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December 2003 Vol. 6, Issue 12

HIV & HEPATITIS
EDUCATION
PRISON
PROJECT

INFECTIOUS DISEASES IN CORRECTIONS

SPONSORED BY THE BROWN MEDICAL SCHOOL OFFICE OF CONTINUING MEDICAL EDUCATION.

ABOUT HEPP

HEPP Report, a forum for correctional problem solving, targets correctional physicians, nurses, administrators, outreach workers, and case managers. Published monthly and distributed by email and fax, HEPP Report provides up-to-the moment information on HIV/AIDS, hepatitis, and other infectious diseases, as well as efficient ways to administer treatment in the correctional environment. Continuing Medical Education credits are provided by the Brown University Office of Continuing Medical Education. HEPP Report is distributed to all members of the Society of Correctional Physicians (SCP) within the SCP publication, CorrDocs (www.corrdocs.org).

CO-CHIEF EDITORS

Joseph Bick, M.D.

*Chief Medical Officer,
California Medical Facility,
California Department of Corrections*

Anne S. De Groot, M.D.

*Director, TB/HIV Research Lab,
Brown Medical School*

DEPUTY EDITORS

Frederick L. Altice, M.D.

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*Director, AIDS Care and Clinical
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University of Texas, Medical Branch*

Stephen Tabet, M.D., M.P.H.

*University of Washington and Northwest
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THE MANAGEMENT OF END STAGE LIVER DISEASE IN THE CORRECTIONAL SETTING

Rachel Maddow, D.Phil., Joseph Bick**, M.D.*

Approximately one-third of hepatitis C- (HCV) infected persons in the United States passed through jail or prison facilities in 1997.¹ In some states, the prevalence of chronic HCV infection among incoming prisoners is as high as 49% (see Table 1). Correctional healthcare providers are on the front line in the diagnosis and management of HCV in this country.

Among those with chronic HCV, the natural history of progression from infection to cirrhosis in an individual patient is uncertain. Ten to 15 percent of those with HCV will develop cirrhosis within 20 years of initial infection.^{6,7} Studies evaluating serial liver biopsies in HCV-infected prisoners have demonstrated distinct cohorts of fast, moderate, and non-progressors.⁸ Numerous studies have demonstrated that coinfection with HIV increases the rate of progression to cirrhosis.

Chronic liver disease and cirrhosis kills more than 25,000 people in the US annually⁹ and is among the 10 leading causes of death for White males, Hispanics, and Native Americans.¹⁰ In patients with HCV and cirrhosis, the five-year death rate is approximately 15%.¹¹ In some correctional facilities, end-stage liver disease (ESLD) is now the leading cause of death among inmates.¹² This article focuses on the treatment of ESLD in the correctional setting, primarily among patients with chronic HCV.

CHRONIC HEPATITIS TREATMENT - SOME PATIENTS LEFT BEHIND?

Advances in combination therapy have improved clinical options for some patients with chronic HCV. However, correctional health providers are still confronted with many patients with cirrhosis and ESLD. Reasons for this include:

(1) Even under ideal treatment conditions, sustained viral response (SVR) rates for the current anti-HCV combination therapy (pegylated interferon plus ribavirin) are less than 50% for genotype 1, and less than 80% for other less common genotypes.¹³

TABLE 1: Proportion of persons entering state prisons found to have HCV infection

	WOMEN	MEN
California: ²	39%	32%
Maryland: ³	39%	25%
Massachusetts: ⁴	44%	27%
Texas: ⁵	49%	27%

(2) Many people cannot tolerate anti-HCV combination therapy because of side effects, co-morbidities (including psychiatric issues), or other factors.

(3) Prisoners are eight to 10 times more likely than the general population to be HIV-infected.¹⁴ Coinfection with HIV is estimated to reduce SVR rates for anti-HCV combination therapy by 20 to 30%, though some of this difference may be due to adherence issues.¹⁵ As highly active antiretroviral therapy (HAART) has reduced HIV-related morbidity and mortality among HIV-infected persons, ESLD has risen in importance as a cause of death among people with HIV/AIDS¹⁶ (see Table 2).

(4) Prisoners in the US are disproportionately African American, and HCV treatment response rates are lower among African Americans than among other racial groups. This treatment disparity has not been adequately explained, and is now the subject of a major federal study.¹⁸

(5) Some correctional healthcare systems do not routinely offer HCV testing or treatment for inmates. The number of such systems is expected to increase.

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ed to decline now that the Centers for Disease Control and Prevention (CDC) has published guidelines for managing viral hepatitis in correctional settings.¹⁹

DIAGNOSIS OF VIRAL HEPATITIS AND CIRRHOSIS

The first step in the diagnosis of liver disease due to viral hepatitis is to offer antibody screening for hepatitis B and C (HBV, HCV). Some clinicians recommend targeted screening based upon risk factor histories. In many correctional systems, the prevalence of chronic hepatitis among inmates is sufficiently high and the reliability of risk factor history information is sufficiently low that all inmates should be offered testing for both viruses.

Most of those infected with HBV will spontaneously clear the virus and be left with antibodies to the viral surface and core antigens. Approximately 5% will develop chronic HBV. Unlike HBV infection, 60-85% of those with HCV infection will develop chronic disease.²⁰ Chronic infection with HCV can be confirmed by detection of HCV RNA in the plasma.

