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SPECIAL ISSUE

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HIV & Mental Health

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STRIBILD®
elvitegravir 150mg/ cobicistat 150mg/ emtricitabine 200mg/ tenofovir disoproxil fumarate 300mg tablets

COMPLERA®
emtricitabine 200mg/rilpivirine 25mg/ tenofovir disoproxil fumarate 300mg tablets

Please see Brief Summaries of full Prescribing Information for STRIBILD and COMPLERA, including **BOXED WARNINGS,** on the following pages.

STRIBILD® (elvitegravir 150 mg/cobicistat 150 mg/ emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) tablets, for oral use

Brief summary of full Prescribing Information.
See full Prescribing Information. Rx only.

WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate (tenofovir DF), a component of STRIBILD, in combination with other antiretrovirals *[See Warnings and Precautions]*.

STRIBILD is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of STRIBILD have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and human immunodeficiency virus-1 (HIV-1) and have discontinued emtricitabine or tenofovir DF, which are components of STRIBILD. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue STRIBILD. If appropriate, initiation of anti-hepatitis B therapy may be warranted *[See Warnings and Precautions]*.

INDICATIONS AND USAGE:

STRIBILD is indicated as a complete regimen for the treatment of HIV-1 infection in adults who are antiretroviral treatment-naive.

DOSAGE AND ADMINISTRATION:

See ***Warnings and Precautions, Adverse Reactions,*** and ***Use in Specific Populations*** for additional information.

Adult Dosage: One tablet taken orally once daily with food.

Renal Impairment: Do not initiate in patients with estimated creatinine clearance (CrCl) <70 mL/min. Discontinue if CrCl declines to <50 mL/min during treatment.

Hepatic Impairment: No dose adjustment is required in patients with mild or moderate hepatic impairment (Child-Pugh Class A or B). No data are available regarding use in patients with severe hepatic impairment (Child-Pugh Class C). STRIBILD is not recommended for patients with severe hepatic impairment.

Testing Prior to Initiation: Test patients for HBV infection and document CrCl, urine glucose, and urine protein.

CONTRAINDICATIONS:

Coadministration: Do not use with drugs highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening adverse events, or with drugs that strongly induce CYP3A as this may decrease STRIBILD plasma concentrations leading to a loss of efficacy and possible resistance to STRIBILD *[See Drug Interactions]*:

- Alpha 1-adrenoreceptor antagonist: alfuzosin. Potential for hypotension.
- Antimycobacterial: rifampin. May lead to a loss of efficacy and possible resistance.
- Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine. Potential for acute ergot toxicity characterized by peripheral vasospasm and ischemia of the extremities and other tissues.
- GI motility agents: cisapride. Potential for cardiac arrhythmias.
- Herbal products: St. John's wort. May lead to a loss of efficacy and possible resistance.
- HMG CoA reductase inhibitors: lovastatin, simvastatin. Potential for myopathy, including rhabdomyolysis.
- Neuroleptics: pimozide. Potential for cardiac arrhythmias.
- PDE-5 inhibitors: sildenafil when dosed as REVATIO for the treatment of pulmonary arterial hypertension. Increased potential for sildenafil-associated adverse events (visual disturbances, hypotension, priapism, and syncope).
- Sedative/hypnotics: orally administered midazolam, triazolam. Potential for prolonged or increased sedation or respiratory depression.

WARNINGS AND PRECAUTIONS:

Lactic Acidosis/Severe Hepatomegaly with Steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with nucleoside analogs, including tenofovir DF, a component of STRIBILD, in combination with other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Particular caution should be exercised when administering nucleoside analogs to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with STRIBILD should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

Patients Coinfected with HIV-1 and HBV: All patients with HIV-1 should be tested for chronic HBV infection before initiating antiretroviral therapy. STRIBILD is not approved for the treatment of chronic HBV infection and the safety and efficacy of STRIBILD have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and HIV-1 and have discontinued emtricitabine or tenofovir DF, two of the components of STRIBILD. In some patients infected with HBV and treated with emtricitabine, the exacerbations of hepatitis B were associated with liver decompensation and liver failure. Patients who are coinfected with HIV-1 and HBV should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment with STRIBILD. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

New Onset or Worsening Renal Impairment: Renal impairment, including acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with tenofovir DF and with STRIBILD. In clinical trials through 96 weeks, 10 (1.4%) subjects in the STRIBILD group (N=701) and 2 (0.3%) subjects in the combined comparator groups (N=707) discontinued study drug due to a renal adverse reaction. Four (0.6%) subjects who received STRIBILD developed laboratory findings consistent with proximal renal tubular dysfunction leading to discontinuation of STRIBILD compared to 0 in the comparator groups. Two of these 4 subjects had renal impairment (CrCl <70 mL/min) at baseline. The laboratory findings in these 4 subjects improved but did not completely resolve in all subjects upon discontinuation. Renal replacement therapy was not required. STRIBILD should be avoided with concurrent or recent use of a nephrotoxic agent (e.g., high-dose or multiple NSAIDs) *[see Drug Interactions]*. Cases of acute renal failure after initiation of high dose or multiple NSAIDs have been reported in HIV-infected patients with risk factors for renal dysfunction who appeared stable on tenofovir DF. Some patients required hospitalization and renal replacement therapy. Alternatives to NSAIDs should be considered in patients at risk for renal dysfunction. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function. ***Monitoring:*** CrCl, urine glucose and urine protein should be documented in all patients prior to initiating therapy. Do not initiate in patients with CrCl <70 mL/min. Routinely monitor CrCl, urine glucose, and urine protein during therapy in all patients. Additionally monitor serum phosphorus in patients at risk for renal impairment. Although cobicistat may cause modest increases in serum creatinine and modest declines in CrCl without affecting renal glomerular function *[See Adverse Reactions]*, patients with a confirmed increase in serum creatinine of >0.4 mg/dL from baseline should be closely monitored for renal safety. Discontinue STRIBILD if CrCl declines to <50 mL/min.

Use with Other Antiretroviral Products: STRIBILD is a complete regimen for the treatment of HIV-1 infection and coadministration with other antiretroviral products is not recommended. Do not coadminister with products containing any of the same active components; with products containing lamivudine; with products containing ritonavir; or with adefovir dipivoxil.

Bone Effects of tenofovir DF: ***Bone Mineral Density (BMD):*** In clinical trials in HIV-1 infected adults, tenofovir DF was associated with decreases in BMD and increases in biochemical markers of bone metabolism, suggesting increased bone turnover relative to comparators. Serum parathyroid hormone levels and 1,25 Vitamin D levels were also higher in subjects receiving tenofovir DF. For additional information, consult the VIREAD (tenofovir DF) full Prescribing Information. The effects of tenofovir DF-associated changes in BMD and biochemical markers on long-term bone health and future fracture risk are unknown. Consider assessing BMD in patients with a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. Although the effect of supplementation with calcium and vitamin D was not studied, such supplementation may be beneficial. If bone abnormalities are suspected appropriate consultation should be obtained. ***Mineralization Defects:*** Cases of osteomalacia associated with proximal renal tubulopathy, manifested as bone pain or pain in extremities and which may contribute to fractures, have been reported in association with the use of tenofovir DF. Arthralgias and muscle pain or weakness have also been reported in cases of proximal renal tubulopathy. Hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered in patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms while receiving products containing tenofovir DF. *[See Adverse Reactions]*

Fat Redistribution: Redistribution/accumulation of body fat including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and "cushingoid appearance" have been observed in patients receiving antiretroviral therapy. The mechanism and long-term consequences of these events are currently unknown. A causal relationship has not been established.

Immune Reconstitution Syndrome (IRS): IRS has been reported in patients treated with combination antiretroviral therapy, including STRIBILD. During the initial phase of combination antiretroviral treatment, patients whose immune system responds may develop an inflammatory response to indolent or residual opportunistic infections (e.g., *Mycobacterium avium* infection, cytomegalovirus, *Pneumocystis jirovecii* pneumonia [PCP], or tuberculosis), which may necessitate further evaluation and treatment. Autoimmune disorders (e.g., Graves' disease, polymyositis, and Guillain-Barre syndrome) have been reported to occur in the setting of immune reconstitution, however, the time to onset is more variable, and can occur many months after initiation of treatment.

ADVERSE REACTIONS:

*See **BOXED WARNING** and **Warnings and Precautions** for additional serious adverse reactions.* The safety assessment of STRIBILD is based on pooled data from two Phase 3 trials in antiretroviral treatment-naive HIV-1 infected adults. A total of 701 subjects received STRIBILD once daily for at least 96 weeks. 4.6% of subjects discontinued STRIBILD due to adverse events, regardless of severity.

Adverse Reactions: Treatment emergent adverse reactions (all grades) reported in ≥5% of subjects receiving STRIBILD (N=701) through week 96 were: nausea (16%), diarrhea (12%), abnormal dreams (9%), and headache (7%). Frequencies are based on all treatment emergent adverse reactions attributed to study drugs. See *Warnings and Precautions* for more information on renal adverse reactions.

