects messenger RNAs coding for the matrix tegument protein pp67 of CMV, a true late protein, which is only expressed during viral replication. The NASBA technology selectively amplifies RNA in a DNA background and allows direct testing in whole blood. The NucliSENS CMV pp67 assay offers both the diagnostic laboratory and the clinician a new tool for CMV diagnosis - for both diagnosis of active CMV infection and monitoring treatment efficacy.

It is a FDA approved assay for the qualitative detection of pp67mRNA in patients having CMV viraemia and HIV quantization.

Total Samples 386



Total Sample	Positive	Nephrology	External	Paediatrics	Oncology	Gastroenterology	Others (Medicine, Neuro)
386	64	41 (64%)	11 (17.18%)	5 (7.8%)	2 (3.1%)	2 (3.1%)	3 (4.6%)

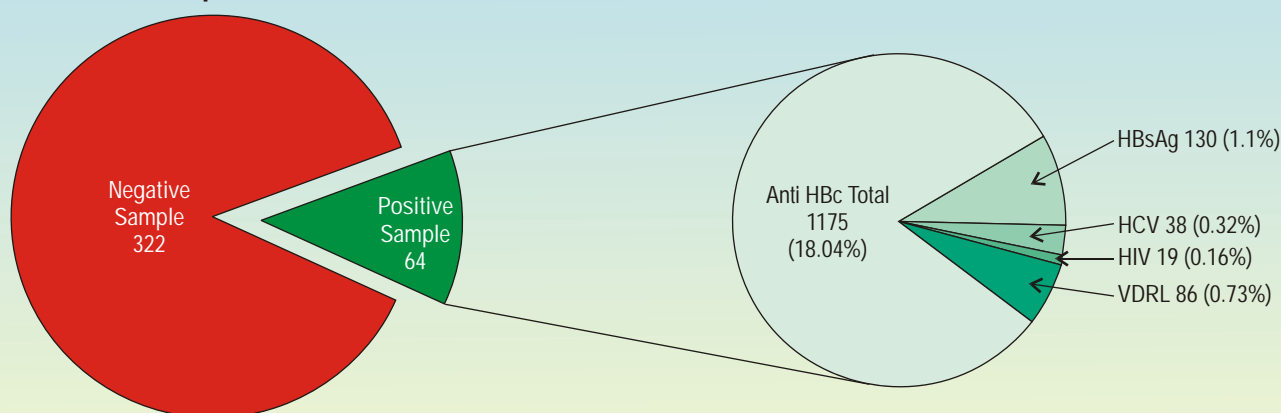
Note: NASBA is being (upgraded) to Real Time NASBA (Nuclisens Easy Q-NASBA) indue course of time.

Status of Transfusion Transmissible Infections among Blood Donors at SGRH

(Jan. - Dec. 2007)

Screening of blood donors for transfusion transmissible infections is an important tool to achieve the goal of safe blood transfusion. The status of these infections among blood donors at Sir Ganga Ram Hospital, from Jan. 07 Dec 07 has been recorded and analysed.

Total Samples 11654



Total Sample	Positive	HBsAg	HCV	HIV	VDRL	Anti HBc Total*
11654	1448	130 (1.1%)	38 (0.32)	19 (0.16%)	86 (0.73%)	1175 (18.04%)

*6512 Samples were screened for Anti HBc (Total) from May 2007.

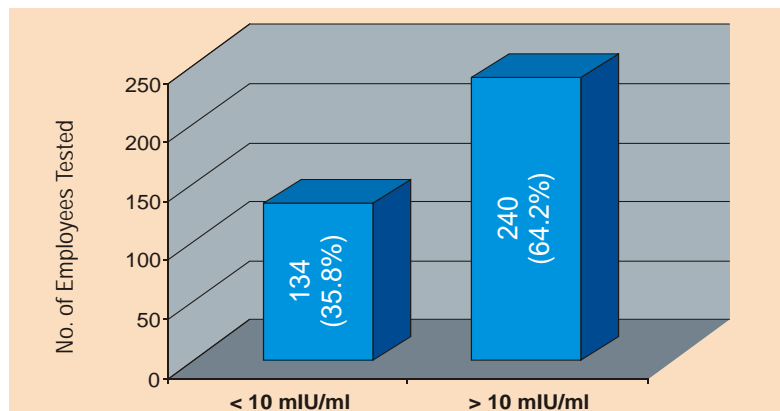
Note: NAT testing for blood bank to start indue course of time.