Among those with chronic viral hepatitis, no single test or panel is sufficient to accurately portray disease severity. A basic lab assessment for patients with liver disease should include complete blood counts (CBC), serum aminotransferase levels (ALT and AST), bilirubin, albumin, prothrombin time/INR, and platelet count. Serial measurements over time offer a more complete portrait of the severity progression of the disease than individual assays. Elevated AST/ALT values reflect inflammation, while prolonged INR and decreased albumin can reflect decreased hepatic function. Elevated direct bilirubin may be indicative of cirrhosis or bile duct obstruction; total bilirubin levels over approximately 2.5 mg/dl are associated with jaundice. Anemia can be due to variceal bleeding, while thrombocytopenia can result from bleeding or sequestration in an enlarged spleen.

Physical examination of patients with advanced liver disease may detect a firm and enlarged liver, though in very advanced cirrhosis, the liver may decrease in size. External physical examination may also detect excess fluid in the abdomen by palpating the flanks and feeling for a shifting wave of fluid. Imaging techniques such as ultrasound, CT scan, and MRI can reveal ascites, an enlarged spleen, reversed portal vein flow, and hepatocellular carcinoma (HCC).

TABLE 2: Before and after HAART: ESLD as a cause of death in HIV-infected persons¹⁷

Setting	Pre-HAART Era		HAART Era	
	# / %	Year	# / %	Year
Brescia, Italy	305/13%	1987	46/35%	1996
Madrid, Spain	312/5%	1991-5	20/45%	2000
Boston, MA (USA)	36/12%	1991	22/50%	1998-9
Paris, France	1327/2%	1995	543/8%	1997

Liver biopsy is the single best technique for determining disease progression, and is the definitive means of confirming cirrhosis and assessing its severity.²¹ Liver biopsy has become a contentious issue in corrections because of cost and the high number of patients with chronic viral hepatitis. Despite advances in noninvasive monitoring techniques, biopsy remains the gold standard for the assessment of severity of cirrhosis.^{22,23,24}

Most of those with serially "normal" ALTs will have minimal inflammation, are likely to be to be slow progressors, and may not need to undergo biopsy. Just as HCV treatment costs may be reduced by price negotiation²⁵, it may be possible to reduce biopsy costs by proactively contracting for biopsies based on HCV prevalence in the facility or system in question. Correctional health providers in Pennsylvania have reportedly reduced biopsy costs to as low as \$400 per patient.²⁶ At the California Medical Facility in the California DOC, on site biopsy costs are less than \$300 per patient.²⁷

PATHOPHYSIOLOGY AND COMPLICATIONS OF CIRRHOSIS

Damage to the liver due to chronic alcohol or other toxins, infection, obstruction, or heart failure can lead pathologic changes including fibrosis and the formation of regenerative nodules. These pathologic changes are termed cirrhosis, and can result in a variety of clinical manifestations. When the liver is cirrhotic but still able to perform most basic functions, cirrhosis is referred to as "compensated". Further loss of functioning hepatocytes can result in "decompensated" cirrhosis, manifest by coagulopathy, jaundice, and edema. Extensive fibrosis can cause portal hypertension, splenomegaly, and gastroesophageal varices. In more severe cases, patients may develop excess fluid within the peritoneal cavity (ascites), spontaneous bacterial peritonitis, and/or encephalopathy. Up to 5% of those with cirrhosis will develop HCC. Deaths associated with HCV are more likely to be due to complications of decompensated cirrhosis such as variceal bleeding, encephalopathy, and peritonitis, than to HCC.²⁸

Portal hypertension: When scar tissue obstructs the normal flow of blood through the liver, pressure within the liver's main blood vessel, the portal vein, is increased. Portal hypertension is responsible for common complications of ESLD, including variceal bleeding and ascites.

Variceal bleeding: When blood cannot flow normally through the portal vein, it must return to the heart using other blood vessels. These other blood vessels, called varices, enlarge to provide an alternative pathway for blood diverted from the liver. Varices often form in the stomach and esophagus. They pose a high risk for rupture and bleeding because they are thin-walled, often abnormally twisted and swollen, and subject to high pressure. Internal variceal bleeding occurs in 20 to 30% of cirrhotic patients and is dangerous, with mortality rates reported between 15 and 50%.²⁹ Vomiting blood or passing black stools can be signs of variceal bleeding.

Ascites: Lowered albumin production from the cirrhotic liver and other physiological processes can result in fluid retention in the peritoneal cavity. Ascites itself is not life-threatening, but it is a marker of severe disease progression. The probability of death within two years in cirrhotic patients hospitalized with ascites is approximately 40%, and is worse for those who develop spontaneous bacterial peritonitis (SBP), a common and potentially fatal complication of ascites.³⁰

Encephalopathy: The exact pathogenesis of hepatic encephalopathy is not clear. A build-up of toxins such as ammonia can affect the brain, causing confusion, memory loss, fatigue, agitation, and possibly coma and death. Early symptoms of encephalopathy can include confusion, drowsiness, lethargy, and difficulty concentrating. The physical examination in those with encephalopathy may demonstrate tremor, asterixis, and slowed coordination.

Hepatorenal syndrome: Hepatorenal syndrome is a potentially life-threatening complication of liver disease in which patients

LETTER FROM THE EDITOR

Dear Colleagues:

I am reminded of the problems addressed in this issue of the HEPP Report every time I visit the inpatient ward of my facility. Several of our ID clinic patients have become long-term residents of that ward, simply because their liver disease cannot be safely managed in the outpatient correctional setting. I have had to revisit published literature in order to learn to manage these patients more effectively. This issue of HEPP Report was conceived with that need for an update in mind - we've now provided you (and me!) with the latest information on the management of inmates presenting with chronic hepatitis and cirrhosis.

