

MDCH Sponsors Bioterrorism Exercise

James Rudrik, Ph.D.
Microbiology Section

On June 3, 2003 the Michigan Department of Community Health (MDCH) held a Strategic National Stockpile (SNS) functional exercise in the greater Lansing area (Ingham, Barry, Eaton, and Clinton counties). The purpose of the exercise was to test procedures to request, receive, and distribute the SNS. The SNS is a containerized system for distribution of pharmaceuticals and medical supplies that can be deployed from strategic locations anywhere in the United States within 12 hours following a terrorist attack using biological or chemical agents. The exercise involved personnel from the Centers for Disease Control and Prevention (CDC), Department of Justice (DOJ), Federal Bureau of Investigation (FBI), Michigan State Police (MSP), Michigan National Guard, area hospitals, MDCH staff from the Office of Public Health Preparedness (OPHP), Bureau of Laboratories (BOL) and Bureau of Epidemiology (BOE), emergency management, law enforcement and health departments for the counties involved.

While the main thrust of the exercise was to test the plan for deploying the SNS, the BOL simultaneously conducted an exercise at four Level A laboratories and at the Level B/C lab in Lansing. Each Level A laboratory was given Gram stain slides and culture plates for five patients. The laboratories were asked to review the Gram stains and plates and then describe how they would handle each culture. A representative from the BOL was on-site to provide additional subculture plates and give the results of any biochemical test(s) requested. The goal was to

have the laboratory recognize a potential agent of bioterrorism and take appropriate action. Two of the four laboratories quickly made a presumptive identification of *Francisella tularensis*, notified appropriate authorities and packed the specimen for delivery to a Level B lab. The state emergency courier system was called to transport a sample from the Jackson area to Lansing for confirmation. Once samples reached the laboratory in Lansing, molecular and conventional tests confirmed the identification of *Francisella tularensis* within two and a half hours.

This exercise demonstrated that good preparation is the key to a safe and successful outcome. How prepared is your laboratory? Here are some simple steps to assure your laboratory is prepared:

- 1) Each laboratory should have written procedures for the presumptive identification of *Bacillus anthracis*, *Yersinia pestis*, *Francisella tularensis*, *Brucella* spp., *Burkholderia mallei* and *Burkholderia pseudomallei*.
- 2) Laboratories should have written specimen collection and transport guidelines for *Clostridium botulinum*, *Variola virus* and all the agents listed above.

- 3) Laboratory staff should have access to a list of contact numbers that, at a minimum, includes the hospital infection control practitioner, the nearest Level B lab, the local health department and the after hours emergency number for MDCH. Staff should know whom to call when, and if, a potential agent of bioterrorism is isolated.
- 4) One or more individuals must be certified to pack and ship infectious substances. Any infectious agent shipped from your laboratory by mail or commercial carrier is subject to stringent federal regulations. Any patient specimen that may contain an agent of bioterrorism or any suspect isolate must be packaged as an infectious substance. (See page 4)
- 5) Appropriate safety precautions should be followed. Any procedure that may create an aerosol (e.g., subculture of a positive blood culture bottle) should be performed in a biological safety cabinet using a gown and gloves. Avoid sniffing plates, particularly plates that contain organisms that require incubation of 48 hours or more to see visible growth. All slow growing, gram-negative organisms should be suspect for *Brucella* or *Francisella* and should be handled in a biological safety cabinet using appropriate personal protective equipment.

Once these procedures are in place, they should be reviewed and updated on an annual basis. They offer a convenient format for annual safety and emergency preparedness training. MDCH sponsors educational programs or can direct you to the resources needed for Level A laboratories to quickly and safely recognize the agents of bioterrorism. For additional information, please contact Valerie Reed, Laboratory Bioterrorism Training Coordinator at 517-335-9653 or at reedv@michigan.gov.



Feedback on SNS Exercise

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On June 3, MDCH coordinated an exercise of the Strategic National Stockpile (SNS) in a four-county region in Mid-Michigan to test preparedness to respond to a bioterrorism incident. The laboratory component of that exercise is detailed on pages 1 and 2 in this issue. As part of the laboratory exercise, a broadcast fax alert was sent to all clinical microbiology laboratories in the state when identification of the organism had been made at MDCH. As part of the analysis of the readiness drill, a second fax was sent the next day asking for feedback on the handling of the notification fax the previous day.