Laboratory Abnormalities: Treatment emergent laboratory abnormalities (Grades 3-4) occurring in ≥2% of subjects receiving STRIBILD (N=701) through 96 weeks were: creatine kinase ≥10.0x ULN (7%); urine RBC (hematuria) >75 RBC/HPF (3%); amylase >2.0x ULN (3%); and AST >5.0x ULN (2%). For subjects with serum amylase >1.5x ULN, lipase test was performed; increased lipase (Grades 3-4) occurring in STRIBILD (N=61) was 15%. Proteinuria (all grades) occurred in 46% of subjects receiving STRIBILD. Cobicistat has been shown to decrease CrCl due to inhibition of tubular secretion of creatinine without affecting renal glomerular function; decreases in CrCl occurred early in treatment with STRIBILD after which they stabilized. Mean ±SD changes after 96 weeks of treatment were: serum creatinine, 0.13 ±0.13 mg/dL; and eGFR by Cockcroft-Gault, -13.2 ±15.7 mL/min. Elevation in serum creatinine (all grades) occurred in 10% of subjects. BMD was assessed by DEXA in a non-random subset; mean decreases in BMD from baseline to Week 96 in the STRIBILD group (N=47) were comparable to the comparator group at the lumbar spine (-2.0%) and the hip (-3.2%). Bone fractures occurred in 14 subjects (2.0%) in the STRIBILD group.

Serum Lipids: In clinical trials, 11% of subjects receiving STRIBILD were on lipid lowering agents at baseline; through Week 96, an additional 8% of subjects were started on lipid lowering agents. Mean changes from baseline in fasting serum lipids in subjects receiving STRIBILD (N=701) through 96 weeks were: total cholesterol: week 96 change +12 (N=571; baseline 166 mg/dL); HDL-cholesterol: week 96 change +7 (N=571; baseline 43 mg/dL); LDL-cholesterol: week 96 change +12 (N=572; baseline 100 mg/dL); triglycerides: week 96 change +8 (N=571; baseline 122 mg/dL). The change from baseline is the mean of within-patient changes from baseline for patients with both baseline and Week 96 values.

Consult the respective full Prescribing Information for each available individual component of STRIBILD for additional information regarding adverse reactions, including laboratory abnormalities and postmarketing events.

DRUG INTERACTIONS:

*See **Contraindications** for additional serious drug interactions.*

STRIBILD is a complete regimen for the treatment of HIV-1 infection. STRIBILD should not be administered with other antiretroviral medications for treatment of HIV-1 infection. Complete information regarding potential drug-drug interactions with other antiretroviral medications is not provided.

Potential for STRIBILD to Affect Other Drugs: Cobicistat is an inhibitor of CYP3A and CYP2D6 and the transporters p-glycoprotein (P-gp), BCRP, OATP1B1 and OATP1B3. Coadministration of STRIBILD with drugs that are primarily metabolized by CYP3A or CYP2D6, or are substrates of P-gp, BCRP, OATP1B1 or OATP1B3 may result in increased concentrations of such drugs. Elvitegravir is a modest inducer of CYP2C9 and may decrease the concentrations of CYP2C9 substrates.

Potential for Other Drugs to Affect STRIBILD: Elvitegravir and cobicistat are metabolized by CYP3A. Cobicistat is also metabolized to a minor extent by CYP2D6. Drugs that induce CYP3A activity are expected to increase the clearance of elvitegravir and cobicistat, resulting in decreased concentrations of cobicistat and elvitegravir, which may lead to loss of efficacy and development of resistance. Coadministration of STRIBILD with other drugs that inhibit CYP3A may decrease the clearance and increase the concentration of cobicistat.

Drugs Affecting Renal Function: Because emtricitabine and tenofovir are primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion, coadministration of STRIBILD with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of emtricitabine, tenofovir, and other renally eliminated drugs, which may increase the incidence of adverse reactions *[see Warnings and Precautions]*.

Established and Other Potentially Significant Interactions: The drug interactions described are based on studies conducted with either STRIBILD, the components of STRIBILD as individual agents and/or in combination, or are predicted drug interactions that may occur with STRIBILD. The list includes potentially significant interactions but is not all inclusive. **An alteration in dose or regimen may be recommended for the following drugs when coadministered with STRIBILD:**

- Acid Reducing Agents: antacids. Separate STRIBILD and antacid administration by at least 2 hours.

STRIBILD® (elvitegravir 150 mg/cobicistat 150 mg/ emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) tablets, for oral use Brief summary (*cont*)

- Antiarrhythmics: amiodarone, bepridil, digoxin, disopyramide, flecainide, systemic lidocaine mexiletine, propafenone, quinidine. Caution warranted and therapeutic concentration monitoring recommended.
- Antibacterials: clarithromycin, telithromycin. Clarithromycin: no dose adjustment required for patients with CrCl ≥60 ml/min; the dose should be reduced by 50% for patients with CrCl between 50 and 60 mL/min. Telithromycin: concentrations of telithromycin and/or cobicistat may be increased.
- Anticoagulants: warfarin. International normalized ratio (INR) monitoring recommended.
- Anticonvulsants: carbamazepine, oxcarbazepine phenobarbital, phenytoin, clonazepam, ethosuximide. Phenobarbital, phenytoin, carbamazepine, and oxcarbazepine: may lead to loss of efficacy and possible resistance to STRIBILD. Alternative anticonvulsants should be considered. Clonazepam and ethosuximide: clinical monitoring recommended.
- Antidepressants: Selective Serotonin Reuptake Inhibitors (SSRIs), Tricyclic Antidepressants (TCAs), trazodone. Dose titration of the antidepressant and monitoring for antidepressant response recommended.
- Antifungals: itraconazole, ketoconazole, voriconazole. Ketoconazole and itraconazole: the maximum daily dose should not exceed 200 mg/day. Voriconazole: an assessment of benefit/risk ratio is recommended to justify use.
- Anti-gout: colchicine. Do not coadminister in patients with renal or hepatic impairment. For other patients, modify the dose and/or regimen as described in the full PI for STRIBILD.
- Antimycobacterials: rifabutin, rifapentine. May lead to loss of efficacy and possible resistance to STRIBILD. Coadministration not recommended.
- Beta-Blockers: metoprolol, timolol. Clinical monitoring recommended and a dose decrease of the beta blocker may be necessary.
- Calcium Channel Blockers: amlodipine, diltiazem, felodipine, nicardipine, nifedipine, verapamil. Caution warranted and clinical monitoring recommended.
- Corticosteroids (Systemic): dexamethasone. May lead to loss of efficacy and possible resistance to STRIBILD.
- Corticosteroids (Inhaled/Nasal): fluticasone. Alternative corticosteroids should be considered, particularly for long term use.
- Endothelin Receptor Antagonists: bosentan. Discontinue bosentan at least 36 hours prior to initiating STRIBILD. For patients taking STRIBILD for at least 10 days, start or resume bosentan at 62.5 mg once daily or every other day based on individual tolerability.
- HMG CoA Reductase Inhibitors: atorvastatin. Initiate with the lowest starting dose and titrate carefully while monitoring for safety.
- Hormonal Contraceptives: norgestimate/ethinyl estradiol. Coadministration with STRIBILD resulted in decreased plasma concentrations of ethinyl estradiol and an increase in norgestimate. The effects of increased progesterone exposure are not fully known. The potential risks and benefits of coadministration should be considered, particularly in women who have risk factors for progesterone exposure. Alternative (non hormonal) methods of contraception can be considered.
- Immunosuppressants: cyclosporine, rapamycin, sirolimus, tacrolimus. Therapeutic monitoring recommended.
- Narcotic Analgesics: buprenorphine, naloxone. Closely monitor for sedation and cognitive effects.
- Inhaled Beta Agonist: salmeterol. Coadministration not recommended due to the increased risk of salmeterol cardiovascular adverse events, including QT prolongation, palpitations, and sinus tachycardia.
- Neuroleptics: perphenazine, risperidone, thioridazine. Decrease in dose of the neuroleptic may be needed.
- Phosphodiesterase-5 (PDE5) Inhibitors: sildenafil, tadalafil, vardenafil. *Dosage for erectile dysfunction:* sildenafil, a single dose not exceeding 25 mg in 48 hours; vardenafil, a single dose not exceeding 2.5 mg in 72 hours; tadalafil, a single dose not exceeding 10 mg in 72 hours; increase monitoring for PDE-5 associated adverse reactions. *Dosage for pulmonary arterial hypertension (PAH):* tadalafil: stop tadalafil at least 24 hours prior to initiating STRIBILD; start or resume at 20 mg once daily in patients receiving STRIBILD for at least 1 week and increase to 40 mg once daily based on individual tolerability.
- Sedative/hypnotics: Benzodiazepines. Parenteral midazolam: coadministration should be done in a setting ensuring close clinical monitoring and appropriate medical management in case of respiratory depression and/or prolonged sedation; dose reduction should be considered, especially if more than a single dose is administered. Other sedative/hypnotics: dose reduction may be necessary and clinical monitoring recommended.

Consult the full PI prior to and during treatment with STRIBILD for potential drug interactions; this list is not all inclusive.

USE IN SPECIFIC POPULATIONS:

Pregnancy: STRIBILD is Pregnancy Category B; however, there are no adequate and well-controlled studies in pregnant women. STRIBILD should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. ***Antiretroviral Pregnancy Registry:*** To monitor fetal outcomes of pregnant women exposed to STRIBILD, an Antiretroviral Pregnancy Registry has been established. Healthcare providers are encouraged to register patients by calling 1-800-258-4263.

