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(210) 531-4500****[www.HeartlandNTBC.org](http://www.HeartlandNTBC.org)****Vitamin D Activates  
Immune Response to  
TB: Study***Agence France Presse (10.12.11)*

While researchers have long known that vitamin D is involved in the body's response to TB, a new study shows it must be present at sufficient levels to trigger the immune response.

"Over the centuries, vitamin D has intrinsically been used to treat tuberculosis," said lead author Mario Fabri. "Sanatoriums dedicated to tuberculosis patients were traditionally placed in sunny locations that seemed to help patients, but no one knew

why this worked."

"Our findings suggest that increasing vitamin D levels through supplementation may improve the immune response to infections such as tuberculosis," said Fabri, who conducted the research while at the University of California-Los Angeles, and who now is at the Department of Dermatology at the University of Cologne, Germany.

Previously, the same research team showed that vitamin D plays an important role in the production of cathelicidin, a molecule that helps the innate immune system kill TB bacteria.

The new study shows that vitamin D is needed for the T-cells in the adaptive immune system to produce the protein interferon, which directs cells to attack the bacteria.

The finding could bolster TB treatment efforts in settings like Africa, as dark-skinned people are more likely to be deficient in vitamin D. This is because dark skin contains more melanin, which shields the body from ultraviolet rays and reduces vitamin D production.

"At a time when drug-resistant forms of tuberculosis are emerging, understanding how to enhance natural innate and acquired immunity through vitamin D may be very helpful," said Barry Bloom, former dean of faculty at the Harvard School of Public Health and a study co-author.

The report, "Vitamin D Is Required for IFN- $\gamma$ -Mediated Antimicrobial Activity of Human Macrophages," was published in *Science Translational Medicine* (10.12.11;3(104):104ra102).

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**Highlighting the Patient Worker Program**

The Texas Center for Infectious Disease (TCID) offers patients an opportunity to participate in a Patient Worker Program (PWP). In order to qualify for participation, they must have a Social Security Card, a valid Identification Card, and not be under respiratory isolation order. Several departments around TCID offer opportunities for patients to gain experience that can be very useful after being discharged from therapy. Some of these departments include, Heartland National TB Center (HNTC), Recreation, Housekeeping, Grounds Keeping, and Community Relations, to name a few. Several opportunities exist that can cater to the patients previous work experience and specific skill sets. According to Dania Reed, Lead of the Patient Worker Program, there have been approximately 100 patients enrolled in this program since its inception in October of 2007. Reed states that this program is beneficial to patients because, "self esteem is increased, it makes the stay seem to go by faster, they gain workplace skills and knowledge that can help them feel more 'in-tune' with society when discharged, they can save money, and it can help some patients qualify for the Earned Income Credit during tax season." There have also been instances when the PWP has been used to counteract behavior problems. When enrolled in the PWP, patients are highly encouraged to behave as they would in a normal job field; if infractions occur there are consequences such as suspension or even termination from the program.

Tana Pradia, one of the patients enrolled in the PWP worked with the Heartland National TB Center from March—October of this year. She worked as an Administrative Assistant under the direction of Delfina Sanchez, Project Coordinator. Her responsibilities included shipping and receiving of educational products, typing and filing office documents, and data entry. Throughout her employment at HNTC Tana proved to be a professional, intelligent, efficient, hard-working and punctual employee; she always went above and beyond what was asked of her. Tana's warm and friendly demeanor made working with her a pleasure – we will miss her greatly.

**IDSA: Boston**

The Infectious Disease Society of America held their 49th Annual Meeting in Boston, Massachusetts this year. The meeting provided three and a half days of broad continuing education courses and comprehensive educational experiences in the major facets of infectious diseases: pathophysiology, diagnosis, treatment, and prevention. Among the invited to present were Dr. Barbara Seaworth and Dr. David Griffith. Dr. Seaworth presented on Management of Complex, Mutidrug-Resistant Tuberculosis; Dr. Griffith presented on Treatment of NTM Lung Infections.