A total of 164 facilities received the fax. Although a number of these facilities do not have on-site microbiology services, almost 70 percent (110) have complete microbiology services. By June 10, responses had been received from 105 of the 164 facilities, the majority from those with full-service microbiology. Sixty-two (59%) of the responses were returned on the day the feedback request was sent. Two respondents did not receive the original fax for 24 hours; five did not receive for 48 hours; one had not received after 72 hours and one was not received for 6 days due to vacation.

As this was labeled as an exercise, people may have handled this differently than a real event. In general, the response was very good. One respondent bravely indicated the fax had not been read. Twenty-four (23%) indicated they read and shared (or would share such notices if real) within their laboratory, while 64 (61%) indicated they did or would share beyond their laboratory with other hospital or facility departments such as Infection Control, Emergency Department or Safety and Security. These responses suggest microbiologists are knowledgeable as to their pivotal role in emergency preparedness.

A number of the comments indicated the fax came too late in the day to be read or to share with other departments or administration, some of which had left for the day. For this exercise the natural unfolding of events were allowed to direct the timing of the communication. The isolates were received at the MDCH lab via emergency courier by late morning. Identification was complete by early afternoon and the fax written and sent within one hour. This exercise points to a weakness in the communications network regarding the conveying of vital information after 3:00 PM. Redundancies built into the Health Alert Network (HAN), a statewide communications system being

implemented, will help address this, as each Level A laboratory, Emergency Department and Infection Control Office will receive alerts directly. MDCH expects to maintain the fax or e-mail link with microbiology departments providing technical updates. Meanwhile, supervision should examine the ability to receive and act upon critical information received after hours or in the absence of supervisory personnel.

Your time in responding to this request for feedback and the helpful comments made were appreciated. Comments will be summarized and included in the report of this exercise to state and federal agencies.

Events in the last several years have demonstrated the importance of emergency preparedness to clinical microbiologists. Anthrax was followed by West Nile Virus, SARS and monkeypox. The clinical microbiology laboratory played a vital role, not only in diagnosing these diseases, but also in communicating timely and accurate information to the medical communities. In an era of emerging infectious diseases, the value of well-trained and well-informed clinical microbiologists will only grow.

Cumulative Antibiogram Data Proves Useful

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CDC has undertaken several initiatives to strengthen and improve the Laboratory Response Network, including a national pilot Microbiology Quality Assurance (QA) project in Michigan. The first year of this QA project reinforced the belief that many clinical microbiology laboratories face difficulties implementing new initiatives and directives. This partnership with CDC affords Michigan the unique opportunity to have input on the national level. MDCH is interested in learning more about what specific hurdles and barriers laboratories face, so that national policymakers get a true picture of the state of our clinical microbiology laboratories.

MDCH chose to look at statewide antimicrobial susceptibility data by collecting antibiograms, to see if meaningful statewide data could be determined, and also whether antibiograms can be used as tools to measure quality improvement. Microbiology laboratories in Michigan were asked to voluntarily submit antibiograms from years 2000-2001 to MDCH. Representative

antibiograms were obtained from 34 of the estimated 108 laboratories that perform susceptibility testing. Twenty-three labs provided data from 2000 and 33 from 2001. Data collected was prior to the publication of the NCCLS document M39-A (May 2002). This is a new guideline for the standardized analysis and presentation of antimicrobial susceptibility testing data.

Laboratories were assured that confidentiality would be strictly maintained if the antibiogram data were to be used for any purpose other than internally at MDCH. No characteristics that could identify the facility would be revealed without permission from the submitting laboratory. The determination of statewide statistics is challenging, but may provide useful data for key select organisms such as MRSA and VRE.

In reviewing these data, we discovered some issues, many of them minor, but also a few major errors that could potentially impact patient care. These errors may demonstrate some fundamental challenges present in the current microbiology laboratory environment. Completing the daily workload is difficult and quality assurance activities may assume a lower priority. An adequate susceptibility quality assurance program may be lacking in many institutions. Factors contributing to this may include:

- P Difficulty in maintaining adequate staffing levels.
- P Shortage of qualified personnel.
- P Replacement of highly experienced specialists with generalists who have little interest in or knowledge of microbiology. Even with automated testing a thorough understanding on the part of the microbiologist is required.
- P Lack of or decrease in administrative support for continuing education.
- P Consolidation of microbiology services among fewer, larger regional reference laboratories that do not perform the antibiogram analysis for individual facilities.