Nursing Mothers: The Centers for Disease Control and Prevention recommend that HIV infected mothers not breastfeed their infants to avoid risking postnatal transmission of HIV. Studies in rats have demonstrated that elvitegravir, cobicistat, and tenofovir are secreted in milk. Emtricitabine and tenofovir have been detected in human milk; it is not known if elvitegravir or cobicistat is secreted in human milk. Because of both the potential for HIV transmission and the potential for serious adverse reactions and/or drug resistance in nursing infants, **mothers should be instructed not to breastfeed if they are receiving STRIBILD.**

Pediatric Use: Safety and effectiveness in children less than 18 years of age have not been established.

Geriatric Use: Clinical studies of STRIBILD did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Caution should be exercised in the administration of STRIBILD in elderly patients.

Renal Impairment: STRIBILD should not be initiated in patients with CrCl <70 mL/min. STRIBILD should be discontinued if CrCl declines to <50 mL/min during treatment with STRIBILD. *[See Warnings and Precautions, Adverse Reactions].*

Hepatic Impairment: No dose adjustment is required in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. STRIBILD is not recommended for use in patients with severe hepatic impairment (Child-Pugh Class C) as no pharmacokinetic or safety data are available in these patients *[See Dosage and Administration].*

OVERDOSAGE:

If overdose occurs the patient must be monitored for evidence of toxicity. Treatment consists of general supportive measures including monitoring of vital signs as well as observation of the clinical status of the patient.

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COMPLERA® (emtricitabine 200 mg/rilpivirine 25 mg/ tenofovir disoproxil fumarate 300 mg) tablets, for oral use

Brief Summary of full Prescribing Information. See full Prescribing Information. Rx Only.

WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate (tenofovir DF), a component of COMPLERA, in combination with other antiretrovirals *[See Warnings and Precautions].*

COMPLERA is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of COMPLERA have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and human immunodeficiency virus-1 (HIV-1) and have discontinued emtricitabine or tenofovir DF, which are components of COMPLERA. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue COMPLERA. If appropriate, initiation of anti-hepatitis B therapy may be warranted. *[See Warnings and Precautions].*

INDICATIONS AND USAGE:

COMPLERA is indicated as a complete regimen for the treatment of HIV-1 infection in antiretroviral treatment-naive adults with HIV-1 RNA ≤100,000 copies/mL at the start of therapy. COMPLERA is not recommended for patients <18 years of age.

Prescribing considerations when initiating therapy with COMPLERA:

- More rilpivirine-treated subjects with HIV-1 RNA >100,000 copies/mL at the start of therapy experienced virologic failure (HIV-1 RNA ≥50 copies/mL) compared to rilpivirine-treated subjects with HIV-1 RNA ≤100,000 copies/mL.
- Regardless of HIV-1 RNA level at the start of therapy, more rilpivirine-treated subjects with CD4+ cell count <200 cells/mm^3 experienced virologic failure compared to rilpivirine-treated subjects with CD4+ cell count ≥200 cells/mm^3.
- The observed virologic failure rate in rilpivirine-treated subjects conferred a higher rate of overall treatment resistance and cross-resistance to the NNRTI class compared to efavirenz.
- More subjects treated with rilpivirine developed tenofovir and lamivudine/emtricitabine associated resistance compared to efavirenz.

DOSAGE AND ADMINISTRATION:

See ***Warnings and Precautions, Adverse Reactions,*** and ***Use in Specific Populations*** for additional information.

Adult Dosage: One tablet taken orally once daily with food.

Renal Impairment: Do not use in patients with estimated creatinine clearance (CrCl) <50 mL/min.

CONTRAINDICATIONS:

Coadministration: Do not use with drugs that induce CYP3A or increase gastric pH as significant decreases in rilpivirine plasma concentrations may occur leading to loss of virologic response and possible resistance to COMPLERA or to the class of NNRTIs *[See Drug Interactions].*

- Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- Antimycobacterials: rifabutin, rifampin, rifapentine
- Proton pump inhibitors: esomeprazole, lansoprazole, dexlansoprazole, omeprazole, pantoprazole, rabeprazole
- Glucocorticoid (systemic): dexamethasone (>1 dose)
- Herbal product: St. John's wort

WARNINGS AND PRECAUTIONS:

Lactic Acidosis/Severe Hepatomegaly with Steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir DF, a component of COMPLERA, in combination with other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Particular caution should be exercised when administering nucleoside analogs to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with COMPLERA should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

Patients Coinfected with HIV-1 and HBV: All patients with HIV-1 should be tested for chronic HBV before initiating antiretroviral therapy. COMPLERA is not approved for the treatment of chronic HBV infection and the safety and efficacy of COMPLERA have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and HIV-1 and have discontinued emtricitabine or tenofovir DF, two of the components of COMPLERA. In some patients infected with HBV and treated with emtricitabine, the exacerbations of hepatitis B were associated with liver decompensation and liver failure. Patients who are coinfected with HIV-1 and HBV should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment with COMPLERA. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

New Onset or Worsening Renal Impairment: Renal impairment, including acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with tenofovir DF. Assess estimated CrCl in all patients prior to initiating therapy and as clinically appropriate during therapy with COMPLERA. In patients at risk of renal dysfunction, including patients who have previously experienced renal events while receiving adefovir dipivoxil, it is recommended that estimated CrCl, serum phosphorus, urine glucose, and urine protein be assessed prior to initiation of COMPLERA, and periodically during COMPLERA therapy. COMPLERA should be avoided with concurrent or recent use of a nephrotoxic agent (e.g., high dose or multiple NSAIDS) *[see Drug Interactions].* Cases of acute renal failure after initiation of high dose or multiple NSAIDs have been reported in HIV-infected patients with risk factors for renal dysfunction who appeared stable on tenofovir DF. Some patients required hospitalization and renal replacement therapy. Alternatives to NSAIDs should be considered in patients at risk for renal dysfunction. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function in at-risk patients. Do not use COMPLERA in patients with estimated CrCl <50 mL/min.

Drug Interactions: Caution should be given when prescribing COMPLERA with drugs that may reduce the exposure of rilpivirine or when coadministered with a drug with a known risk of Torsade de Pointes. In healthy subjects, supratherapeutic doses of rilpivirine (75 mg once daily and 300 mg once daily) have been shown to prolong the QTc interval of the electrocardiogram (ECG) *[See Contraindications and Drug Interactions].*

Depressive Disorders: Depressive disorders (depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, suicidal ideation) have been reported with rilpivirine. Through 96 weeks in Phase 3 trials (N=686), the incidence of depressive disorders (regardless of causality, severity) was 9% (most events were mild or moderate in severity); Grades 3 and 4 depressive disorders (regardless of causality) was 1%; and discontinuation due to depressive disorders was 1%; suicidal ideation was reported in 4 subjects and suicide attempt was reported in 2 subjects. Patients with severe depressive symptoms should seek immediate medical evaluation to assess the possibility that the symptoms are related to COMPLERA, and if so, to determine whether the risks of continued therapy outweigh the benefits.

Hepatotoxicity: Hepatic adverse events have been reported with rilpivirine. Patients with underlying hepatitis B or C, or marked elevations in serum liver biochemistries prior to treatment may be at increased risk for worsening or development of serum liver biochemistries elevations with use of COMPLERA. A few cases of hepatic toxicity have been reported in patients receiving a rilpivirine containing regimen who had no pre-existing hepatic disease or other identifiable risk factors. Appropriate laboratory testing prior to initiating therapy and monitoring for hepatotoxicity during therapy with COMPLERA is recommended in patients with underlying hepatic disease such as hepatitis B or C, or in patients with marked elevations in serum liver biochemistries prior to treatment initiation. Serum liver biochemistries monitoring should also be considered for patients without pre-existing hepatic dysfunction or other risk factors.

Bone Effects of Tenofovir DF: ***Bone mineral density (BMD):*** In clinical trials in HIV-1 infected adults, tenofovir DF was associated with decreases in BMD and increases in biochemical markers of bone metabolism, suggesting increased bone turnover relative to comparators. Serum parathyroid hormone levels and 1,25 Vitamin D levels were also higher in subjects receiving tenofovir DF. For more information, please consult the VIREAD (tenofovir DF) full Prescribing Information. The effects of tenofovir DF-associated changes in BMD and biochemical markers on long-term bone health and future fracture risk are unknown. Consider assessing BMD in patients with a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. Although the effect of supplementation with calcium and Vitamin D was not studied, such supplementation may be beneficial. If bone abnormalities are suspected, appropriate consultation should be obtained. ***Mineralization defects:*** Cases of osteomalacia associated with proximal renal tubulopathy manifested as bone pain or pain in extremities and which may contribute to fractures, have been reported in association with the use of tenofovir DF. Arthralgias and muscle pain or weakness have also been reported in cases of proximal renal tubulopathy. Hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered in patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms while receiving products containing tenofovir DF.

Coadministration with Other Products: COMPLERA should not be administered concurrently with other products containing any of the same active components, emtricitabine, rilpivirine, or tenofovir DF; with products containing lamivudine; or with adefovir dipivoxil.