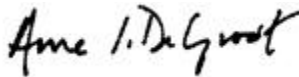
Unfortunately, HCV-related liver disease is only likely to become even more common in correctional settings as time goes on. While the incidence of HCV (the rate of new infections) is slowly decreasing, HCV-related liver disease is becoming more common as HCV infections "mature". The prevalence of HCV-related liver disease is expected to peak in the year 2010 both inside and outside of correctional settings. Given the fact that the cost for hospitalizations related to HCV in the United States was 1.6 billion dollars in 1998, 10 to 12 years before the expected peak, it is clear that we are about to witness a major shift in prison health care expenditures.

Given that potential scenario, aggressive treatment of HCV-infected patients in correctional environments should be viewed as potentially cost saving. One decision analysis study has demonstrated that HCV treatment resulted in a net savings in the range of \$400 to \$3500 over the lifetime of each patient, in the same range of cost effectiveness as stool guaiac testing, pneumococcal vaccination, coronary bypass surgery, and mammography. According to a more recent publication, combination HCV therapy resulted in improvements in Quality Adjusted Life Year (QALY) for both men and women. QALY measures improvements in health-related quality of life, meaning less chronic illness and fewer laboratory tests and clinic visits. These are the same types of benefits that have been observed over the past 10 years following improvements in HIV care. More aggressive management of HCV infection in the near term may therefore affect the "bottom line" for correctional health care in years to come.

My visits to the inpatient ward in my facility hint at our collective future. We anticipate that this issue of HEPP Report will provide you with an overview of prevention, diagnosis and treatment of viral hepatitis and cirrhosis, and approaches that may be efficacious in preventing common complications of end-stage liver disease.

And let us not forget to celebrate the season! The entire staff of HEPP Report wishes you a wonderful holiday and a happy and healthy 2004!

Sincerely,



Annie De Groot, M.D.,
Co-chief Editor, HEPP Report

FACULTY DISCLOSURE

In accordance with the Accreditation Council for Continuing Medical Education Standards for Commercial Support, the faculty for this activity have been asked to complete Conflict of Interest Disclosure forms. Disclosures are listed at the end of articles. All of the individual medications discussed in this newsletter are approved for treatment of HIV and hepatitis unless otherwise indicated. For the treatment of HIV and hepatitis infection, many physicians opt to use combination antiretroviral therapy which is not addressed by the FDA.

Senior Advisors

Karl Brown, M.D.
Rikers Island Jail

John H. Clark, M.D., M.P.H., F.S.C.P.
Los Angeles County Sheriff's Department

Theodore M. Hammett, Ph.D.
Abt Associates

Ned E. Heltzer, R.Ph., M.S.
Heltzer Associates

Ralf Jürgens
Canadian HIV/AIDS Legal Network

Joseph Paris, Ph.D., M.D.
CCHP Georgia Dept. of Corrections

Renee Ridzon, M.D.
Bill & Melinda Gates Foundation

Mary Sylla, J.D.
CorrectHELP: Corrections HIV
Education and Law Project

David Thomas, M.D., J.D.
Division of Correctional Medicine,
NovaSoutheastern University
College of Osteopathic Medicine

Louis C. Tripoli, M.D., F.A.C.F.E.
Correctional Medical Institute,
Correctional Medical Services

Lester Wright, M.D.
New York State Department of
Corrections

Associate Editors

Scott Allen, M.D.
Rhode Island Department of Corrections

Peter J. Piliro, M.D.
Associate Professor of Medicine,
Consultant, New York State Department of
Corrections, Albany Medical College

Dean Rieger, M.D.
Indiana Department of Corrections

Josiah Rich, M.D.
Brown University School of Medicine,
The Miriam Hospital

Steven F. Scheibel, M.D.
Regional Medical Director
Prison Health Services, Inc.

David A. Wohl, M.D.
University of North Carolina

Michelle Gaseau
The Corrections Connection

Layout

Kimberly Backlund-Lewis
The Corrections Connection

Distribution

Screened Images Multimedia

Managing Editor

Julia Noguchi
HIV/Hepatitis Education Prison Project

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develop oliguria, hyponatremia, hypotension, and renal failure manifest by increases in BUN and creatinine. The exact etiology of this syndrome is not clear, but it can be precipitated by sepsis, severe variceal bleeding, aggressive diuresis or paracentesis.

Patients with advanced cirrhosis also commonly develop malnutrition, gallstones, and coagulopathy due to impaired hepatic synthesis of clotting factors and thrombocytopenia.

PREVENTION AND TREATMENT OF COMPLICATIONS

The prevention and treatment of complications associated with ESLD can be challenging for even experienced generalist physicians. In general, the management of those with ESLD should be done in consultation with a gastroenterologist or hepatologist. In one recent study, hospitalized patients with decompensated cirrhosis managed by a generalist in consultation with a gastroenterologist fared better than patients managed by generalists alone. Better outcomes included shorter length of hospitalization, lower cost of hospitalization, lower rates of hospital readmission, and improved survival.³¹

Patients with chronic hepatitis should be protected from further hepatic insult. Those who are not immune to hepatitis A and hepatitis B should be vaccinated.³² Those with liver disease should receive annual influenza vaccinations and a pneumococcal vaccine. Patients should avoid hepatotoxic medications whenever possible. Large doses of acetaminophen should be avoided, however, low doses (less than 2,000 milligrams per day) are generally well-tolerated. Non-steroidal anti-inflammatory drugs such as ibuprofen (Advil®), naproxen (Aleve® or Naprosyn®), or aspirin should be used with caution both because of hepatotoxic potential and the risk for bleeding. The dosage of medications that are hepatically metabolized may need to be adjusted. Because of the increased prevalence of HIV infection among those with viral hepatitis, patients should also be encouraged to test for HIV.