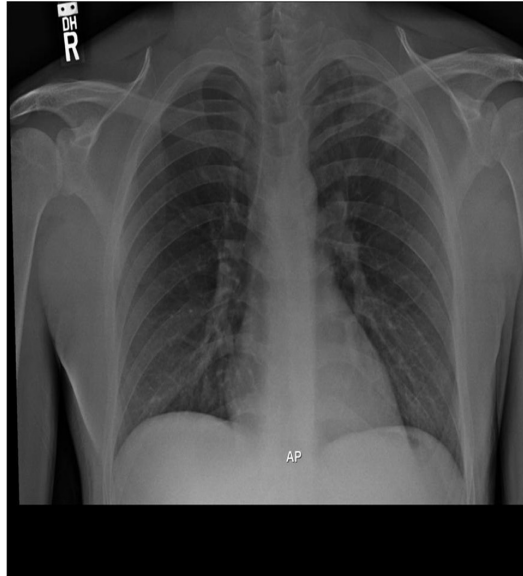
**The MISSION of the Heartland National TB Center is to build capacity with our partners. We will share expertise in the treatment and prevention of tuberculosis by: developing and implementing cutting-edge trainings, delivering expert medical consultation, providing technical assistance, and designing innovative educational and consultative products.**

## CASE PRESENTATION

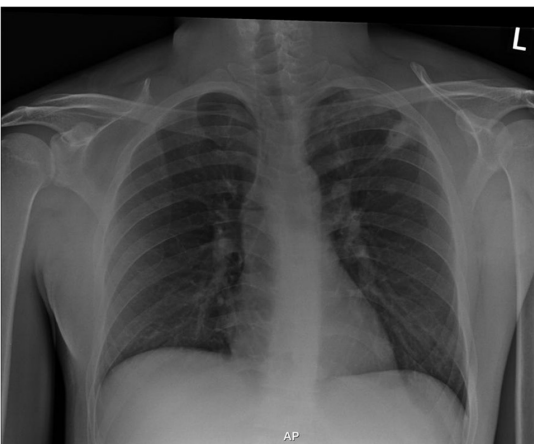
### CASE HISTORY

On 9/8/2010 a 27 year old Hispanic man was admitted to a psychiatric facility for treatment of undifferentiated schizophrenia. The patient received treatment with risperidone 3 mg daily. The patient's psychiatric issues were well controlled and he tolerated the medication well.

On 12/02/2010 the patient developed a cough and was referred for a chest radiograph. The chest radiograph was abnormal and consistent with pulmonary tuberculosis. The patient had a history of a positive tuberculin skin test and QuantiFERON TB Gold In-Tube (QFT-GIT). Treatment for latent tuberculosis infection was not documented in the patient's history. Sputum was collected and found to be acid fast bacilli (AFB) smear negative. Culture results were pending. The primary provider began treatment for latent tuberculosis infection (LTBI) on 12/02/2010 with 300 mg of isoniazid daily.



(A lesion consistent with cavitory tuberculosis was present in the upper lobe of the left lung.)



After initiation of LTBI treatment the patient's cough continued and the patient developed fever and malaise. A repeat chest radiograph 12/13/10 revealed a thickening of the wall of the cavitory lesion. A bronchoalveolar lavage was performed on 12/14/10. The sample was Nucleic Acid Amplification test (NAAT) positive for *Mycobacterium tuberculosis* and later grew MTB.

The patient was started on standard antituberculosis therapy with a regimen that consisted of Rifampin, Isoniazid, Pyrazinamide and Ethambutol daily. Pyrazinamide was discontinued after 5 days due to symptomatic hepatotoxicity. Isoniazid was discontinued 3 days later when INH resistance was reported. Moxifloxacin was added to strengthen the regimen.

*Continued on next page*

The VISION of Heartland National TB Center is to provide *excellence, expertise, innovation* in training, medical consultation, and product development to reduce the impact of tuberculosis in our region.

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## CASE HISTORY (continued)

The symptoms of pulmonary tuberculosis (cough, fever and malaise) subsided rapidly after the implementation of the multi-drug regimen. A repeat chest radiograph noted improvement. The patient converted to culture negative after 2 weeks of therapy.

After initiation of TB treatment the patient began to exhibit psychiatric symptoms. He became reclusive and spent extended periods of time in his darkened room, rarely interacting with the staff and other patients. The patient also noted the re-emergence of auditory hallucinations. A drug-drug interaction between risperidone and rifampin was identified. A pharmacist and psychiatrist were consulted. Following the consultation, the risperidone dosage was increased. The psychiatric symptoms improved as a result of the dosage adjustment.