Fat Redistribution: Redistribution/accumulation of body fat including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and "cushingoid appearance" have been observed in patients receiving antiretroviral therapy. The mechanism and long-term consequences of these events are unknown. A causal relationship has not been established.

Immune Reconstitution Syndrome (IRS): IRS has been reported in patients treated with combination antiretroviral therapy, including the components of COMPLERA. During the initial phase of combination antiretroviral treatment, patients whose immune system responds may develop an inflammatory response to indolent or residual opportunistic infections (e.g., *Mycobacterium avium* infection, cytomegalovirus, *Pneumocystis jirovecii* pneumonia [PCP], or tuberculosis), which may necessitate further evaluation and treatment. Autoimmune disorders (e.g., Graves' disease, polymyositis, and Guillian-Barré syndrome) have also been reported to occur in the setting of immune reconstitution, however, the time to onset is more variable, and can occur many months after initiation of treatment.

ADVERSE REACTIONS:

See ***BOXED WARNING*** *and* ***Warnings and Precautions*** *for additional serious adverse reactions.*

The safety assessment of rilpivirine, used in combination with other antiretroviral drugs, is based on the week 96 pooled data from two Phase 3 trials in antiretroviral treatment-naive HIV-1 infected adults. A total of 686 subjects received rilpivirine in combination with other antiretroviral drugs as background regimen; 550 of whom received emtricitabine/tenofovir DF. The median duration of exposure for subjects was 104 weeks.

Adverse Reactions: Treatment emergent adverse reactions (Grades 2-4) reported in ≥2% of subjects receiving rilpivirine + emtricitabine/tenofovir DF (N=550) through week 96 were: depressive disorders (2%; includes depressed mood, depression, dysphoria, major depression, mood altered, negative thoughts, suicide attempt, and suicidal ideation), headache (2%), and insomnia (2%). Frequencies of adverse reactions are based on all Grades 2-4 treatment emergent adverse reactions assessed to be related to study drug. No new adverse reactions were identified between weeks 48 and 96. The adverse reactions observed in this subset of subjects were generally consistent with those seen for the overall patient population (for additional information, consult the EDURANT [rilpivirine] full Prescribing Information). Two percent of subjects discontinued treatment with rilpivirine + emtricitabine/tenofovir DF due to adverse reactions (regardless of severity). The most common adverse reactions leading to discontinuation were psychiatric disorders (9 [1.6%] subjects); rash led to discontinuation in 1 (0.2%) subject. ***Rilpivirine adverse reactions:*** Treatment emergent adverse reactions (≥Grade 2) occurring in <2% of subjects receiving rilpivirine (N=686) were (grouped by Body System): vomiting, diarrhea, abdominal discomfort, abdominal pain, fatigue, cholecystitis, cholelithiasis, decreased appetite, somnolence, sleep disorders, anxiety, glomerulonephritis membranous, glomerulonephritis mesangioproliferative, and nephrolithiasis.

Laboratory Abnormalities: Treatment emergent laboratory abnormalities (Grades 1, 2, 3, and 4, respectively) occurring in subjects receiving rilpivirine + emtricitabine/tenofovir DF (N=550) through week 96 were: increased creatinine (6%, 1%, <1%, 0%), increased AST (16%, 4%, 2%, 1%), increased ALT (19%, 5%, 1%, 1%), increased total bilirubin (6%, 3%, 1%, 0%), increased fasting total cholesterol (14%, 6%, <1%, 0%), increased fasting LDL cholesterol (13%, 5%, 1%, 0%), and increased fasting triglycerides (0%, 1%, 1%, 0%).

Adrenal Function: Mean changes from baseline in basal cortisol and ACTH-stimulated cortisol at week 96 (N=686) were -19.1 nmol/L (95% CI: -30.9; -7.4) and +18.4 ± 8.36 nmol/L, respectively; both values were within normal range. Effects on adrenal function were comparable by background N(t)RTIs. No serious adverse reactions, deaths, or treatment discontinuations were attributed to adrenal insufficiency.

Serum Creatinine: Mean change from baseline in serum creatinine at week 96 (N=686) was 0.1 mg/dL (range: -0.3 mg/dL to 0.6 mg/dL); most increases occurred within the first four weeks of treatment. Observed serum creatinine increases were similar among subjects with baseline mild or moderate renal impairment and subjects with baseline normal renal function; increases were comparable by background N(t)RTIs. No changes were considered to be clinically relevant and no subject discontinued treatment due to serum creatinine increases.

Serum Lipids: Mean changes from baseline in fasting serum lipids at week 96 were: total cholesterol: +2 mg/dL (N=430; baseline 162 mg/dL); HDL-cholesterol: +4 mg/dL (N=429; baseline 42 mg/dL); LDL-cholesterol: -1 mg/dL (N=427; baseline 97 mg/dL); and triglycerides: -14 mg/dL (N=430; baseline 123 mg/dL). The change from baseline is the mean of within-patient changes from baseline for patients with both baseline and week 96 values. Subjects receiving lipid lowering agents during treatment were excluded from these lipid analyses.

Subjects Coinfected with Hepatitis B and/or Hepatitis C Virus: In patients coinfected with hepatitis B or C virus receiving rilpivirine, the incidence of hepatic enzyme elevation was higher than in subjects receiving rilpivirine who were not coinfected. The pharmacokinetic exposure of rilpivirine in coinfected subjects was comparable to that in subjects without coinfection.

Consult the respective full Prescribing Information for each individual component of COMPLERA for additional information regarding adverse reactions, including laboratory abnormalities and postmarketing events.

DRUG INTERACTIONS:

See ***Contraindications*** *for additional serious drug interactions.*

COMPLERA is a complete regimen for the treatment of HIV-1 infection and should not be administered with other antiretroviral medications. Information regarding potential drug interactions with other antiretroviral medications is not provided.

Drugs Inducing or Inhibiting CYP3A: Rilpivirine is primarily metabolized by CYP3A, thus drugs that induce or inhibit CYP3A may affect the clearance of rilpivirine. Coadministration of rilpivirine and drugs that induce CYP3A may result in decreased plasma concentrations of rilpivirine leading to loss of virologic response and possible resistance to rilpivirine or to the class of NNRTIs. Coadministration of rilpivirine and drugs that inhibit CYP3A may result in increased plasma concentrations of rilpivirine. Rilpivirine at a dose of 25 mg once daily is not likely to have a clinically relevant effect on the exposure of drugs metabolized by CYP enzymes.

Drugs Increasing Gastric pH: Coadministration of rilpivirine with drugs that increase gastric pH may decrease plasma concentrations of rilpivirine leading to loss of virologic response and possible resistance to rilpivirine or to the class of NNRTIs.

Drugs Affecting Renal Function: Because emtricitabine and tenofovir are primarily eliminated by the kidneys through a combination of glomerular filtration and active tubular secretion, coadministration of COMPLERA with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of emtricitabine, tenofovir, and other renally eliminated drugs, which may increase the incidence of adverse reactions *[See Warnings and Precautions].*

QT Prolonging Drugs: There is limited information available on the potential for a pharmacodynamic interaction between rilpivirine and drugs that prolong the QTc interval of the ECG. In a study of healthy subjects, supratherapeutic doses of rilpivirine (75 mg once daily and 300 mg once daily) have been shown to prolong the QTc interval of the ECG. COMPLERA should be used with caution when coadministered with a drug with a known risk of Torsade de Pointes.

Established and Other Potentially Significant Drug Interactions: The drug interactions described are based on studies conducted with individual components of COMPLERA or are predicted drug interactions that may occur with COMPLERA; no drug interaction studies have been conducted using COMPLERA as a fixed-dose combination tablet. The list includes potentially significant interactions but is not all inclusive. For additional information, consult the EDURANT, VIREAD or EMTRIVA (emtricitabine) full Prescribing Information. **An alteration in dose or regimen may be recommended when the following drugs are coadministered with COMPLERA:**

- Antacids: aluminum, magnesium hydroxide, calcium carbonate. Antacids should be taken ≥2 hours before or ≥4 hours after COMPLERA.
- Azole Antifungals: fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole. No dose adjustment required; monitor for breakthrough fungal infections.
- H_2-Receptor Antagonists: cimetidine, famotidine, nizatidine, ranitidine. H_2-receptor antagonists should be taken ≥12 hours before or ≥4 hours after COMPLERA.
- Macrolide/Ketolide Antibiotics: clarithromycin, erythromycin, telithromycin. Consider alternatives (e.g., azithromycin) when possible.
- Narcotic Analgesic: methadone. No dose adjustment required at therapy initiation; monitor during treatment; methadone maintenance dose may need adjustment.

Consult the full Prescribing Information prior to and during treatment with COMPLERA for potential drug interactions; this list is not all inclusive.

USE IN SPECIFIC POPULATIONS:

Pregnancy: COMPLERA is Pregnancy Category B; however, there are no adequate and well-controlled studies in pregnant women. COMPLERA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. ***Antiretroviral Pregnancy Registry:*** To monitor fetal outcomes of pregnant women exposed to COMPLERA, an Antiretroviral Pregnancy Registry has been established. Healthcare providers are encouraged to register patients by calling 1-800-258-4263.