MDCH plans to increase personal visits to clinical laboratories in order to document the burdens and challenges they face. The information gained regarding workforce issues and the working environment in clinical laboratories in Michigan will be shared with policy makers at CDC. To address some immediate needs, MDCH has developed several in-service programs on antibiograms, antimicrobial resistance and susceptibility testing. The issues found in the antibiogram project have resulted in a list of specific, practical tips and strategies for checking the accuracy of the cumulative antibiogram before it is printed. Please

contact Marty Boehme at (517)-335-9654 (or Boehmem@Michigan.gov) for this list or more information on these programs, or to schedule a presentation or visit to your laboratory.

To continue the quality assurance project MDCH is again requesting a copy of your facilities antibiogram data from year 2002. Please forward them to MDCH, attention: Martha Boehme, P.O. Box 30035, Lansing, MI 48909, or fax on white stock to: 517-335-9631. Your input is appreciated.

Cavanagh Joins MDCH

On July 7, 2003, Kevin Cavanagh, Ph.D. joined MDCH and the Bureau of Laboratories as the new director of the Division of Chemistry and Toxicology overseeing the newborn screening, trace metals and analytical chemistry units. Previously, Cavanagh was the technical supervisor and clinical laboratory operations manager at Ingham Regional Medical Center in Lansing, Michigan and a laboratory consultant at McLaren Regional Medical Center in Flint, Michigan.

Cavanagh received his Ph. D. in clinical chemistry from the University of Windsor in Ontario, Canada. He is certified by the American Board of Clinical Chemistry and is a fellow in the National Academy of Clinical Biochemistry. He is a member of the American Association for Clinical Chemistry, the American Association for the Advancement of Science and the American Chemical Society. Cavanagh is also a College of American Pathologists (CAP) laboratory accreditation inspector. He holds one patent and has 27 publications in peer-reviewed journals.

Dr. Cavanagh may be reached at 517-335-9490 or at cavanaghk@michigan.gov. Please join us in welcoming him to the world of public health laboratories.

Revisions to U.S. Postal Regulations Effective June 12, 2003

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Quality Assurance Section

Over the past few years, the United States Postal Service has encountered increasing difficulties with the commercial carriers who are contracted to provide air transportation services for the carriage of U.S. mail. Many carriers have refused to transport mail pieces containing mailable hazardous materials. In some instances, an air carrier has established a corporate policy not to carry hazardous materials. In other cases, an air carrier has refused to carry a specific type of hazardous material (e.g., diagnostic specimens) because Postal Service packaging standards, which met federal standards, did not meet the international standards followed by the air carrier industry.

Postal Service revisions adopt many of the regulatory and packaging changes for infectious substances that the U.S. Department of Transportation (DOT) made in their final rule, which was published August 14, 2002. There is a phase in period through January 1, 2004 for mailers using a business reply mail format for diagnostic (clinical) specimens.

Brief Summary of Changes

- Revisions and modifications in the DOT federal regulations related to the definitions of division 6.2 materials and clarification of the use of the biohazard symbol on regulated and non-regulated material.
- New classification criteria for Division 6.2 infectious substances. The World Health Organization (WHO) criterion provides four Risk Groups used to rank the degree of risk associated with different Division 6.2 materials.

Risk group means a ranking of a microorganism's ability to cause injury through disease. A risk group is defined by criteria developed by the WHO based on the severity of the disease caused by the organism, the mode and relative ease of transmission, the degree of risk to both an individual and a community and the reversibility of the disease through the availability of known and effective preventive agents and treatment.

| Risk Group | Pathogen | Risk to Individuals | Risk to Community |
|------------|---|---------------------|-------------------|
| 4 | A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly, and for which effective treatments and preventive measures are not usually available. | High | High |
| 3 | A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another, and for which effective treatments and preventive measures are available. | High | Low |
| 2 | A pathogen that can cause human or animal disease but is unlikely to be a serious hazard, and, while capable of causing serious infection on exposure, for which there are effective treatments and preventive measures available and the risk of spread of infection is limited. | Moderate | Low |
| 1 | A microorganism that is unlikely to cause human or animal disease. A material containing only such microorganisms is not subject to regulation as a hazardous material. | None or Very Low | None or Very Low |

The sender is responsible for accurately ranking a mailable material within the correct risk group. Assignment to a risk group is based on the known medical condition and history of the source patient or animal, endemic local conditions, symptoms of the source patient or animal, or professional judgment concerning individual circumstances of the source patient or animal.