Pre-vaccination Screening of High Risk Hospital Population for Specific Anti HBV Antibody

(Jan. - Dec. 2007)

An anti-HBsAg level of greater than or equal to 10mIU/ml is recommended by ACIP (Advisory committee on immunological practices) as standard for demonstrating post vaccination protection for hepatitis B virus. Total hospital employee 374 screened between Jan 07 - Dec 07 of which 240 had protective levels. The rest 134 needed vaccination. The HBs Ag screening test was avoided on the patients with protective levels thus decreasing the expense on the cost per assay and the work load of the department.

Total Employee screened 374, 35.8% needed vaccination and the rest (64.1%) had protective antibodies.



TORCH Assay / Avidity Testing

(Jan. - Dec. 2007)

Seroprevalance of TORCH was almost similar to the previous year.

Avidity assays have shown promise in distinguishing recent primary infections from past infections and has often shown to correlate with patient viraemia.

We have started doing the Avidity tests for CMV, Rubella, Toxoplasma which helps differentiating primary recent from past infections. The assay should be done on patients with both IgM and IgG positive status in the first trimester following the screening of TORCH. The data for Avidity Assay will be reflected in 2008 Newsletter.

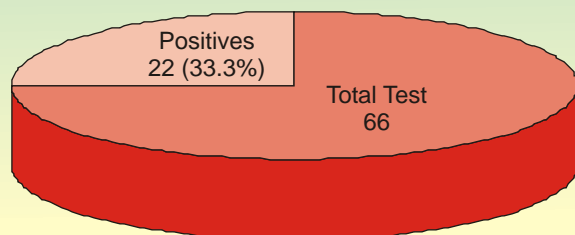
Name of Test	Total	Obs. & Gyn.	IgM (%) Positive		IgG (%) Positive	
Toxo	932	800	14	1.7%	78.4	9.8%
CMV	2412	1500	29	1.91%	1332	88.8%
Rubella	1800	1500	17	1.1%	1320	88%
Herpes	3616	800	352	44%	224	28%

The TORC assays are done by MINIVIDAS which uses an automated Enzyme linked Immunofluorescent assay. Herpes assay is done by ELISA.

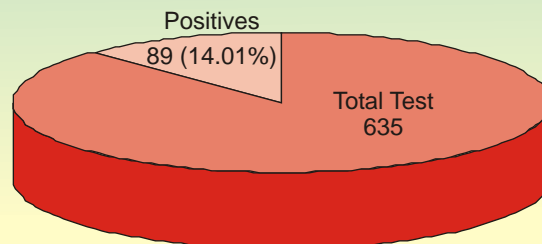
Dengue

(Jan. - Dec. 2007)

Dengue Antigen



IgM Dengue Antibody



Enzyme-linked immunosorbent assay (ELISA) directed against the NS1 antigen has demonstrated high concentrations of this antigen in the sera of dengue virus-infected patients during the early clinical phase of this disease.

Dengue NS1 Ag test (BioRad) and MAC ELISA (Pan bio Diagnosis) are currently routinely used for the serodiagnosis of dengue fever; however, the IgM antibodies do not usually become positive before 5 days of fever. NS1 is detected concomitant with viremia and may be detectable even when RT-PCR is still negative suggesting that NS1 protein may circulate at higher levels than virus particles. NS1 appears in the sera before IgM antibodies.

Though NS1 antigen and IgM antibodies both develop during the acute phase, but from day1 to day3, NS1 in our hands, was found to be more sensitive.* The use of NS1 detection as a first-line test during the first 4 days of fever could help in earlier diagnosis of dengue fever.

* "Evaluation of Dengue NS1 Antigen detection in the diagnosis of dengue virus infection".
Poster presented in Indian Institute of Science, Bangalore 2006.