Nursing Mothers: The Centers for Disease Control and Prevention recommend that HIV infected mothers not breastfeed their infants to avoid risking postnatal transmission of HIV. Studies in rats have demonstrated that rilpivirine and tenofovir are secreted in milk. Emtricitabine and tenofovir have been detected in human milk; it is not known if rilpivirine is secreted in human milk. Because of both the potential for HIV transmission and the potential for serious adverse reactions and/or drug resistance in nursing infants, **mothers should be instructed not to breastfeed if they are receiving COMPLERA.**

Pediatric Use: COMPLERA is not recommended for patients <18 years of age because not all the individual components of the COMPLERA have safety, efficacy and dosing recommendations available for all pediatric age groups.

Geriatric Use: Clinical studies of emtricitabine, rilpivirine, or tenofovir DF did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for the elderly patients should be cautious, keeping in mind the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Renal Impairment: COMPLERA should not be prescribed for patients with moderate, severe or end stage renal impairment (CrCl <50 mL/min) or patients who require dialysis *[See Warnings and Precautions].*

Hepatic Impairment: No dose adjustment of COMPLERA is required in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. COMPLERA has not been studied in patients with severe hepatic impairment (Child-Pugh Class C).

OVERDOSAGE:

If overdose occurs the patient must be monitored for evidence of toxicity. Treatment of overdose with COMPLERA consists of general supportive measures including monitoring of vital signs and ECG (QT interval) as well as observation of the clinical status of the patient.

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BY JAMES M. FRIEDMAN, MHA, EXECUTIVE DIRECTOR, AAHIVM

Progress: Past and Present

APPROXIMATELY 25 YEARS AGO, I was on the senior staff of the Assistant Secretary for Health in the U.S. Public Health Service. Prior to becoming the Assistant Secretary for Health, Dr. James O. Mason was the Director of the Centers for Disease Control, and was very involved with HIV/AIDS prevention.

James M. Friedman

In one of his 8 a.m. daily senior staff meetings, Dr. Mason turned to me and said, "Jim, I want you to go to Chicago and find out whether the Alcohol, Drug Abuse and Mental Health Administration (now the Substance Abuse & Mental Health Services Administration or SAMHSA) is doing enough to combat the spread of HIV/AIDS." Unfortunately, I didn't have much to report upon my return from Chicago. It is safe to say SAMHSA is doing a much better job now.

As you know, substance abuse and mental illness are closely associated with HIV—both as a transmitter and a co-morbid condition. In this issue, we have partnered with the American Psychological Association (APA) and several of APA's HIV experts to address many of these important issues. Dr. David J. Martin, Senior Director of APA's Office on AIDS, has been instrumental in identifying relevant topics and expert authors, and of invaluable assistance as we developed this edition.

I hope this issue of the *HIV Specialist* is the first of many joint projects between the Academy and APA.

As we near the end of 2013, it is useful to take stock of what a good year this has been for the Academy and for the HIV community in general. First and foremost is the implementation of the Affordable Care Act (ACA). Yes, there have been substantial problems with the ACA website—severely limiting the ability to sign up participants. Hopefully these problems are behind us.

We at the Academy have invested an enormous amount of effort in helping HIV practitioners prepare for ACA. In September, we launched the Health Reform Resource Center for HIV Providers on our website, which assists practitioners in learning about the specific developments in the health care systems in their state, including the State Insurance Exchanges (Marketplaces), any Medicaid Managed Care plans offered in the state, and their state's decisions on the Medicaid Expansion Option.

Our Credentialing Program continues to grow in numbers and recognition. There are now over 2000 HIV credentialed practitioners and pharmacists in the United States. That number should expand further in 2014.

Membership in the Academy has now surpassed 1600. We have opened up a dialogue with the American Academy of Physician Assistants in an attempt to increase Academy PA membership and are considering doing the same for Nurse Practitioners.

In the policy arena, we have been active at both the national and state level. For example, we worked with 16 other HIV advocacy organizations to pass the HOPE Act, which opens the doors to federal research that could help hundreds of HIV patients currently awaiting a transplant. We also worked with our New York members to hold a "White Coat Day" in Albany to fight the lurking threat to the "Prescriber Prevails" rules in New York's Medicaid program. We also supported Assembly legislation to protect HIV medications from prior authorization and preferred drug lists.

The *HIV Specialist* magazine continues to evolve and grow—with a circulation of 11,000.

We continued the AAHIVM/Institute for Technology in Health Care HIV Practice Award, which provides $10,000 grants to two practices demonstrating innovative use of technology in the HIV care setting. We look forward to the third year of the award in 2014.

We also have some new programs scheduled for the first quarter of 2014. We will launch a new membership campaign, with a goal of increasing membership by 10 percent in 2014. And following up on our 2011 project with the American Geriatrics Society (*Recommended Treatment Strategies for Clinicians Managing Older Patients with HIV*), we will launch a new, multi-faceted HIV and Aging Blog funded by the Archstone Foundation.

Finally, the staff of the Academy and I wish all of you and the patients you serve a happy and healthy holiday season and a bright 2014. HIV

IN THE NEWS

Aggressive New Strain of HIV Discovered by Scientists

A new strain of HIV that appears to progress much faster than most previously identified variations of the virus has been identified by Swedish scientists, according to a study published in the *Journal of Infectious Diseases*.

The HIV-1 recombinant strain A3/02, a fused form of the 02AG and A3 strains, moves from HIV to AIDS development in five years, much faster than previously known strains.

The two strains that recombined to form this new one are the most common strains in Guinea-Bissau in West Africa. So far the new infection appears confined to West Africa, but experts fear that recombinants are becoming more common and could start spreading globally.

"HIV is an extremely dynamic and variable virus," said study researcher Patrik Medstrand, professor of clinical virology at Lund University. "New subtypes and recombinant forms of HIV-1 have been introduced to our part of the world, and it is highly likely that there are a large number of circulating recombinants of which we know little or nothing. We therefore need to be aware of how the HIV-1 epidemic changes over time."

In the study, *Faster Progression to AIDS and AIDS-Related Death Among Seroincident individuals infected With Recombinant HIV-1 A3/CRF02_AG Compared With Sub-subtype A3*, the researchers stated:

"Infection with A3/02 was associated with a close to three-fold increased risk of AIDS and AIDS-related death compared to A3 (HR = 2.6 [P = 0.011] and 2.9 [P = 0.032], respectively). The estimated time from seroconversion to AIDS and AIDS-related death was 5.0 and 8.0 years for A3/02, 6.2 and 9.0 years for CRF02_AG, and 7.2 and 11.3 years for A3.Conclusion. Our results show that there are differences in disease progression between HIV-1 A-like subtypes/CRFs. Individuals infected with A3/02 have among the fastest progression rates to AIDS reported to date. Determining the HIV-1 subtype of infected individuals could be important in the management of HIV-1 infections."

The findings are based on data from 152 HIV-1 infected people from Guinea-Biussau who were followed as they developed AIDS and died from AIDS-related causes. The A3/02 subtype of HIV was identified in 13 percent of those in the study. HIV

CDC Cites Progress in Reaching HIV Prevention Goals

The Centers for Disease Control and Prevention (CDC) recently published online a report indicating that 62 percent of current HIV prevention targets were met or exceeded.

According to the National HIV Prevention Progress Report, comparing 2008 to 2010, new HIV infections decreased 15 percent among heterosexuals, 21 percent among African American women, and 22 percent among injection drug users. The study also showed a 9 percent decline in the HIV transmission rate. During this time, testing efforts succeeded in increasing the percentage of people living with HIV who know their serostatus from 80.9 percent to 84.2 percent, which means that five out of six people living with HIV in 2010 knew their status.

The report also draws attention to indicators for which more improvement is necessary. For example, there are an estimated 180,000 people in the United States living with undiagnosed HIV infection, racial/ethnic disparities persist, and new infections remain unacceptably high and are increasing among gay, bisexual, and other men who have sex with men (MSM).

Comparing 2008 and 2010, there was a 12 percent increase in new infections among MSM and a 22 percent increase among young MSM aged 13-24 years. In 2009, three out of four persons in medical care had a suppressed viral load, but across all racial and ethnic groups, the 2015 goal was met by whites only. HIV

THINKSTOCK

NIH to Redirect Funds to Seek a Cure for HIV/AIDS

MARKING THE 25TH ANNUAL WORLD AIDS DAY December 2, President Obama revealed that the National Institutes of Health (NIH) will redirect AIDS research funds to expand efforts aimed at finding a cure for HIV. NIH will invest an additional $100 million over the next three fiscal years on this area of HIV/AIDS research, the President said.

In the three decades since AIDS was first reported, NIH-funded researchers—in partnership with academia and the biotechnology and pharmaceutical industries—have helped develop more than 30 life-saving antiretroviral drugs and drug combinations for treating HIV infection.

Important recent advances in basic and therapeutics research aimed at eliminating viral reservoirs in the body are spurring scientists to design and conduct research aimed at a cure or lifelong remission of HIV infection. Key stakeholders from academia, government, foundations, advocacy groups and industry have concluded that developing a cure for HIV is one of the most important biomedical challenges of the 21st century. This will require an extraordinary, collaborative global effort, including public-private partnerships and innovative alliances to share scientific expertise and accelerate the search for a cure.