Packaging of Division 6.2 Infectious Substances – Summary of Changes

Division 6.2 materials include infectious substances (etiologic agents), biological products, cultures or stocks, and toxins known or suspected to contain a Risk Group 2, 3, or 4 pathogen. It also includes diagnostic specimens known or suspected to contain a Risk Group 4 pathogen.

The primary receptacle(s) and the secondary container must be marked with the international biohazard symbol. Each mail piece must bear a DOT

Class 6 label for infectious substances (etiologic agents), proper United Nations package specification markings and orientation markings. A shipping paper is required. The red and white etiologic agent label is no longer required when shipping via U.S. Mail.

Packaging for Diagnostic Specimens in Risk Group 2 or 3 – Summary of Changes

Such materials must be packaged in a triple container, consisting of a primary receptacle, secondary container, and outer shipping container, subject to the following specific requirements:

Liquid Diagnostic (Clinical) Specimens

- (1) The secondary container must be marked with the international biohazard symbol.
- (2) The primary receptacle(s) or the secondary container must be capable of withstanding, without leakage, an internal pressure producing a pressure differential of not less than 0.95 bar, 14 psi (95 kPa).
- (3) The address side of the outer shipping container must be clearly and durably marked "Diagnostic Specimen." **Note:** No international biohazard symbol on the outer shipping container.

Solid (or Dried) Diagnostic Specimens.

- (1) Either the primary receptacle or secondary/inner container must be marked with the international biohazard symbol.
- (2) The outer shipping container must be clearly and durably marked "Diagnostic Specimen." **Note:** No international biohazard symbol on the outer shipping container.

Packaging for Diagnostic Specimens in Risk Group 1 – Summary of Changes

Non-regulated materials must be properly packaged. Materials must be held within a securely sealed primary receptacle surrounded by sufficient absorbent material (for liquids) and cushioning material to protect the primary receptacle from breakage. Either the primary receptacle or secondary/inner container must be marked with the international biohazard symbol.

View the U.S. Postal Service final rule at: http://www.access.gpo.gov/su_docs/fedreg/a030606c.html. Scroll down to Postal Service; Domestic Mail Manual: Restricted or non-mailable articles and substances - Infectious substances; mailing and packaging standards, pages 33858-33873.

New HCV Testing Algorithm Introduced at MDCH

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 Viral Serology/Viral Isolation Unit
 Jeff Massey, Dr. P.H.
 Molecular Biology Section

On February 7, 2003, the Centers for Disease Control and Prevention (CDC) published new guidelines for laboratory testing and reporting Hepatitis C virus antibody assays. These guidelines were published in the MMWR Recommendations and Reports, 52(RR03);1-16, entitled "Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus."

CDC had previously recommended that testing algorithms for anti-HCV antibody should combine the use of a screening assay with a more specific supplemental assay. Because of substantial variation in reflex supplemental testing practices among laboratories, an anti-HCV positive lab report did not uniformly represent a confirmed positive result. Prior to making these new recommendations, CDC examined testing data from volunteer blood donors and generated additional data from other populations to determine a specific signal to cutoff (s/co) ratio to predict a true antibody positive result 95 percent or more of the time, regardless of the anti-HCV prevalence or characteristics of the population being tested. It was determined that a s/co ratio of 3.8 or greater would predict a true antibody positive result 95 percent or more of the time. These new guidelines expand recommendations for anti-HCV testing to include an option for reflex supplemental testing based on the screening test positive s/co ratio.