Tests for Syphilis

(Jan. - Dec. 2007)

TESTS AVAILABLE:

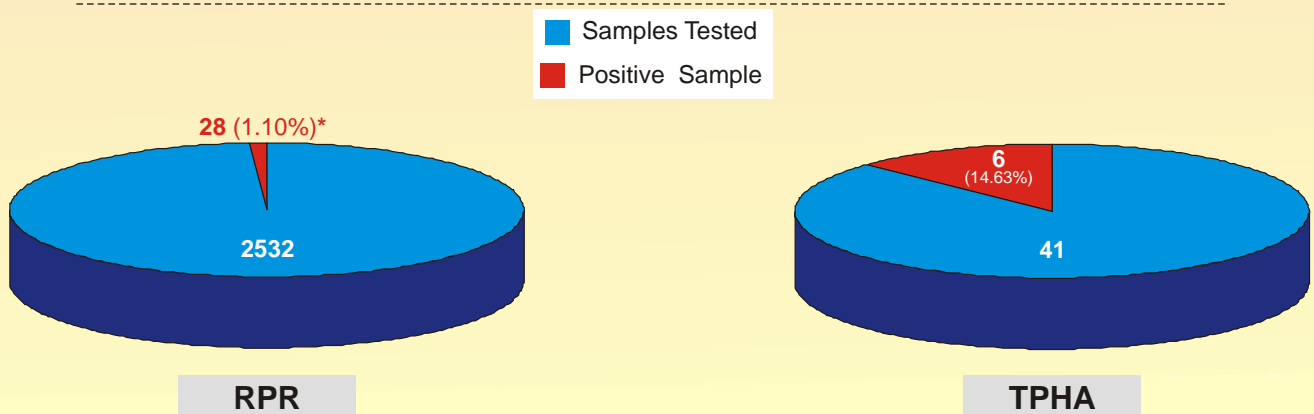
1. Rapid Plasma Reagin (RPR) Test
2. Treponema Pallidum Haemagglutination (TPHA)

Rapid Plasma Reagin (RPR)

The conventional VDRL test was replaced with RPR for the screening of blood donors and pregnant women from 2004 onwards. In the year 2007 a total of 2532 samples mainly obtained from the department of Obstetrics and Gynaecology, of our hospital were screened by RPR. Out of them 28 (1.10%) were reactive. The percentage reactivity detected last year was almost in the same range i.e. 1.95%.

Treponema Pallidum Haemagglutination (TPHA)

All RPR reactive patients are tested by TPHA for the confirmation of syphilis. In the year 2007, only 41 samples were tested by TPHA, of which 06 were found positive for *Treponema pallidum* antibodies.



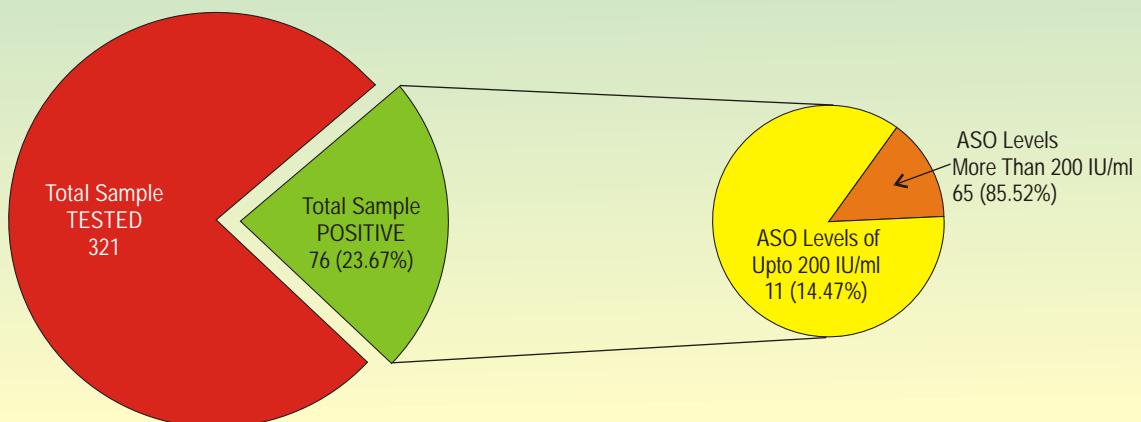
*Out of these 28, only 10 were tested by TPHA and only 02 (20%) were found positive.