Alcohol

Because alcohol is commonly covertly manufactured and ingested in prison, all patients should be educated about the extreme importance of avoiding alcohol. Even moderate ingestion of alcohol hastens the progression of liver disease in those with cirrhosis. Correctional physicians should link their patients to drug and alcohol abuse treatment

programs both within the correctional system and at the time of release.

Nutrition

Maintaining adequate nutrition for patients with advanced liver disease can be difficult in the community, and poses particular challenges in the prison setting. Adequate dietary protein is important for patients with ascites and for repairing lost muscle mass. However, excess protein may pose a risk for encephalopathy. In those prone to encephalopathy, vegetable proteins may pose fewer risks than animal proteins. Iron supplementation and excessive sodium intake should be avoided in those with cirrhosis. Patients with ascites may require fluid and salt restriction.

Variceal bleeding

Beta-blockers can reduce heart rate, lower portal vein pressure, and reduce the threat of variceal bleeding. Patients with diabetes, asthma, emphysema and chronic bronchitis may be unable to tolerate beta-blockers. Options for treatment of variceal bleeding and prevention of recurrence also include endoscopic sclerotherapy, vasoactive drugs, and band ligation. Surgical shunts and Transjugular Intrahepatic Portosystemic Shunt (TIPS) are other options to eliminate variceal bleeding. TIPS is a less invasive procedure in which the shunt is inserted through a catheter.

Ascites

Patients with ascites may require a reduced salt diet, reduced fluid intake, and diuretics. Spironolactone in doses of 100-400 milligrams per day can be used to achieve diuresis. In those who fail to respond to diuretics, fluid may be drained with a catheter or plastic drainage tube inserted into the abdominal wall (paracentesis). Paracentesis should be accompanied by albumin infusion to prevent circulatory dysfunction and other complications.³³ TIPS is also an option in ascites patients for whom paracentesis is ineffective, intolerable, or contraindicated.³⁴

Bacterial Peritonitis

Patients with SBP may present with fever, hypotension, abdominal discomfort, and/or encephalopathy. Often the clinical findings are very subtle, and the clinician must act presumptively to prevent death of the patient. Gram stain and culture of ascitic fluid often fails to demonstrate the presence of an organism. To diagnose SBP, ascitic fluid should be examined by microscope and inoculated directly into blood culture bottles. An ascitic fluid neutrophil count of 250 polymorphonuclear cells/mm³ is diagnostic of SBP.³⁰ In suspected cases, treatment should

TABLE 3:
Signs and Symptoms of Cirrhosis

Many patients with cirrhosis have no symptoms, and are only determined to be cirrhotic by physical examination and liver biopsy. When signs or symptoms are present, they can include:

- ♦ enlargement of the liver
- ♦ loss of appetite
- ♦ unusual weight loss or weight gain
- ♦ nausea and vomiting
- ♦ fatigue
- ♦ jaundice
- ♦ enlargement of the spleen
- ♦ abdominal swelling
- ♦ swelling of the legs
- ♦ amenorrhea (absence of menstrual periods)
- ♦ intense itching
- ♦ vomiting blood
- ♦ palmar erythema (reddish and blotchy palms)
- ♦ loss of body hair
- ♦ spider angiomas (pinhead-sized red spots on the skin with tiny visible blood vessels, blanch with pressure)

be initiated with cefotaxime, ceftriaxone, or a fluoroquinolone. Patients who have already had a previous episode of SBP are at high risk for recurrence, and should be provided prophylaxis with trimethoprim -sulfamethoxazole, ciprofloxacin, or norfloxacin.

Encephalopathy

Precipitating factors for encephalopathy in advanced liver disease can include gastrointestinal bleeding, excess dietary protein, constipation, or infection. The goal of treatment for encephalopathy is to lower the level of toxic substances affecting the brain by reducing or eliminating dietary protein and removing nitrogenous material from the gut, often by using lactulose.³⁵

Fulminant hepatic failure is manifest as encephalopathy, worsening jaundice, gastrointestinal bleeding, sepsis, coagulopathy, hypoglycemia, renal failure, and electrolyte abnormalities. Patients with fulminant hepatic failure should be managed in the ICU setting, and should urgently be evaluated for candidacy for liver transplant.³⁶

Transplantation

More than 3,000 liver transplants are performed annually in the US. For patients with cirrhosis, the two commonly used indices of liver disease severity are Child-Turcotte-Pugh (CTP) and Model for End Stage Liver Disease (MELD). CTP and MELD are designed to direct organ allocation to liver transplantation candidates based on the

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severity of disease. CTP score is determined using albumin, bilirubin, prothrombin time (INR), ascites, and hepatic encephalopathy. MELD score is determined using bilirubin, creatinine, and INR. MELD uses a wider range of assay values and a more complicated formula than CTP. A MELD calculator is available online at the website of the United Network for Organ Sharing: www.unos.org. Every correctional system should have policies in place that address the appropriate evaluation and referral of selected patients for consideration for transplant.

