Mississippi State Department of Health

Mississippi Morbidity Report

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Treatment of Latent Tuberculosis Infections and Drug Interactions

Introduction: Several Mississippi physicians recently queried the recommended duration of Isoniazid (INH) treatment for Latent Tuberculosis Infection (LTBI) among Tuberculin (PPD) skin test (TST)-reactive and/or QuantiFERON®-TB-Gold (QFT-G)-positive patients who are also prescribed an anti-tumor necrosis factor α (anti-TNF α) medication for treatment of rheumatoid arthritis. Their question offers an opportunity to address this and several related issues, including the use of INH and selective serotonin reuptake inhibitors for the treatment of depression.

Anti-TNF α Agents and Similar Medications: The anti-TNF α medications have proved to be very effective additions to the clinical management of refractory rheumatoid arthritis, psoriasis, psoriatic arthritis, Crohn's Disease, ankylosing spondylitis, sarcoidosis, and ulcerative colitis. Anti-TNF α agents include infliximab (Remicade®), etanercept (Enbrel®), and adalimumab (Humira®). Anakinra (Kineret®), an interleukin 1 binding inhibitor, and abatacept (Orencia®), a T cell inhibitor, are other new agents for the treatment of rheumatoid arthritis. Some of these medications, however, particularly the anti-TNF α agents, have been associated with activation of old LTBI or exacerbation of recently acquired active TB. In some patients, activation of latent, INH-resistant strains has emerged after documented receipt of the usual full recommended 9-month course of INH preventive treatment.

All the major authorities including the Centers for Disease Control and Prevention (CDC), the American Thoracic Society (ATS), the Infectious Diseases Society of America (IDSA), and the American College of Rheumatology advise thorough TB evaluations including TST's and/or QFT-G assays, assessment of TB risk factors, and appropriate clinical and radiologic assessment of any patients with signs and symptoms suggestive of active TB, prior to beginning anti-TNF α agents.

Patients who have clear risk factors for TB should be considered for preventive treatment prior to initiation of these medications even if they have a non-reactive TST or QFT-G assay (i.e., a patient who is HIV+ and is a household contact of a person with smear-positive cavitary TB). Results of a QFT-G assay may help decide whether additional preventive treatment is needed for documented prior TST reactors who have previously received the full recommended course of INH, or among those with a history of prior BCG vaccine receipt.

Patients identified with active TB must complete treatment prior to initiation of anti-TNF α or similar medications. Newly-identified LTBI patients, particularly those with positive QFT-G tests, should complete any needed INH preventive treatment prior to initiation of anti-TNF α therapy or similar medications, if feasible. Consultation with a physician experienced in the treatment of TB is urged prior to initiating anti-TNF α or similar medications in patients with a history of prior active TB.

The recommendations of the CDC, the ATS, the IDSA, and the American College of Rheumatology for at least 9 months' INH treatment for most LTBI patients prescribed these drugs remains the standard of care. Physicians may balance the risks and benefits of longer durations of LTBI treatment (i.e., 12 months' INH) in managing some LTBI patients (i.e., those with TST reactions $\geq$ 15 mm induration, household contacts of known, smear-positive TB patients, younger patients with a lesser risk of INH-associated hepatitis, and HIV+ patients). Alternative preventive regimens with rifampin for 4 months may be considered in some circumstances. As with all LTBI patients, assurance of compliance with

preventive treatment is a must. Directly-observed preventive treatment (DOPT) should be considered when compliance may be an issue.

The various manufacturers' package inserts contain appropriate warnings and precautions. Regardless, patients who receive these medications must be monitored carefully for signs and symptoms of emerging TB during their course of treatment.

SSRI's: Another recent inquiry involved a patient under multi-drug treatment for active TB, which included INH, and who was also prescribed a selective serotonin reuptake inhibitor (SSRI), in this case citalopram (Celexa®). Although not a strong monamine oxidase inhibitor (MAOI), INH does have some MAOI activity and manufacturers' package inserts for the various SSRI's state that they are considered contraindicated among patients on MAOI's. INH and the SSRI's compete for Cytochrome 2D6 in their metabolic pathways. Telephone consultation with the manufacturer of Celexa® indicated that they consider the contraindication for concomitant use of an MAOI and an SSRI to apply in the case of INH. However, neither they, nor we, are aware of any reported adverse effects attributed to concomitant use of INH with Celexa® or any other SSRI. Consultation with nationally-renowned TB experts further supports the lack of any recognized adverse interaction, though theoretically possible. The SSRI's have proven vital adjuncts to the treatment of many heretofore difficult-to-treat depressed patients. Nevertheless, for now, caution is advised and alternative behavioral/mood-stabilizing medications or alternative TB preventive regimens (e.g., rifampin -- see above) should be considered among patients requiring treatment for both LTBI and conditions responsive to SSRI treatment. Patients on an SSRI who require treatment for active TB should be managed in consultation with a knowledgeable expert. Patients prescribed both INH and an SSRI should be closely monitored for the theoretical possibility of increased risk of serotonin syndrome.

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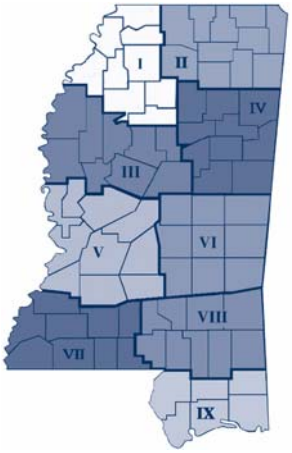
References Available on Request

Update—2008-2009 Influenza Season (continued on back)

U.S.: The ongoing U.S. 2008-2009 influenza season has been relatively mild when compared to the previous season. The proportion of deaths attributed to pneumonia and influenza has remained below the epidemic threshold for the entire season and the rate of laboratory confirmed influenza-associated hospitalizations is lower than last season for all age groups. The percentage of outpatient visits for influenza-like illness (ILI) has steadily declined since a peak of 3.6% in mid-February (compared to a peak of 6.4% in 2007-2008) and has remained below the national baseline of 2.4% for much of the season.