Test for Group A - Streptococcus

(Jan. - Dec. 2007)

Anti-Streptolysin O - Test (ASO)**

Elevated levels of ASO (> 200 IU/ml) indicate acute infection. ASO levels are also monitored for impact of treatment. A total of 321 samples were tested, of which 20.24% showed raised ASO (> 200 IU/ml) levels. There was no significant difference between the percentage positivity of the year 2006 (21.79%) and 2007 (23.67%). However the percentage of patients with ASO levels more than 200 IU/ml was significantly higher in the year 2007. It may be due to the change in detection system from the slide agglutination test to nephelometric system, which is more sensitive and accurate.



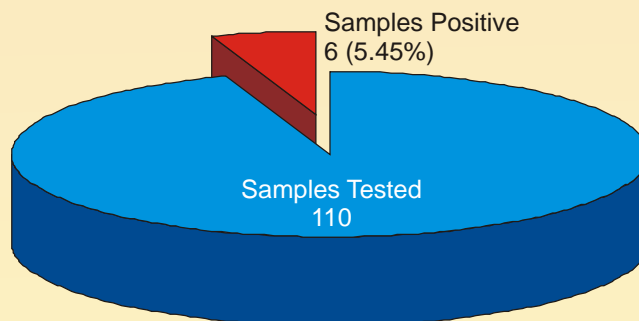
**From June 2007, the ASO testing has been replaced with Nephelometry detection system.

Test for Detecting Anti-Leptospira Antibodies

(Jan. - Dec. 2007)

Lepto Tek Dri-Dot

The Lepto Tek Dri-Dot assay is aimed at the detection of *Leptospira*-specific antibodies, i.e. total immunoglobulin, in human sera. The percentage positivity is comparatively less as compared to last year (9.37%).



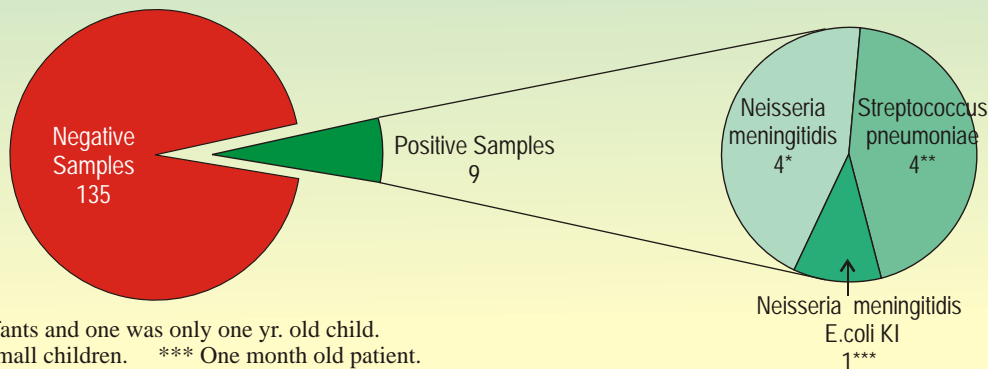
Test for Detecting Bacterial Antigen in C.S.F.

(Jan. - Dec. 2007)

Bacterial Antigen Test

The percentage positivity is significantly less as compared to last year. It was 22.34% in 2006 where as it is only 6.66 % in 2007. It was probably due to the higher prevalence of *Neisseria meningitides* cases in Delhi during the year 2006.

Total CSF Samples Tested: 144



* 2 out of 4 were infants and one was only one yr. old child.

** 2 out of 4 were small children. *** One month old patient.

Complement Levels

TESTS AVAILABLE: Detection of C3 and C4 Levels in Blood by Nephelometry.