In a presentation at the White House event, Anthony S. Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases, discussed the public health and scientific rationale for expanded research in this area.

"Although the HIV/AIDS pandemic can theoretically be ended with a concerted and sustained scale-up of implementation of existing tools for HIV prevention and treatment, the development of a cure is critically important, as it may not be feasible for tens of millions of people living with HIV infection to access and adhere to a lifetime of antiretroviral therapy," Dr. Fauci said. "Our growing understanding of the cellular hiding places or 'reservoirs' of HIV, the development of new strategies to minimize or deplete these reservoirs, and encouraging reports of a small number of patients who have little or no evidence of virus despite having halted antiretroviral therapy, all suggest that the time is ripe to pursue HIV cure research with vigor."

THINKSTOCK

Funding for the new initiatives will come from existing resources and a redirection of funds from expiring AIDS research grants over the next three years, according to NIH Director Francis S. Collins, M.D., Ph.D.

"Flat budgets and cuts from sequestration have had a profound and damaging impact on biomedical research, but we must continue to find ways to support cutting-edge science, even in this environment," he said. "AIDS research is an example of an area where hard-won progress over many years has resulted in new and exciting possibilities in basic and clinical science in AIDS that must be pursued."

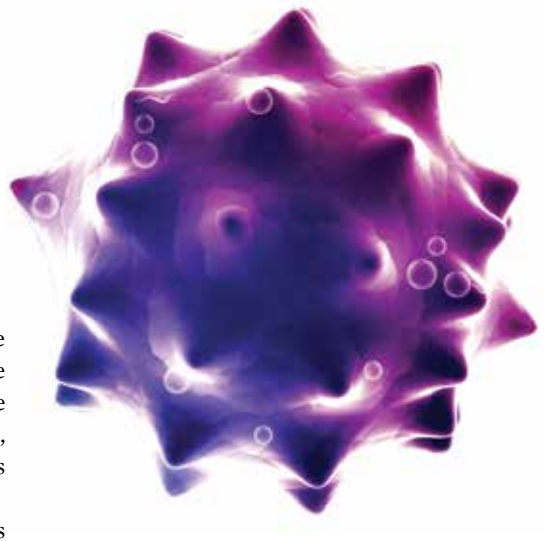
Jack Whitescarver, Ph.D., director of the Office of AIDS Research, a component of the Office of the Director of NIH, said, "We have listened very carefully to the scientific consensus of experts from within the NIH and around the world. We have been building the portfolio of HIV cure research over the past few years, and now is the time to accelerate our research focused specifically toward the goal of sustained or lifelong remission, in which patients control or even eliminate HIV without the need for lifelong antiretroviral therapy."

It is anticipated that a significant portion of the new investment will support basic research, which will also benefit all other areas of AIDS research, as well as research on other diseases. These studies will include research on viral reservoirs, viral latency, and viral persistence, as well as studies of neutralizing antibodies. Research on animal models, drug development and preclinical testing of more potent antiretroviral compounds capable of diminishing viral reservoirs, and clinical research, including studies on therapeutic vaccines and other immune enhancers, will also be supported.

Other high-priority AIDS research will continue to be supported, the White House said. These priorities include: prevention research, including vaccines, microbicides, and other biomedical and behavioral prevention strategies, such as the use of antiretroviral drugs as prevention; research to develop better, less toxic treatments and to investigate how genetic determinants, sex, gender, race, age, nutritional status, treatment during pregnancy, and other factors, including stigma and adherence, interact to affect treatment success or failure and/or disease progression; and studies to address the increased incidence of malignancies, cardiovascular, neurologic, and metabolic complications, and premature aging associated with long-term HIV disease and antiretroviral treatment. **HIV**

IN THE NEWS

Study: Older HIV+ MSMs at Increased Risk of Anal Cancer



Human papillomavirus, or HPV, which can cause cervical cancer in women, is also known to cause anal cancer in both women and men. Now, a study led by researchers at the UCLA School of Nursing has found that older HIV-positive men who have sex with men are at higher risk of becoming infected with the HPVs that most often cause anal cancer.

The researchers also report that smoking increases the risk of infection with specific types of HPV among both HIV-infected and uninfected older men by up to 20 percent. This is the first large U.S. study of a group of HIV-infected and uninfected men between the ages of 40 and 69 who have sex with men. Study participants were examined twice a year for up to 25 years.

"Invasive anal cancer is a health crisis for gay, bisexual and other men who have sex with men," said Dorothy J. Wiley, associate professor at the UCLA School of Nursing and lead author of the study, which was published Nov. 20 in the journal PLOS ONE. "Right now, invasive anal cancer rates among HIV-infected men who have sex with men surpass rates for seven of the top 10 cancers in men."

The study, which involved more than 1,200 participants, was performed at four sites in the United States. Nearly 49 percent of the men were HIV-positive. During semi-annual visits, all the men were examined for demographic, sexual, behavioral and HIV-infection characteristics and were tested for HPV.

The researchers found that HPV infections were common among all the men in the study and that the proportion of men affected by HPV remained consistently high across the 40-69 age range. However, HIV-infected men between the ages of 40 and 69 showed a higher risk for HPV infection than HIV-uninfected men.

The study also found that for HIV-positive men, taking antiretroviral therapies as prescribed appeared to lower their risk for the HPV infections that cause cancers. Avoiding tobacco use also lowered the risk of HPV infections among all the men.

"This study highlights the benefit of adhering to HIV treatment, which among HIV-infected men who have sex with men, is important for cancer-prevention strategies," Wiley said.

The next step in this research is to begin looking at ways to develop better, more effective HPV infection prevention strategies, including vaccination for age-eligible males and screening and treatment programs for high-risk men who have sex with men to prevent invasive cancers.

"Right now, we perform colonoscopies to prevent colon cancer, where 53 men per 100,000 are diagnosed annually," Wiley said. "Unfortunately, we do not provide screening tests routinely for anal cancer for men who have sex with men, where the numbers are much higher—78 men per 100,000."

The study was funded by the National Cancer Institute and the National Institute of Allergy and Infectious Diseases.

In addition to Wiley, researchers included Dr. Roger Detels, Otoniel Martinez-Maza, Hilary Hsu, Katherine DeAzambuja, Kristofer Chua and Shehnaz K. Hussain from UCLA; Xiuhong Li, Gypsyamber D'Souza and Eric Seaberg from Johns Hopkins University; Dr. Ross D. Cranston of the University of Pittsburgh; and Stephen Young of the University of New Mexico. HIV

President Signs PEPFAR Reauthorization

President Obama, also on December 2, signed legislation enacted in November to extend the 10-year-old President's Emergency Plan for AIDS Relief (PEPFAR), which was started during President George W. Bush's administration.

Obama said PEPFAR has exceeded the goal he set on World AIDS Day two years ago of getting anti-HIV treatment to six million people in developing countries, saying treatment has been provided to 6.7 million people.

At the same event, the President pledged to give up to $5 billion to the Global Fund to Fight AIDS, Tuberculosis and Malaria over the next three years, saying an "AIDS-free generation may be within reach." The President said the United States would contribute $1 for every $2 pledged by other donors to support the fund, with a ceiling of $5 billion. HIV