This new algorithm proposed in the CDC guidelines recommends screening serum samples for anti-HCV antibody using one of two enzyme immunoassays (EIA): the Abbott HCV EIA 2.0 (Abbott Laboratories, Abbott Park, N. Chicago, IL) or the Ortho HCV v. 3.0 ELISA (Ortho-Clinical Diagnostics, Raritan, NJ); or an enhanced chemiluminescence immunoassay (CIA): the VITROS anti-HCV assay (Ortho-Clinical Diagnostics, Raritan, NJ). The indication for supplemental testing is based upon calculation of an s/co ratio. This ratio is derived by dividing the Optical density (OD) value of the sample being tested (s-signal) to the mean absorbance of negative control plus 0.600, (co-cutoff). An s/co ratio of ≥ 3.8 in an EIA and ≥ 8 in a CIA test differentiates a positive (reactive) from a negative (non-reactive) test result.

In brief the CDC guidelines recommend that if the:

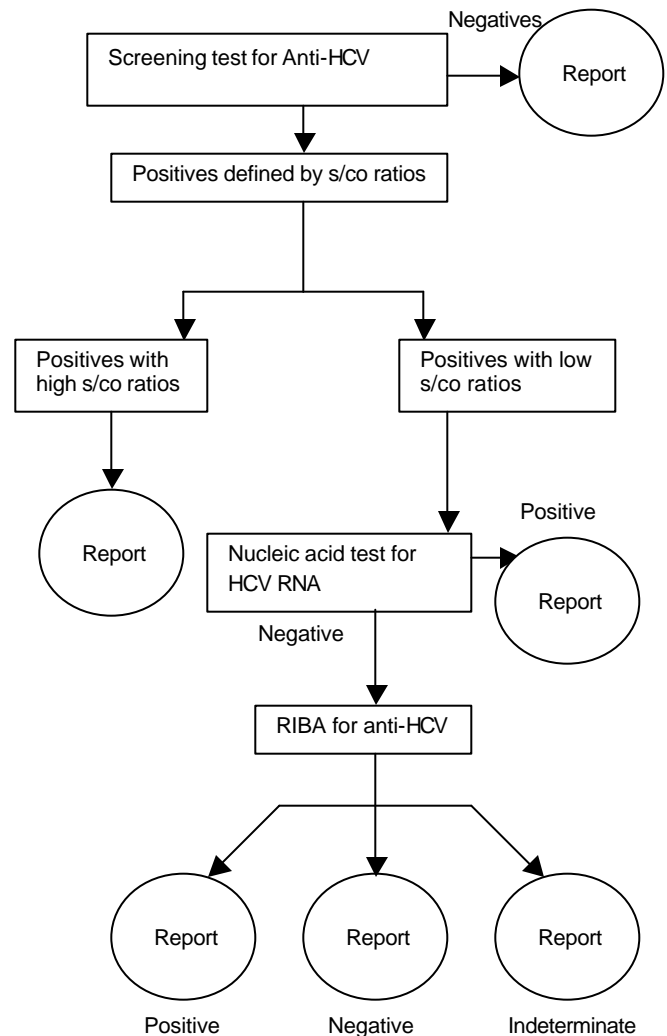
- Screening assay is negative; the patient result is reported as **Non-reactive** and no further testing is recommended.
- Screening assay is reactive with a s/co ratio less than 3.8, additional supplemental assays are recommended and no report is generated until all supplemental testing has been completed.

- Screening assay is positive with a s/co ratio greater than or equal to 3.8, the patient result is reported as **Reactive** and supplemental testing is not recommended.

HCV testing performed at MDCH incorporates these new guidelines. Clinical laboratories should compare the CDC guidelines to their HCV testing algorithm or the reference laboratory algorithm where their HCV testing is performed.

MDCH offers HCV testing free of charge for local health department clients, who were transfused prior to 1992 and cannot afford this testing in the private sector. There is a fee-for-service for HCV screening for institutions that wish to add this test to their blood borne pathogens program. To access this fee-for-service testing, phone the MDCH accounting section at 517-241-5583.

Algorithm adopted at MDCH for HCV testing as per the new Guidelines.