C3 and C4 Levels:

Raised C3 and C4 levels are found in acute phase reactions and in chronic inflammation. Decreased serum C3 and C4 levels are associated with Factor I deficiency, recurrent infections, Systemic Lupus Erythematosus (SLE), Glomerulonephritis and repeated infections. Raised C3 and normal C4 indicates an acute phase response e.g. RA. Low C3 and/ or C4 suggest immune complex mediated disease phase or complement activation. Low C3 and C4 levels may also be found in pneumococcal infection, gonococcal infection, cirrhosis, and post splenectomy, and connective tissue disorders etc. Decreased C3 in the presence of normal C4 is seen in Gram-negative septicemia and membranoglomerulonephritis. Normal or raised C4 occurs in RA. In hereditary angioedema C4 levels are decreased during attacks whilst C3 levels remain normal. Thus detection of C3 and C4 levels is very helpful in the diagnosis and management of various diseases. We are detecting these complement levels by Nephelometry.

NAME OF THE TEST	TOTAL SAMPLES	NORMAL LEVELS	RAISED LEVELS	REDUCED LEVELS	NORMAL VALUES (MG/L)*
C3	472	112	151	209	Male: 970-1576 Female: 1032-1495
C4	403	191	102	110	Male: 162- 445 Female: 167- 385

*Source Product Insert of The Binding Site.

Diagnosis of Rheumatoid Arthritis

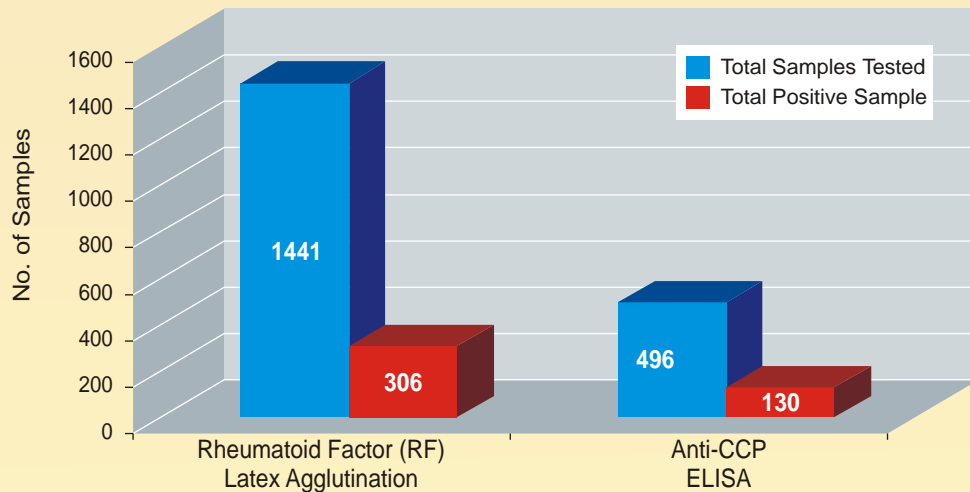
TEST AVAILABLE: 1. Rheumatoid Factor (RF) Test

2. Anti-CC Plus ELISA Test

The concomitant presence of RF and Anti-CCP antibodies has higher specificity for Rheumatoid Arthritis (RA). Therefore, a combined testing for Anti-CCP antibodies and RF may be helpful in the diagnosis of RA. Considering the importance of Anti-CCP as an early marker of the disease and a test with higher specificity, an ELISA test for the detection of Anti-CCP antibodies in suspected RA patients was introduced in the year 2005. From June 2007 the Slide test for RF was replaced by Nephelometric detection system. There was no significant difference in the results when compared to previous year results.

Results of Rheumatoid Factor (RF) Nephelometric latex agglutination test and Anti-CCP Elisa for Rheumatoid arthritis for the year 2007.

RF and Anti-CCP ELISA (Jan. - Dec. 2007)