## DRUG INTERACTION OVERVIEW

Risperidone is an atypical anti-psychotic that is widely used to treat psychosis associated with schizophrenia, bi-polar disorder and a variety of other psychiatric conditions. It is a potent antagonist for 5-HT<sub>2</sub> receptors and Dopamine D2 receptors. It is effective in reducing both the positive symptoms (symptoms that reflect an excess or distortion of normal functions, i.e. auditory hallucinations) and negative symptoms (symptoms that reflect a suppression or absence of normal function, i.e. catatonic state) of schizophrenia.

Risperidone displays a high interindividual variability in treatment responses. This variability is thought to be due to pathophysiological, environmental, genetic factors and a variety of other factors. One consistent factor that contributes to the differences in treatment effectiveness is the variability of drug metabolism. Risperidone is mainly metabolized in the liver by the polymorphic cytochrome enzyme P450 2D6. Recent studies have indicated the involvement of the cytochrome P3A4 enzyme in the metabolism of risperidone and cytochrome P3A4 in the small intestine (1, 2).

Rifampin (rifampicin) is a semi-synthetic derivative of the bacteria: *Amycolatopsis mediterranei*. Rifampin is a member of the rifamycin class of antibiotics. It is considered to be the most potent and important antituberculosis drug. Rifampin is a potent inducer of the hepatic and intestinal cytochrome P3A4 enzyme. As a result rifampin reduces the plasma concentration which decreases the therapeutic effects of risperidone (1, 2). When dealing with a patient who is receiving risperidone and rifampin concurrently, adjusting the risperidone dosage may be required to reach therapeutic effect.

Rifabutin is another member of the rifamycin class of antibiotics; it is similar to rifampin in many aspects including a similar mechanism of action. Rifabutin is also an inducer of the p450 enzyme system but its induction is much less potent than that of rifampin and consequently it has less effect on the metabolism and therapeutic effect of other medications. TB patients being treated for other medical or psychiatric conditions may benefit from substitution of rifabutin for rifampin if significant drug-drug interactions involving rifampin and the patient's other medications are present.

## CLINICAL IMPLICATIONS OF INTERACTION

In a recent study published in the Journal of Clinical Pharmacology (2) healthy volunteers received co-administered rifampin and risperidone. Rifampin considerably decreased the plasma concentration of risperidone. This may result in the re-emergence of previously controlled psychiatric symptoms. These include but are not limited to:

- Auditory Hallucinations
- Apathy
- Social Withdrawal
- Delusions
- Disorganized speech and behavior
- Neurocognitive deficits (eg. memory loss, loss of cognitive abilities)

Adequate treatment of psychiatric illness is essential for maximizing the quality of life of an individual. TB patients with well-controlled psychiatric illness have better adherence to TB medications and therefore better TB treatment outcomes.

## DIFFERENTIATING BETWEEN ACTIVE TUBERCULOSIS AND LTBI

Correct management of the TST or IGRA positive person depends on making the correct diagnosis. Active TB disease must always be excluded before a diagnosis of LTBI can be made and treatment of LTBI initiated. Evaluation of those with a positive TST or IGRA includes a medical assessment and a CXR. Persons with LTBI have no evidence of active disease on CXR and have no symptoms; they are not infectious. Some individuals are at risk of progression to active TB without treatment of their LTBI. The following factors are known to increase the risk of progression from LTBI to active disease:

- Recent contact with an infectious TB case
- Substance abuse
- Low BMI
- Diabetes mellitus
- Recent immigration
- Chronic renal failure

Patients with active pulmonary TB disease are generally infectious and pose a public health risk. Those with an abnormal CXR or symptoms should be identified as TB suspects and have sputum examined for AFB smear and culture. If the smear is positive, the individual is coughing, or the CXR is suggestive of active TB disease, treatment with the standard four drug regimen of INH, rifampin, ethambutol, and PZA should be started pending the results of the sputum culture. If the diagnosis of TB disease is less likely, the smears are negative and the individual is not coughing, the person can be observed and treatment can be held pending the results of the cultures. Whenever a decision is made to initiate treatment before the culture report is final, treatment should be with the four drug regimen. Treatment of active disease with a single drug may lead to acquisition of drug resistance.