THINKSTOCK

The Psychology of HIV

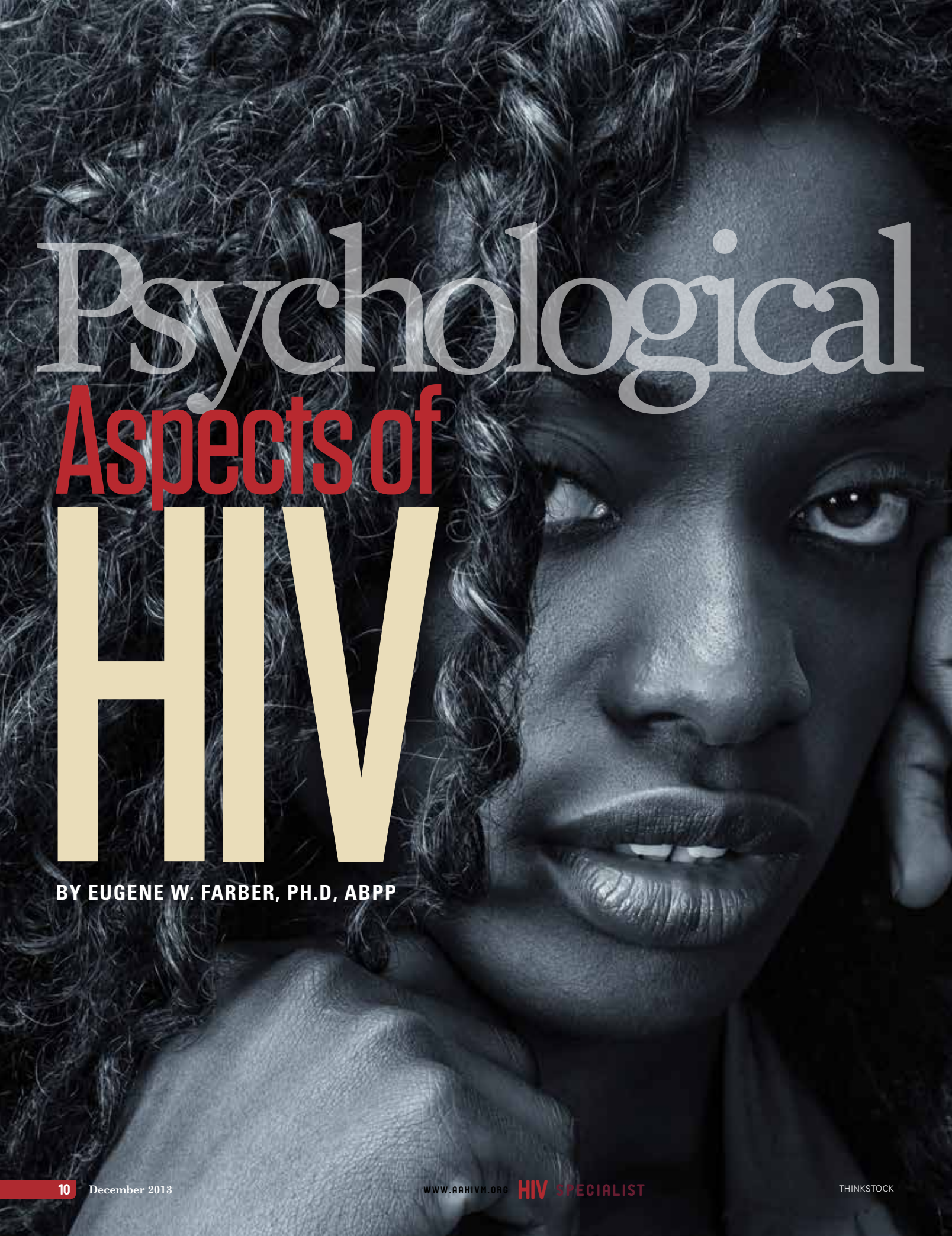
by David Martin, Ph.D, ABPP

SENIOR DIRECTOR,
OFFICE ON AIDS, PUBLIC INTEREST DIRECTORATE,
AMERICAN PSYCHOLOGICAL ASSOCIATION

I AM PLEASED TO INTRODUCE this group of expert psychologists and their perspectives on mental health for people with HIV. The articles included in this issue of *HIV Specialist* were written largely by members of the American Psychological Association's (APA) Committee on Psychology and AIDS (COPA). COPA was authorized by the APA Board of Directors in 1990 to provide policy direction and oversight for current APA activities related to AIDS, to advise APA staff and establish liaisons with governance groups regarding AIDS issues, and to formulate new APA initiatives to meet the continually changing challenges posed by the epidemic. Over the years, COPA has been active in advising APA in ways of responding to HIV, informing APA public policy initiatives, and in educating APA membership and outside groups on issues related to HIV/AIDS including prevention and treatment. APA's *Resolution on Combination Biomedical and Behavioral Approaches to Optimize HIV Prevention,* advocating the inclusion of behavioral interventions in biomedical approaches to prevention, was passed by the Board of Directors in 2012 and was a COPA initiative.

This effort represents an extension of those efforts. As Dr. Farber notes in his introduction to this special issue, psychology has been central in responding to challenges posed by the HIV epidemic, contributing to prevention and education initiatives, testing and counseling, and medical management efforts (including supporting medical treatment adherence and diagnosis and management of HIV-related neurocognitive deficits). As treatment for HIV evolves, new challenges will also emerge; psychology will continue to represent an important part of prevention and treatment efforts.

The articles provide an overview of mental health issues including behavioral health psychology as it relates to HIV; trauma, depression and HIV; neuropsychological/cognitive issues in HIV care; pain management; substance abuse; and transgender issues. Although not exhaustive, these articles touch on several important topics in the management of HIV disease. I hope you find them helpful in caring for your patients. HIV



Psychological Aspects of HIV

BY EUGENE W. FARBER, PH.D, ABPP

THINKSTOCK

The role of behavioral health in optimizing HIV care and prevention

BEHAVIORAL HEALTH, which encompasses both mental health services to ameliorate emotional distress and psychological interventions to facilitate health promoting behavior, has played a key role in the overarching response to HIV disease throughout the history of the epidemic[1].

In the earliest years, as medical science was urgently attempting to respond to what was then a mysterious and devastating new illness, mental health providers became psychological and emotional first responders, offering crisis intervention, emotional palliation, and grief-oriented psychotherapies. As emerging approaches to HIV medical management began to take hold, mental health services focused increasingly on instilling hope, enhancing coping, and supporting engagement in medical care, while behavioral scientists began ramping up HIV prevention efforts aimed at reducing transmission risk behavior.

With the advent of game-changing combination antiretroviral therapies, the psychological and emotional implications of changing life trajectories became a focal point of mental health intervention as a generation of individuals living with HIV, who had assumed a foreshortened lifespan, now experienced the possibility of extended life. Given the complexity of early antiretroviral regimens and the prospects of viral resistance associated with missed medication doses, the development of adherence strategies became a behavioral science priority.

A Contextual View of HIV Disease

As the HIV epidemic has unfolded, a key lesson has been that maximizing the reach of beneficial biomedical treatment and prevention efforts requires a comprehensive multipronged response undergirded by a contextual conceptual framework for understanding HIV disease.

HIV is quintessentially a biopsychosocial illness, wherein biological/biomedical factors intersect with psychological/behavioral and social/cultural phenomena. Biomedical contributors to the biopsychosocial complexity of HIV include such factors as prevalence rates in a given community, infectiousness, impact on physical functioning, and medical treatment exigencies. Temperament, coping resources, health beliefs/behavior, HIV transmission risk behavior, and psychological disorder are examples of factors that fall within the psychological/behavioral domain. Social/cultural factors include socio-demographic and cultural background, social role expectations, community context, availability/quality of social support, and salience of HIV stigma. Within a biopsychosocial framework, the experience of any given individual living with HIV must be understood in the context of the unique intersection of these factors in the life of that person.

This contextual biopsychosocial framework for conceptualizing HIV relates closely to syndemic theory, which posits that interacting health-relevant variables exert a synergistic and collective impact within a given community, ultimately contributing to health disparities such as those that typify the HIV epidemic[2].

Examples of this include social marginalization, economic disenfranchisement, interpersonal violence, and substance abuse. A syndemic perspective provides a useful way to think about the remarkably high rates of HIV infection in adults with severe psychological disorders, a population for whom reported prevalence rates range from 3 to 23 percent[3]. Even prevalence rates that fall at the low end of this range are substantially elevated relative to the general population rates of HIV infection, suggesting a clear intersection of severe mental illness and HIV.

The Role of Psychological/Behavioral Health

Viewed through a biopsychosocial and syndemic lens, a comprehensive approach to HIV prevention and care necessitates a holistic response that combines biomedical, psychological/behavioral, and social/structural strategies, with the alignment of these three domains being critical to optimizing outcomes[2].

As a part of this overall configuration, behavioral health resources have an important role to play in addressing key challenges in the current landscape of HIV treatment and prevention. These challenges are underscored by the fact that,

in the current era of the epidemic in which HIV disease can now be successfully medically managed as a long-term chronic illness, significant numbers of persons living with HIV are not in care and, therefore, do not experience the full benefits of state-of-the-art HIV treatments.

The so-called HIV treatment cascade[4] shows that only about 33 percent of the 1.1 million individuals living with HIV in the United States receive antiretroviral therapy and only 25 percent have achieved viral suppression. The cascade also reveals significant gaps related to HIV diagnosis and linkage and retention in HIV care, with 82 percent of those living with HIV successfully tested and diagnosed, 66 percent linked to care, and only 37 percent retained in care.

The cascade illustrates specific points along the spectrum of HIV disease management where behavioral health intervention, in coordination with biomedical and social/structural approaches, can be applied in ways that advance current efforts to address existing gaps in prevention and treatment efforts.

First, behavioral health strategies can contribute to efforts to facilitate early HIV diagnosis and support linkage to care in the context of emerging "test-and-treat" strategies with a focus on ensuring the availability of high quality HIV test counseling in expanded HIV testing programs.

Additionally, behavioral intervention has a key role in emerging biomedical prevention approaches, including treatment as prevention, given expertise in behavioral approaches to supporting medical treatment adherence. Behavioral health also remains an essential component of comprehensive HIV care, for the treatment of mental health disorders that commonly co-occur with HIV, and for cultivating psychological/behavioral practices that support long-term health and emotional well-being in living with HIV as a chronic illness.

HIV Testing and Linkage to Care

As reflected in the HIV treatment cascade, nearly one in five individuals living with HIV in the United States are unaware of their seropositive status. Given that individuals who are aware of their HIV serostatus tend to take precautions to avoid transmission of the virus and to protect their health, HIV testing efforts are being expanded to facilitate early diagnosis of HIV as part of the Centers for Disease Control's high impact prevention efforts[5].

This approach is in line with emerging "test-and-treat" strategies aimed at identifying new HIV cases and engaging people in care. As noted earlier, the HIV treatment cascade tells us that while 82 percent of individuals living with HIV know their diagnosis, only 66 percent are linked to care, underlining the significant need to bolster linkage to care strategies as part of the HIV testing process.