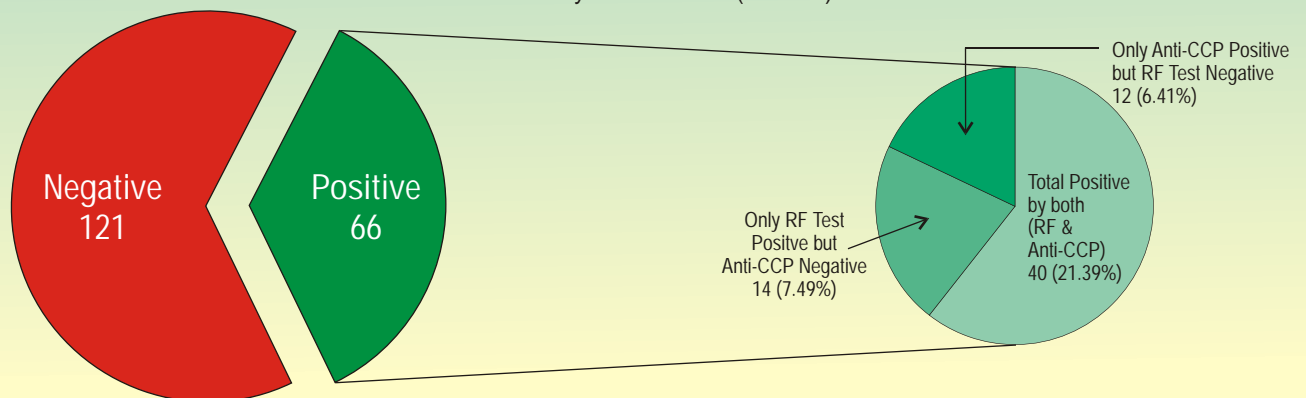
Comparison of Anti-CCP ELISA Test with RF Factor Test

(Jan.-Dec. 2007)

Total No. of Samples Tested by both RF Test and Anti-CCP ELISA = 187

Total Positive by Anti-CCP = 52 (27.08%)

Total Positive by RF Test = 54 (28.87%)



Cryptococcal Antigen Assay

(Crypto-LA Test, Laboratories Fumouze, France)

(Jan. - Dec. 2007)

	Total Samples	Positive Samples	Percentage %
CSF	119	4*	3.36%

*3 Samples grew *cryptococcus neoformans*

Following tests are available in our department.

1. Microscopical Tests:

- i) Direct stool microscopy for parasite ova/cyst
- ii) Formal Ether Concentration Method
- iii) Kinyoun's staining for *Cryptosporidium*/ *Microspora*/ *Isospora* sps. etc.
- iv) Direct smear from Liver abscess aspiration for seeing amebic trophozoites
- v) Direct smear from Hydatid fluid/Sputum for seeing hooklets and scolices.

2. Serological Tests:

Quantitative Antibody (IgG) detection assay for Amebiasis, Echinococcosis and Cysticercosis by ELISA.

Stool Microscopy Findings:

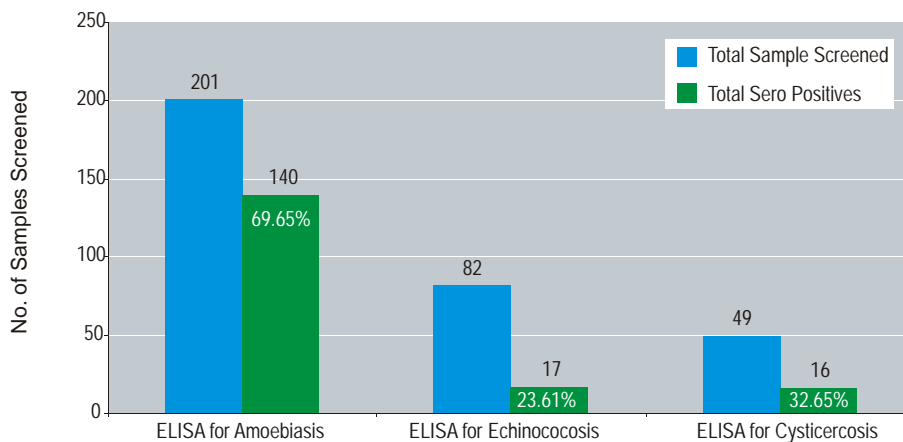
Total Sample Screened	Positive for WBC/RBC	Type of Ova / Cyst Found						Samples screened by Kinyoun's for <i>Cryptosporidium</i> Oocysts	
		<i>Giardia</i>	<i>Entamoeba histolytica</i>	<i>Hymenolepis nana</i>	<i>Ascaris lumbrocoides</i>	<i>Hook worm</i>	Total Positives	Total Samples	Total**** Positive Samples
844*	246 (29.14)**	30	2	6	5	2	45 (5.33)**	112	80 (71.04)**