Anti-HCV Maintenance Therapy

There is little clinical basis for recommendations about continued anti-HCV therapy in patients with advanced cirrhosis. Nevertheless, some studies have shown that patients with compensated cirrhosis can achieve high rates (43%) of SVR on combination therapy,³⁷ and that anti-HCV therapy may cause histological improvement even in patients who are virological non-respon-

ders.³⁸ Whether or not treatment of compensated cirrhotics will translate into decreased morbidity, improved quality of life, or prolonged survival remains to be seen.

Anti-HCV treatment of patients with decompensated cirrhosis may raise significant safety issues and should not generally be recommended except in the setting of clinical trials.

Hepatocellular Carcinoma (HCC)

Chronic HCV infection is a major risk factor for HCC. The risk for HCC is greatest among patients with at least 20 years of HCV infection, cirrhosis or advanced fibrosis, male sex, older age, HBV coinfection, and heavy alcohol use.³⁹ One to 6% of cirrhotic patients develop HCC annually.⁴⁰ Screening techniques for HCC in cirrhotic patients are serum alpha-fetoprotein (AFP) testing (twice yearly) and hepatic ultrasound or CT.

Surgical liver resection and liver transplant are the main treatment strategies for HCC. Alternative approaches include percutaneous alcohol injection, arterial chemoembolization, or radiofrequency ablation.⁴¹

Palliative Care, Compassionate Release
Patients with ESLD, especially those who are not candidates for liver transplantation, should be considered for hospice care and compassionate parole or release. Patients dying with ESLD report a high pain burden, comparable to that of patients dying with lung and colon cancer.⁴² Physicians working with such patients should be aware of available palliative care options, and should initiate compassionate release or medical parole proceedings where appropriate.

CONCLUSIONS

Over the past 20 years, correctional health-care providers have become increasingly important in our nation's response to tuberculosis and HIV. With one-third of HCV-infected individuals in the US passing through our jails and prisons, correctional clinicians are now faced with a new challenge. As we become experts in the antiviral treatment of those with chronic hepatitis, we must also be cognizant of the management of those with ESLD. By doing so, we can decrease ESLD associated morbidity and prolong the lives of our patients suffering with this serious illness.

DISCLOSURES: *Nothing to disclose, **Nothing to disclose.

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Dosing of pegylated interferon for the treatment of hepatitis C infection

Pegasys® (pegylated interferon alfa-2a) and Copegus™ (Ribavirin, USP) dosing recommendations

HCV Genotype	Pegasys Dose	Copegus Dose	Duration
1 or 4	180 µg subcutaneously once a week	<75 kg: 1000 mg daily in two divided doses	48 weeks
		≥75 kg: 1200 mg daily in two divided doses	
2 or 3	180 µg subcutaneously once a week	800 mg daily in two divided doses	24 weeks

PEG-Intron™ (pegylated interferon alfa-2b) monotherapy dosing recommendations

The recommended dose of PEG-Intron™ regimen is 1.0 µg/kg/week for one year. The volume of PEG-Intron to be injected depends on the vial strength used and the patient's weight. (See table below)

Body weight (kg)	PEG-Intron vial strength	Amount of PEG-Intron (µg) to administer	Volume (mL)* of PEG-Intron to administer
≤45 46-56	50 µg per 0.5 mL	40	0.4
		50	0.5
57-72 73-88	80 µg per 0.5 mL	64	0.4
		80	0.5
89-106 107-136	120 µg per 0.5 mL	96	0.4
		120	0.5
137-160	150 µg per 0.5 mL	150	0.5

*When reconstituted as directed

PEG-Intron™ (pegylated interferon alfa-2b) and Rebetol® (Ribavirin, USP) dosing recommendations

When administered in combination with Rebetol®, the recommended dose of PEG-Intron™ is 1.5 µg/kg/week. The volume of PEG-Intron™ to be injected depends on the vial strength used and the patient's weight. The recommended dose of Rebetol® is 800 mg/day in two divided doses. (See table below)

Body weight (kg)	PEG-Intron vial strength	Amount of PEG-Intron (µg) to administer	Volume (mL)* of PEG-Intron to administer
<40	50 µg per 0.5 mL	50	0.5
40-50 51-60	80 µg per 0.5 mL	64	0.4
		80	0.5
61-75 76-85	120 µg per 0.5 mL	96	0.4
		120	0.5
>85	150 µg per 0.5 mL	150	0.5

MANAGEMENT OF END STAGE...

(references continued from page 5)

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SPOTLIGHT: Methicillin-Resistant *Staphylococcus Aureus* (MRSA)

Lou Tripoli*, M.D. and Joseph Bick**, M.D.

Infections caused by methicillin resistant *Staphylococcus aureus* (MRSA) have long been a problem in hospitals and nursing homes. Over the past decade, MRSA has also emerged as a cause of skin and soft tissue infections in the community.¹ Not surprisingly, this organism is now being increasingly recognized as a cause of infections in residents of jails and prisons.^{2,3,4} This article summarizes basic concepts of MRSA diagnosis and management and reviews recent experiences with MRSA in the correctional environment.

Staphylococcus aureus (SA)

Staphylococcus aureus (SA) is a bacterium commonly found on the skin or in the nose of healthy individuals. Although it is often a colonizer causing no disease, it can be responsible for minor to life-threatening infections of the skin, bone, blood, heart valves, and lungs. SA is easily spread by contact with the skin of a person infected or colonized with the bacteria. SA can also be acquired from inanimate objects that have been in contact with a person carrying the organism.