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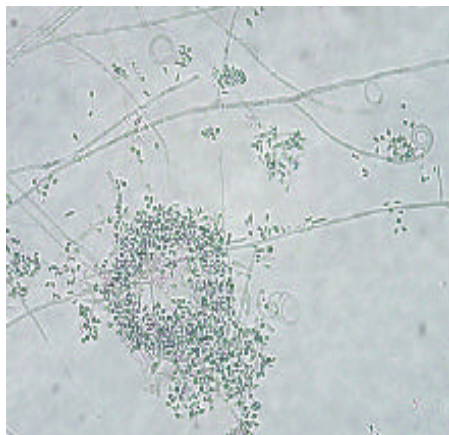
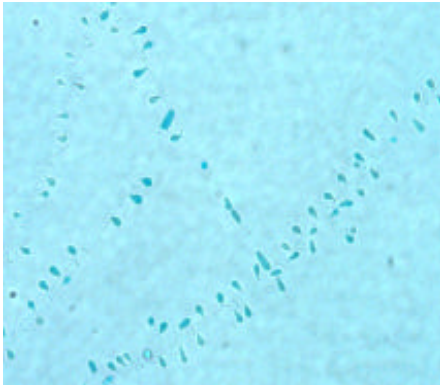
Differentiating *Trichophyton rubrum* From *Trichophyton mentagrophytes*.

Sandy Arduin MT(ASCP) & Bruce Palma MT(ASCP) - Mycobacteriology/Mycology Unit

Trichophyton rubrum

Trichophyton rubrum is a dermatophyte that causes infection of the groin, glabrous skin (trunk), hands, feet and nails. It rarely causes infection of the scalp. Colony growth is slow to moderately rapid and downy, but can occasionally be granular in texture. Colonies have a white to pale pink surface and a yellow, wine red or brown-red reverse. Microscopically *T. rubrum* produces microconidia that are clavate (club shaped) to pyriform (pear shaped), growing solitarily along the hyphae. Some strains of *T. rubrum* sporulate poorly which may impair identification. The macroconidia are multiseptate, pencil-shaped to cigar shaped in appearance and typically absent.

Trichophyton rubrum



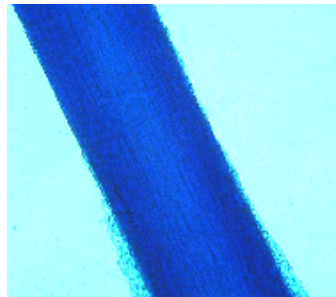
Trichophyton mentagrophytes

Trichophyton mentagrophytes

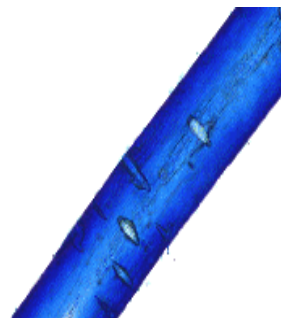
Trichophyton mentagrophytes is both anthropophilic (grows preferentially on humans) and zoophilic (grows preferentially on animals). Anthropophilic isolates typically cause infection of the feet, nails, and groin. Zoophilic isolates causing human infection are associated with inflammatory lesions of the scalp, nails and beard. Colony growth is moderately rapid, and typically powdery to granular in texture. Colonies are white to cream on the surface with a yellowish, brown or red brown reverse. Microscopically, microconidia are numerous, unicellular, round to pyriform and found in grape-like clusters. Spiral hyphae are often present. Macroconidia are multiseptate, club-shaped and often absent.

Differentiating *Trichophyton rubrum* from *Trichophyton mentagrophytes*

Microscopically, *T. mentagrophytes* produces numerous globose conidia and spiral hyphae. *T. rubrum* lacks spiral hyphae and typically has few club shaped microconidia. On rare occasions, variants of both species are difficult to differentiate. There are tests, which can aid in differentiating whether the isolate is *T. rubrum* or *T. mentagrophytes*. One such test is the urease test. *T. rubrum* is urease negative, whereas, *T. mentagrophytes* is urease positive typically turning the urease media pink within 1-3 days. A pure culture is essential because bacteria can cause a false positive urease result in *T. rubrum* cultures. More time consuming but accurate is the hair perforation test. *T. rubrum* is hair perforation negative and *T. mentagrophytes* is hair perforation positive.