*This data is only from July to Dec. 2007

**Figures in parenthesis show percentage (%).

*** More specific assays are in pipeline.

Parasitic Serology Results:



Name of Test	Total Sample Screened	Total Sero Positives	Percentage Sero positivity
ELISA for Amoebiasis	201	140	69.65%
ELISA for Echinococcosis	82	17	23.61%
ELISA for Cysticercosis	49	16	32.65%

Invasive Aspergillosis - A Diagnostic Challenge

(contd. from page 1)

barrier for widespread application of PCR.⁹ Thus, the focus in studies is on detection of circulating *Aspergillus* antigens, particularly galactomannan (GM), in blood and body fluids (CSF, serum, urine, or bronchoalveolar lavage).^{2,7,8}

Galactomannan is a heat stable hetero polysaccharide cell-wall component of *Aspergillus* produced in vivo and can be detected in biological fluids as well. Many serological tests have been developed for detection of GM in high-risk patients of IA.³ The GM assay (Platelia *Aspergillus* EIA kit, Bio-Rad, France) employs a double-sandwich ELISA that incorporates the -1-5 galactofuranose specific EBA2 monoclonal antibody as both the detector and acceptor for galactomannan. The double sandwich ELISA test has a high sensitivity with a threshold of 0.5-1.0 ng/ml.³

Studies evaluating the role of Galactomannan have largely been done in patients undergoing chemotherapy for cancer or transplant recipients. A sensitivity of 67-100% and specificity of 86-98% has been documented.³ When serially monitored the test has preceded the diagnosis on basis of radiologic examination or *Aspergillus* isolation by 6-14 days. Sensitivity of 55.6% and specificity of 93.9% has been documented in liver transplant recipients.¹⁰ Lung transplant recipients have a sensitivity of 30% but a high specificity of 95% with this assay.¹¹ In neutropenic or leukemic patients the antigen test has a sensitivity of 93% and a specificity of 95%.¹²

Inadequate sampling strategies could conceivably compromise clinical sensitivity; the optimal sampling frequency for screening has not been rigorously defined but twice weekly determination of antigen levels has been generally used in high risk patients.

The use of antifungal agents may lower Galactomannan levels by reducing the fungal load. The specificity of Galactomannan in neonates and children appears to be lower, which is possibly due to ingestion of extraneous Galactomannan in food and water and translocation across a damaged or immature gut wall.¹³

Though cross reactivity has been noted with *Penicillium* species, but is of little clinical relevance as they are rare pathogens in humans. False positive results with concomitant use of piperacillin-tazobactam has been reported.¹⁴ Reactivity is less likely in samples collected at trough levels or prior to administration of dose.

Out of 152 patients tested in year 2007 at SGRH, 62 patients were diagnosed as having IA and were categorized into proven, probable and possible cases as per EORTC/ MSG criteria.¹⁵ In these, galactomannan antigen was positive in 2/2 proven, 32/37 probable and 14/23 possible cases showing sensitivities of 100%, 86.4% & 60.8% respectively.

The use of GM assay for screening and diagnosis of IA is attractive as it may detect evidence of IA before the clinical signs and symptoms in high-risk patients are seen.² Besides being used as a prognostic tool, it has been suggested that the GM assay should be routinely used when there is a high pretest probability of IA.

Reflections

Thanks for your (SGRH) Newsletter of May 2008. It is good as usual. The cases of Brucellosis are interesting. I was wondering if *Brucella* Serology is not included in your PUO screen.

Lt. Gen. D. Raghunath

Dir Dorabji Tata Centre for Research in Tropical Diseases, Bangalore

Thank you very much for having me on your mailing list. Your articles be it Dengue or Brucellosis are wonderful and extremely informative. I wish this kind of information is available in more widely read medical publications for better reach in general medical practitioner. Your department is doing great job in field of Microbiology. Keep it up...

Dr. K.K. Garg, Pvt Practitioner

Kindly accept my sincere thanks in response to the Microbiology Newsletter. I regularly read on your website.

It's beautiful experience to read it and take on with the comprehensive database.

Dayal Mehta, Superhouse Group, Noida

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