Methicillin resistant *Staphylococcus aureus* (MRSA)

Penicillin resistance in SA is due to the production of beta lactamase, an enzyme that breaks down penicillin's beta lactam ring and renders the drug inactive. Within a few years of the first clinical use of penicillin in the 1940s, resistance due to beta lactamases was identified. Within a year of the introduction of the semisynthetic, beta lactamase-stable, penicillin methicillin in 1960, MRSA strains were identified. By the 1990s, over half of SA isolated in some hospitals were MRSA. Nursing homes and other long-term care facilities have been identified as reservoirs. Risk factors for infection with MRSA include prolonged hospitalization, having been in an intensive care unit, contact with other patients who have MRSA, having had surgery or another invasive procedure, injection drug use, and underlying illnesses such as diabetes.

Many microorganisms that develop high-level resistance pay a competitive price to carry that antibiotic resistance and are less fit. However, MRSA appears to be as virulent in its resistant form as it is in its wild type. Most MRSA infections are minor infections of the skin that take the form of pustules, furuncles or boils. Generally, these conditions are mild and self-limited. It is not always necessary to treat every infection aggressively.

Methicillin resistant strains are resistant to all beta lactam antibiotics, including penicillins and cephalosporins. In addition, MRSA strains often carry plasmids that lead to resistance to multiple other antibiotics. Many MRSA strains are susceptible to trimethoprim-sulfamethoxazole and rifampin. Virtually all SA are fully susceptible to vancomycin. However, the first clinical isolate of SA with reduced susceptibility to vancomycin was reported from Japan in 1996.⁵ The first documented case of infection caused by vancomycin-resistant *S. aureus* (VRSA) (vancomycin MIC >32 µg/mL) in a patient in the United States was reported in 2002.⁶

Is it just a spider bite?

In the correctional setting, there has been significant amount of misinformation on the "inmate grapevine" that attributes these otherwise unremarkable lesions to arachnid bites. In reality, spiders rarely bite people, and most of the bites are inconsequential. Most spiders only bite when provoked such as when they are trapped in clothing or in a shoe. Spider bites characteristically occur at areas where the spider might settle in the clothing, such as the waistband. It is unusual for a spider to bite multiple times.

The brown recluse spider, or *Loxosceles reclusa*, in particular, has been blamed for lesions among the incarcerated. Found in the Midwest and Southeast, this arachnid prefers isolated areas and is rather shy and timid. It hibernates during the winter, so bites, which are generally painless, occur between March and October. Following a bite, the skin may exhibit a urticarial lesion (hive), a papule, or a pustule. In severe reactions, patients may develop systemic signs including rash, fever, headache, and other flu-like symptoms. Only a small proportion of bites become necrotic, and the progression follows a characteristic pattern termed the "red, white, and blue" sign: a central blister with purple-gray discoloration (in Caucasians), surrounded by a white ring of blanched skin and a much larger halo of red. If skin breakdown occurs, the site becomes painful, usually progressing to a black eschar and may be slow to heal.

The misinterpretation of minor skin lesions as spider bites has ironically led to actions that potentially increase health risks for many inmates. The use of chemicals to eradicate the falsely accused spiders only serves to eliminate an ally in the war against mosquitoes, which are known to carry illnesses such as West Nile virus.

Recent MRSA outbreaks

Outbreaks of MRSA infections are being increasingly recognized in jails and prisons throughout the country.^{2,3,4} Factors that may have contributed to the problem include: limited access to soap or bathing, mental illness among prisoners leading to poor hygiene, inadequate laundry procedures, co-payments for medical care which may limit access to medical care, infrequent collection of wound cultures, and the misperception that lesions were due to spider bites.

Georgia: In 2001 and 2002, the Georgia Division of Public Health, the Georgia Department of Corrections, and local health departments investigated outbreaks of MRSA skin infections in three correctional facilities. Risk factors identified included prolonged incarceration, previous antimicrobial use, self-draining of boils, skin laceration (intentional or accidental), washing clothes by hand, and sharing soap. Beta lactam antibiotics were not uncommonly used, even after the identification of MRSA. A number of measures were implemented, with limited success. These included wide spread screening for skin disease, implementation of standardized antimicrobial treatment recommendations, changes in laundry practices, inmate education, the use of chlorhexidine containing soaps, and the use of alcohol-based hand rubs.

Los Angeles: In 2002, the Los Angeles (L.A.) County jail experienced an increase in reports of spider bites. In response, a protocol was initiated that called for culturing all suspected spider bite lesions. Between January of 2002 and June of 2003, over 1,600 MRSA skin infections were identified. In collaboration with the L.A. County Department of Health Services, the jail recommended changes to include enhanced skin lesion surveillance, standardized treatment protocols including empiric treatment with non-beta-lactam antimicrobials for all wound infections, inmate hygiene education, environmental cleaning, and more frequent laundry changes.

Texas: In 1996, the Texas Department of Criminal Justice (TDCJ) implemented a comprehensive set of treatment and prevention guidelines for MRSA skin infections that included 1) surveillance, 2) hygiene education for inmates, 3) access to proper wound care, 4) standardized antimicrobial therapy based on drug susceptibility data (including directly observed therapy), 5) early treatment of skin dis-

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CASE STUDY... (continued from page 7)

ease, and 6) eradication of MRSA from asymptomatic carriers who have recurrent MRSA infections. Since 1998, TDCJ has required culturing of all draining skin lesions and reporting of results to the TDCJ Office of Preventive Medicine. The proportion of SA infections that were methicillin-resistant increased from 24% (864 of 3,520) in 1998 to 66% (5,684 of 8,633) in 2002. Implementation of guidelines and a continued multidisciplinary approach to MRSA infections has not led to substantial decreases in the incidence of MRSA.