Influenza A (H1 and H3) and B viruses co-circulate and cause illness each season. As of April 4, 2009, influenza A (H1) viruses predominated early in the season, accounting for 36.3% of all positive samples. As influenza activity decreases nationally, the relative proportion of influenza B viruses is increasing, accounting for 32.1% of all positive samples this season.

The CDC antigenically characterizes influenza viruses collected in the U.S. All influenza A (H1) and A (H3) viruses are related to the components in the 2008-2009 vaccine. However, the influenza B viruses currently circulating are of two distinct lineages, of which only 19% are related to the vaccine component. Additionally, 99.3% of all influenza A (H1) isolates tested are resistant to oseltamivir (compared to 10.2% in 2007-2008). No resistance to oseltamivir has been noted in influenza A (H3) or B viruses. All isolates tested (A and B) are sensitive to zanamivir. The CDC issued recommendations for the use of antivirals for the 2008-2009 season, available at
http://www.cdc.gov/flu/professionals/antivirals/index.htm



Mississippi
Provisional Reportable Disease Statistics
March 2009

		Public Health District									State Totals*			
		I	II	III	IV	V	VI	VII	VIII	IX	Mar 2009	Mar 2008	YTD 2009	YTD 2008
Sexually Transmitted Diseases	**Primary & Secondary Syphilis**	2	0	5	0	8	0	0	5	3	23	9	48	23
	Total Early Syphilis	7	3	8	1	24	4	0	10	7	64	22	125	58
	Gonorrhea	65	41	102	43	190	83	42	49	46	661	525	1,830	1,680
	Chlamydia	263	177	334	165	656	162	162	230	162	2,311	1,353	5,954	4,358
	HIV Disease	7	1	5	6	15	3	4	5	7	53	38	169	150
Myco-bacterial Diseases	**Pulmonary Tuberculosis (TB)**	0	0	1	0	7	0	1	0	0	9	7	15	14
	Extrapulmonary TB	0	0	1	0	0	1	0	0	0	2	1	3	3
	Mycobacteria Other Than TB	5	3	3	1	9	0	2	2	4	29	17	86	56
Vaccine Preventable Diseases	**Diphtheria**	0	0	0	0	0	0	0	0	0	0	0	0	0
	Pertussis	0	0	0	0	0	0	0	0	2	2	6	19	26
	Tetanus	0	0	0	0	0	0	0	0	0	0	0	0	0
	Poliomyelitis	0	0	0	0	0	0	0	0	0	0	0	0	0
	Measles	0	0	0	0	0	0	0	0	0	0	0	0	0
	Mumps	0	0	0	0	0	0	0	0	0	0	0	0	0
	Hepatitis B (acute)	1	0	0	0	2	0	0	0	1	4	7	12	11
	Invasive *H. influenzae* b disease	0	0	0	0	0	0	0	0	0	0	1	0	1
	Invasive Meningococcal disease	0	0	1	0	0	0	0	0	0	1	2	1	5
Enteric Diseases	**Hepatitis A (acute)**	0	0	1	0	0	0	0	1	0	2	0	4	0
	Salmonellosis	0	0	0	1	1	0	0	0	1	3	26	74	85
	Shigellosis	0	0	0	0	0	0	0	0	0	0	42	5	133
	Campylobacteriosis	0	0	1	0	0	0	0	0	0	1	7	19	21
	***E. coli* O157:H7/HUS**	0	0	0	0	0	0	0	0	0	0	1	1	2
Zoonotic Diseases	**Animal Rabies (bats)**	0	0	0	0	0	0	0	0	0	0	0	0	1
	Lyme disease	0	0	0	0	0	0	0	0	0	0	0	1	0
	Rocky Mountain spotted fever	0	0	0	0	0	0	0	0	0	0	1	1	1
	West Nile virus	0	0	0	0	0	0	0	0	0	0	1	0	1

*Totals include reports from Department of Corrections and those not reported from a specific District.

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Update—2008-2009 Influenza Season (continued)

Mississippi: The Mississippi 2008-2009 influenza season has also been mild. The Mississippi State Department of Health (MSDH) monitors seasonal influenza activity through an active ILI surveillance program. Sentinel providers, located throughout the state, report weekly numbers of non-trauma patients with symptoms consistent with an ILI. Influenza activity peaked in mid-February, with an ILI rate of 11%, compared to a peak ILI rate of 20.68% in the 2007-2008 season. Influenza activity has steadily declined since mid-February, to a rate of 5.7% for the week ending April 4, 2009. ILI providers are supplied with kits for PCR influenza testing at the Public Health Laboratory (PHL). To date, 37 (59%) specimens submitted to the PHL have been positive. The predominant strain for the season is influenza A (H1) at 62% of all positive samples. The last positive sample at the PHL was influenza B on 3/19/09.

Surveillance activities remain important to continue to monitor the overall geographic spread of influenza for the remainder of this season, and to detect potential late season outbreaks. The mild 2008-2009 season should not be considered a predicator for the next season. Influenza vaccination, especially in high risk groups, will still be an important segment of the preventive strategy for the 2009-2010 influenza season.

References:
-CDC. Flu Activity and Surveillance. Available at http://www.cdc.gov/flu/weekly/fluactivity.htm Accessed 4/10/09.