## TEACHING POINTS

1. Treatment for Latent Tuberculosis infection (LTBI) should not be initiated until active disease has unequivocally been ruled out. Not doing so and treating active TB Disease with one drug may lead to the development of drug resistance.
2. Untreated mental illness places patients at high risk for treatment failure. Poorly controlled disease places patients at risk for poor adherence to therapy and decrease the chances of successful cure.
3. When a patient is on a variety of medications (and there is high probability of multiple drug–drug interactions) rifabutin should be considered as a substitute for rifampin. Rifabutin has considerably less potent interactions than rifampin (e.g. when a patient is receiving protease inhibitors as part of an HIV treatment regimen).
4. When a patient is being treated concurrently with rifampin and risperidone, the dosage of risperidone may have to be adjusted to achieve therapeutic levels. The dosage of risperidone will also need to be re-adjusted after the discontinuation of rifampin treatment. Risperidone dosage will usually need to be decreased ten to fourteen days following the discontinuation of rifampin to avoid the development of adverse effects as a result of high risperidone serum levels.

*WRITTEN BY ROBERT PETROSSIAN AND ADRIANA VASQUEZ, MD*

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**TB LINKS****TB Education and Training Network**

<http://www.cdc.gov/tb/education/Tbetn/default.htm>

**Find TB Resources**

[www.findtbresources.org](http://www.findtbresources.org)

**Tuberculosis Epidemiologic Studies Consortium (TBESC)**

<http://www.cdc.gov/tb/topic/research/TBESC/default.htm>

**Regional Training and Medical Consultation Centers' TB Training and Education Products – (Joint RTMCC Products Page)**

<https://sntc.medicine.ufl.edu/rtmccproducts.aspx>

**Program Collaboration and Service Integration (PCSI)**

<http://www.cdc.gov/nchhstp/programintegration/Default.htm>

\*\*\*\*If your organization has any additional links for TB resources you would like published, please send them to [Alysia.gibbons@uthct.edu](mailto:Alysia.gibbons@uthct.edu)\*\*\*\*

## 2011–2012 HNTC Training Calendar

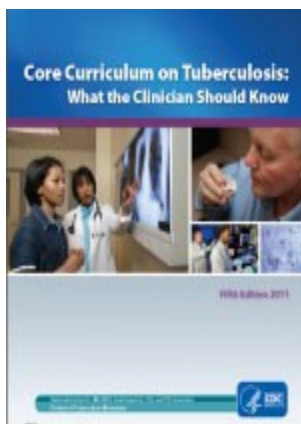
Date	Course	Location
November 29 – December 2	TB Intensive	San Antonio, Texas
February 22 – 25	RTMCC Pre-Conference Course & IUATLD North America Meeting	San Antonio, Texas
February 9, 16 March 1	Introduction to TB Nurse Case Management	ONLINE COURSE
March 7 – 9 or 14 – 16	TB Nurse Case Management	San Antonio, Texas
April 3 – 6	TB Intensive	San Antonio, Texas
May 31, June 7, 21	Introduction to TB Nurse Case Management	ONLINE COURSE

\*\*The calendar will be updated in every newsletter as well as on the website to show trainings that have been confirmed\*\*

Please visit our website: <http://www.heartlandntbc.org/training.asp> to find detailed information concerning registration and participation. Proposed topics are subject to change; check website for the latest updates.

Products from the Heartland National TB Center are available for download at <http://www.heartlandntbc.org/products.asp>

TBeat Volume 6 Issue 3 November 2011



The Centers for Disease Control and Prevention (CDC), Division of Tuberculosis Elimination (DTBE) is pleased to announce the release of the 5<sup>th</sup> edition of the *Core Curriculum on Tuberculosis: What the Clinician Should Know*. The *Core Curriculum* is intended for use as a self-study guide or reference manual for clinicians and other public health professionals caring for people with or at high risk for TB disease or infection. In addition, the *Core Curriculum* includes a slide set designed to be useful in developing educational programs.

Originally developed in 1989 and last updated in 2000, the *Core Curriculum* required further revisions to reflect new guidelines for TB prevention, treatment, testing, diagnosis, and patient management and public health practice.

To view the *Core Curriculum*, please visit:  
<http://www.cdc.gov/tb/education/corecurr/default.htm>

To view or download the *Core Curriculum* slide set, please visit:  
<http://www.cdc.gov/tb/publications/slidesets/corecurr/default.htm>

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