Mississippi: An evaluation of MRSA cases at a state prison in Mississippi revealed that 19 of 21 (90%) of infected inmates with wound dressings changed their dressings themselves. Fifteen (33%) of infected inmates reported helping or being helped by other inmates with wound care or dressing changes. Twenty-six (58%) reported lancing their own boils or other inmates' boils with fingernails or tweezers; forty (89%) shared personal items (e.g., linen, pillows, clothing, and tweezers) that potentially were contaminated by a wound.

Treatment of MRSA infections

Some correctional systems have developed guidelines for the management of MRSA. In July 2003, the federal Bureau of Prisons issued guidelines to prevent and control MRSA in correctional facilities⁷. This document recommends the reporting and tracking of patients with MRSA and offers a convenient form to do so. In addition, a useful patient education handout can be found at the end of the document.

Facilities detecting a substantial number of MRSA infections should implement improved hygiene, infection-control, and treatment practices. Skin lesions should be cultured to determine the infecting organism. Drainage of abscesses is important to facilitate cure. Empiric antibiotic selection should be made with MRSA in mind. Treatment should be adjusted as needed based upon the infecting organism's antibiotic susceptibility pattern.

Trimethoprim-sulfamethoxazole (Bactrim, Septra) in a dose of one double-strength tablet twice daily is usually effective in patients who have MRSA. Some clinicians also add rifampin in a dose of 600 mg once daily. Due to the rapid development of resistance, rifampin should not usually be used alone to treat infections due to SA. For more serious infections, intravenous vancomycin or oral linezolid may be used. A new antibiotic, daptomycin, (Cubicin™) has recently been approved for treatment of skin infections due to SA. Daptomycin is given parenterally, and has a spectrum of activity that includes virtually all Gram-positive organisms including *E. faecalis*, *E. faecium* (including VRE) and SA including MRSA. Daptomycin should not be used for pneumonia due to higher failure in clinical trials, and should not be relied upon for CNS or bone infections due to poor penetration of these tissues.

Clinicians are reminded that oral vancomycin is non-absorbable and is, therefore, not useful in the treatment of skin and soft tissue infections due to SA.

Eradication of nasal carriage

SA and MRSA commonly inhabit the anterior nares of otherwise healthy asymptomatic individuals. Routine eradication of this carriage is neither efficacious nor recommended. In some cases of recurrent active disease, clearance of the organism from the nose can be beneficial. Mupirocin (Bactroban®) ointment, applied to both anterior nares bid for 5-7 days, is commonly used for this purpose.

Education and Infection Control

Inmates should be educated about personal hygiene, and advised to avoid touching other persons' wounds or wound drainage. Inmates should be provided access to soap, showers, and sinks. Clinical staff that provides wound care should follow Standard Precautions. Infection control measures can never be overemphasized, as even in the hospital setting many healthcare professionals neglect hand washing. The restrooms in many hospitals and public settings are poorly designed, leading people to re-contaminate their hands immediately after washing them.

In an effort to improve hand hygiene, the use of alcohol-containing antiseptic scrubs is increasingly being encouraged. However, security concerns may lead to these particular disinfectants not being universally embraced in the correctional setting. Surfaces that are used by multiple people should be routinely decontaminated. Laundry should be washed in hot water for at least 25 minutes to be sure that most bacteria have been exterminated. Custody staff should be educated to refer inmates who have even minor-appearing skin infections so that an appropriate evaluation can be performed.

The involvement of experts in infection control and infectious diseases can be useful in both managing individual patients and establishing protocols specific to the unique needs of each facility.

Correctional facilities experiencing outbreaks of MRSA should seek assistance from their local and state health departments. MRSA outbreaks can be reported to CDC (telephone [800] 893-0485) through state departments of corrections and state health departments. Preventing MRSA disease in inmates might be an important measure for preventing MRSA in the community outside the correctional facility. Additional information about MRSA is available at <http://www.cdc.gov/ncidod/hip/aresist/mrsa.htm>

In conclusion, the recent experience with MRSA in jails and prisons reminds us that antibiotic-resistant organisms will continue to be a significant problem in this country. Lessons learned from the MRSA experience may also be applicable to other infections to come. Correctional healthcare providers' responsibility to public health cannot be underestimated. It is important to strengthen our relationships with outside public health agencies as we strive to contain this growing threat to the health of those patients entrusted to our care.

Disclosures: *Nothing to disclose.

**Nothing to disclose.

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INSIDE NEWS

Magic Johnson visits California prison for World AIDS Day

Continuing his commitment to reaching out to at-risk populations, Earvin "Magic" Johnson visited California Medical Facility in Vacaville, CA on Dec. 3, 2003. After a private meeting with the prison's inmate peer educators, Magic spoke to an appreciative audience of over 600 inmates, recounting his own personal journey following his diagnosis with HIV in 1991. The audience responded enthusiastically to Magic's messages concerning testing, treatment, and prevention. Earlier in the week, the prison was host to Assemblyman Mark Leno, Senator Gloria Romero, and 35 members of the San Francisco Gay Men's Chorus. Senator Romero took the opportunity to call upon the CA DOC to evaluate the feasibility of distributing condoms to inmates.