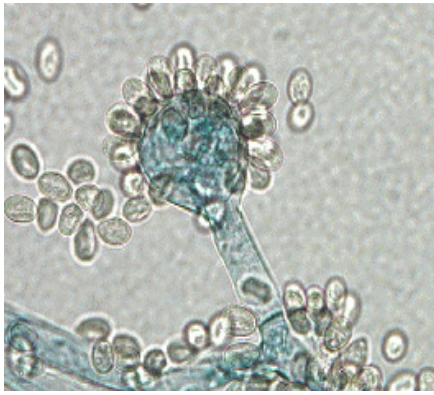


T. rubrum hair perforation negative



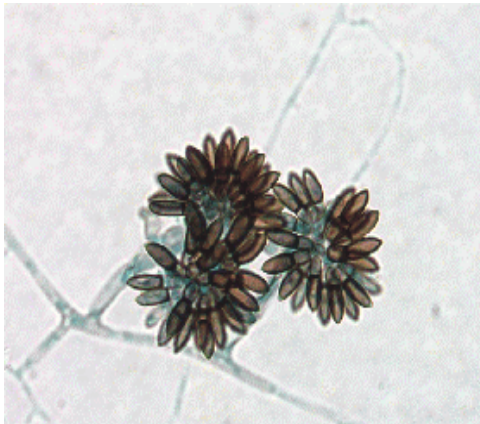
T. mentagrophytes hair perforation positive

Last Issue's Picture Quiz Answer:



The photo is of the mould *Cunninghamella* spp. The colony grows rapidly and is typically gray and wooly with a pale yellow reverse. Microscopically, the hyphae are broad and aseptate, occasionally with infrequent septa. The sporangiophores are branched and terminate in a vesicle. One celled spores form on denticles on the surface of the vesicle. *Cunninghamella* spp. is occasionally an agent of pulmonary or disseminated zygomycosis in immunocompromised patients.

This Issue's Picture Quiz: What Mould is this?



This mould was received as a referred culture from a toe web. The colony was pink/gray, wrinkled and powdery. The hyphae were hyaline and the conidiophores were branched. The sporogenous cells bear apical clusters of dark ellipsoidal conidia. The conidiogenous cells are globose to barrel shaped and produce several conidia. The conidia are generally 2-celled and constricted at the septum. The apical cell is twice as long as the basal cell.

Arboviral Serology Testing 2003

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Virology Section

The Arboviral serology test panel consisting of West Nile (WNV), Eastern Equine encephalitis (EEE), California group (LaCrosse) encephalitis (CGV) and St. Louis encephalitis (SLE) antigens will be offered at MDCH from May 1 until November 1 for patients hospitalized with any of the following clinical presentations.

- 1) Viral encephalitis or meningitis without recovery in 72 hours. Aseptic meningitis due to enterovirus is typically of short duration and has a benign clinical course.
- 2) Guillain-Barre syndrome with atypical features such as fever, altered mental status, and/or pleocytosis.
- 3) Patients presenting with febrile illness of sudden onset accompanied by malaise, anorexia, nausea, vomiting, headache, myalgia, rash, lymphadenopathy or eye pain.

If the patient has donated blood in the two weeks prior to onset of illness, please include date and place of donation on the test requisition form.

Cerebrospinal fluid is the preferred specimen for the IgM MAC-ELISA procedure. A single serum is not the preferred specimen for the IgM MAC-ELISA test procedure. Presence of IgM antibodies in a single serum sample will not confirm a recent infection. IgM antibodies have been detected in serum for up to 500 days post-onset. Single serum specimens from cases who have CNS symptoms with documented lumbar puncture failure will be accepted for testing for IgM only after consultation with virology manager. Patients who have been recently vaccinated against or recently infected with related arboviruses (e.g., yellow fever, Japanese encephalitis, dengue, etc.) or those who had a WNV infection in 2002 might have positive WNV MAC-ELISA results unrelated to recent WNV infection.

In areas, like Michigan, where WNV has been identified in the recent past, testing of serially collected paired sera is the only way to differentiate between a past or current infection. An acute sample drawn at least 8 days post onset and a convalescent specimen drawn at least 22 days post onset are needed for testing. Such paired sera, which show a four-fold increase or rising titers of IgG antibody in the IgG MAC-ELISA procedure, are indicative of a recent infection. A single serum sample will be held for testing until submission of a convalescent serum sample.

Positive sera will be tested further by the plaque reduction neutralization (PRNT) to rule out cross-reactions between WNV and other arbovirus infections (SLE, EEE and CGV). The results of this test are reported as neutralizing antibody present or absent for the respective arbovirus.

For more information, Contact Dr. Hema Kapoor at 517-335-8099 or visit www.michigan.gov/westnilevirus.