Study: Long Term Adefovir in HBeAg Negative Chronic Hepatitis B Results in Significant Virological, Biochemical, and Histologic Improvement

This study presented from the Henry Dunant Hospital, Athens, Greece and Gilead Sciences showed that Adefovir dipivoxil (ADV) 10 mg has demonstrated significant histological, virological, and biochemical improvement as compared to placebo (PLB) through 48 weeks of therapy in HBeAg positive and HBeAg negative patients. Study authors concluded that Adefovir for 96 weeks resulted in significant and continued reduction in HBV DNA and ALT; and additional histologic improvement beyond that seen at week 48. Discontinuation of ADV resulted in loss of HBV DNA and ALT suppression and reversion of histologic improvement. Emergence of adefovir resistance was delayed and infrequent. Adefovir has a distinct resistance profile from lamivudine. *Marcellin, Patrick et al. 54th AASLD October 2003 Poster 1156.*

Sexual Transmission of HCV in Heterosexual Monogamous Couples

The aim of this study is to determine the potential for sexual transmission of HCV among monogamous heterosexual couples by identifying the factors (sexual and non-sexual) associated with anti-HCV positivity among partners, and the relatedness of virus strains among concordant couples. The prevalence of anti-HCV among sexual partners of persons with HCV was 4% (95% CI: 2.3%-5.7%) but 40% of partners had discordant types indicating lack of sexual transmission. The majority of type concordant couples lacked per-

cutaneous risk factors for HCV, suggesting sex may be the route of transmission but phylogenetic analysis of viral strains will ultimately determine whether sexual transmission occurred.

Terrault, NA et al. 54th AASLD. October 2003 Abstract 716.

Weight Loss and Exercise Can Improve Fibrosis

Obesity is a risk factor for the progression of fibrosis in chronic liver diseases such as non-alcoholic fatty liver disease (NAFLD) and hepatitis C (HCV). The aim of this study was to investigate the longer-term effect of weight loss on liver biochemistry, serum insulin levels and quality of life in overweight patients with liver disease and the effect of subsequent weight maintenance or regain and to determine factors associated with successful weight maintenance. It was demonstrated that lifestyle interventions reduced risk factors associated with progression of liver disease, decreased abnormal liver enzymes, improved quality of life and in a proportion of patients improved histological features of liver injury. Importantly, these changes were achievable and sustainable with relatively small but persistent changes in lifestyle. Treatment of overweight should form an important component of the management of patients with chronic liver disease.

Hickman, IJ et al. 54th AASLD. October 2003 Abstract 716.

Study: Survival of HIV-Infected Liver Transplant Recipients

With immune function restoration made possible by HAART (Highly Active Antiretroviral Therapy), a study from the University of Pittsburgh evaluated 24 HIV positive subjects with ESLD who were undergoing Orthotopic liver transplantation (OLT). In contrast to the finding of past inferior survival observed among HIV-infected transplant recipients, this study found that successful liver transplantation is possible for HIV-infected subjects, and that for HIV-infected subjects, post-OLT survival with ART is similar to that for HIV negative subjects. Data from this study provide a scientific rationale to justify that HIV infection should no longer be considered an absolute contraindication to transplantation, which is consistent with recent transplantation arguments based on ethical considerations.

Ragni, MV et al. Journal of Infectious Diseases 188 (2003) pp. 1412-1420.

RESOURCES

For more information on hepatitis:

- ♦ www.hivandhepatitis.com/hiv_hcv_co_inf/080403a.html
- ♦ www.cdc.gov/hepatitis

For more information on MRSA:

- ♦ www.cdc.gov/ncidod/hip/aresist/mrsa.htm
- ♦ www.ojp.usdoj.gov/bjs/prisons.htm

Immunization questions?

- ♦ Email nipinfo@cdc.gov
- ♦ Call CDC's Immunization Information Hotline at (800) 232-2522
- ♦ Call your state health dept., (phone numbers at: www.immunize.org/coordinators)

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1. The rate of progression to cirrhosis in those with HCV is increased in those who are co-infected with HIV.
 - a) True
 - b) False

2. Common laboratory abnormalities in those with end-stage liver disease include:
 - a) Hypoalbuminemia
 - b) Prolonged INR
 - c) Elevated serum ammonia
 - d) Thrombocytopenia
 - e) All of the above

3. The percentage of HCV-infected individuals in the US who spend time in a prison or jail each year is closest to:
 - a) 5%
 - b) 15%
 - c) 30%
 - d) 50%

4. Approaches that may be efficacious for the treatment of variceal bleeding include:
 - a) beta blockers, sclerotherapy, banding of varices
 - b) ace inhibitors, lactulose, low protein diets
 - c) beta blockers, low protein diets, paracentesis

5. Risk factors for acquiring methicillin-resistant *Staphylococcus aureus* (MRSA) include:
 - a) Injection drug use, recent surgery and hemodialysis
 - b) Diabetes, hemodialysis and HIV-infection
 - c) Spider bites, indwelling catheters or other hardware
 - d) None of the above

6. Antibiotics that may retain efficacy for the treatment of MRSA include:
 - a) vancomycin, linezolid, ceftriaxone
 - b) vancomycin, trimethoprim-sulfamethoxazole, linezolid
 - c) vancomycin, trimethoprim-sulfamethoxazole, ticarcillin
 - d) vancomycin, dicloxacillin, linezolid

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