The evidence base suggests that HIV test counseling, a type of behavioral intervention, is an effective means of encouraging access to medical care for people who receive a positive HIV test result[6]. HIV test counseling serves multiple functions, including education on how to interpret the meaning of positive or negative test results, provision of emotional support, and active linkage to community HIV treatment resources. As such, it can play a critical role as a behavioral tool for optimizing efforts to link patients to care in the context of a "test and treat" framework.

Recent research, however, showed that individuals who receive a positive test result often perceive that the counseling element of the HIV testing process, including active linkage to care, is not sufficiently emphasized[7]. These findings point to the need to redouble efforts to provide high quality HIV test counseling as part of expanded testing programs. Those who conduct HIV testing and counseling also need to be alert for possible co-occurring mental health or substance abuse concerns that might complicate linkage to care and make appropriate treatment referrals as needed.

Behavioral Considerations

While historically the absence of a biomedical cure for HIV meant that efforts to prevent the spread of HIV focused primarily on the development and implementation of behavioral interventions, emerging biomedical prevention strategies have gained increasing attention. Examples include the development of antiretroviral microbicides[8] and pre-exposure prophylaxis (PrEP)[9], each of which has been shown to reduce HIV transmission rates. Evidence that viral suppression through antiretroviral therapy reduces HIV transmission has contributed to the conceptualization of HIV treatment as a significant means of HIV prevention[10].

These biomedical advances represent important contributions to efforts to reduce new HIV infections. However, the effectiveness of these strategies is in part dependent on psychological and behavioral contingencies. These approaches require attitudes that support their acceptability for use by individuals for whom they may benefit (i.e., treatment uptake), comprehension and knowledge regarding how to use them, and capacity and motivation to remain adherent.

Thus, adherence counseling has been incorporated into the protocols for research on both PrEP[9] and antiretroviral treatment as prevention[10]. Also, in reporting the results of a microbicide study[8], the authors described differential reductions in HIV incidence as a function of degree of adherence to the intervention, with high adherence resulting in greater HIV incidence reductions than low adherence. These findings demonstrate the importance of attending to behavioral factors in the implementation of biomedical prevention strategies, and illustrate the usefulness of combining behavioral interventions with biomedical prevention approaches as a way of optimizing outcomes.

More broadly, mental health services for those with psychological disorders co-occurring with HIV can support a treatment as prevention approach in the context of general HIV medical care. Specifically, the psychological symptom relief and enhancement of adaptive functioning resulting from mental health intervention increases the likelihood of favorable self-care activities, including adherence to antiretroviral medicines and medical appointments.

Behavioral/Mental Health Services in HIV Care

Because of the remarkably high prevalence rate of psychological disorders co-occurring with HIV disease, providers of HIV medical care services are likely to encounter patients who require mental health intervention.

Past-year and past-month prevalence of a psychological disorder diagnosis of 50 percent and 33 percent, respectively, have been reported in HIV primary care samples, with 50 percent of those with past-year and 40 percent of those with past-month diagnoses meeting criteria for more than one diagnosis[11].

These numbers reflect both the disproportionately high rates of HIV infection in psychiatric populations and the stress burden associated with HIV, which can be a precipitant to clinically significant psychological distress or disorder. Untreated mental health disorders are associated with decreased HIV primary care access, reduced medical adherence, lower retention in care, and poor overall health outcomes[1].

Assessing for mental health and substance abuse disorders and coordinating with mental health clinicians to provide the appropriate treatment are, therefore, critical parts of a comprehensive biopsychosocial approach to providing HIV care.

When making outside referrals for mental health treatment is wise to regularly communicate with mental health providers in order to coordinate care. Where feasible, it can be advantageous to integrate mental health services into HIV medical care settings, as this enhances service accessibility as well as ease of coordination and collaboration between medical and mental health providers.

Integrated care approaches can take various forms, including co-location of primary care and behavioral/mental health providers in the same physical plant with degree of care coordination and collaboration determined at the discretion of the primary care and behavioral/mental health providers. Alternatively, mental health providers can be included as members of interdisciplinary provider teams that meet regularly for joint treatment planning and care coordination. Behavioral/mental health and primary care providers also can work side by side at the point of service, yielding opportunities for real time coordination and collaboration on behalf of their patients.

Depending on clinical circumstances and needs, the level and intensity of behavioral/mental health provider involvement may vary along a continuum that ranges from a consulting role to the primary care provider without the patient present, to brief intervention with the patient, to ongoing mental health services, including psychotherapy and/or psychiatric medication management.

Within a biopsychosocial treatment framework, behavioral/mental health assessment and intervention focuses on three intersecting domains of functioning.

The first is on the ways in which the biomedical aspects of HIV interface with psychological/emotional functioning, including physical symptom profile, pain syndromes, tolerance of medication side effects, medical co-morbidities, and neurocognitive sequelae.

A second focus is on psychological resources and functioning, including self/role functioning, life trajectory concerns, personal strengths, and adaptive coping strategies. Addressing the impact of psychological disorder and emotional distress on health behaviors, HIV medical adherence, and retention in care also is encompassed within this area of focus.

Behavioral/mental health assessment and intervention focus thirdly on the social environment, including the availability of social support, the quality of relationships (including intimate partners, family, and social networks), the impact of HIV stigma, financial and material resource concerns, and spiritual/religious life. This area of focus also addresses overarching sociodemographic and cultural influences (e.g., age, gender, race, ethnicity, nationality, sexual orientation, socioeconomic status, language, literacy, and disability) on HIV-related health beliefs, attitudes, and behaviors.

Behavioral/mental health services also focus on the promotion of overall health and well-being, along with prevention of psychological and substance use disorders. The aim of these services is to build and reinforce patient strengths and resources that contribute to sustaining a long-term healthy lifestyle pattern.

Consistent with a biopsychosocial framework of service delivery, examples of behavioral health wellness services include consumer friendly psycho-educational programs on the biomedical aspects of HIV (e.g., basic HIV education, education on the links between stress and immune functioning), psychological resources that support emotional well-being (e.g., stress management techniques, coping skills training), and psychosocial resource development (e.g., relationship skills, building support networks, negotiating service systems).

A Comprehensive Response to HIV

Despite the availability of state-of-the-art HIV treatment, formidable and persistent prevention and treatment gaps remain across the spectrum of illness represented in the HIV treatment cascade. From a contextual biopsychosocial perspective, comprehensive efforts to maximize the reach of HIV health services require coordination across biomedical, psychological/behavioral, and social spheres.

As a part of this multifaceted approach, behavioral interventions can be invaluable in supporting and optimizing biomedical interventions to prevent and treat HIV disease. Additionally, given the prevalence of mental health challenges that co-occur with HIV, behavioral/mental health assessment and intervention, including treatments for psychological disorders and wellness interventions to encourage positive health behavior, are critically important to successful outcomes in the overall clinical management of HIV disease. HIV

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Trauma & HIV

BY AMANDA HOUSTON-HAMILTON, DMH

Releasing the 'straightjacket that binds the mind and body in frozen fear'

THE SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION (SAMHSA) estimates that up to half of people with HIV suffer mental illness such as Major Depressive Disorder (MDD), but only 13 percent receive care for the condition, and many are under-diagnosed. Successful treatment of HIV/AIDS requires addressing the emotional-behavioral health of patients such as trauma, a common impediment to care. Frequently characterized by depression that increases and that is more complex with histories of multiple disruptive, distressful events, trauma in people living with HIV/AIDS (PwHIV/AIDS) is associated with chronic physical pain, poor cognitive functioning, disability, frequency and length of hospitalization, and number of ER visits.

Patients with trauma histories have roughly twice the negative health outcomes as those without trauma histories. In fact, the presence of these psychological problems can predict mortality, independent of variables such as CD4 count, viral load, age, baseline clinical stage, time since HIV diagnosis, social support, and adherence. Depressed PwHIV/AIDS have higher death rates from both HIV and non-HIV causes than PwHIV who are not depressed, even when compliant with HAART.

In prevention, passive forms of coping with prior trauma and depression such as denial and avoidance, have been associated with contraction of HIV through risky behaviors. Tissue injury from sexual violence can increase the risk for HIV infection. Isolation or negative social networks leave individuals at risk of exploitation and re-traumatization.

Once infected, patients with trauma histories are at increased risk for treatment non-adherence, treatment dropout, and inconsistent provider-patient relationships because, although they may seek help for medical symptoms, severely traumatized patients often experience intervention as intrusive and re-traumatizing.[1]

Typically, healthcare systems are not designed for such ambivalent and challenging patients; successful clinics are aware of the need to conduct quality improvement (QI: obtaining institutional commitment to the integration of mental health care into primary care; training local leaders—primary-care physicians, nursing supervisors and mental health specialists; delivery of integrated interventions, evaluating outcomes)[2]

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and to create trauma-informed practices acknowledging and integrating the role of trauma in all aspects of patients' lives.

PwHIV without apparent previous traumatic events can show first signs well into their disease. Stigma stemming from on-going abuse, shame, helplessness, and internalized anger are precursors to depression. PwHIV also may be at risk of MDD by virtue of their responses to diagnosis, chronic illness, "death anxiety", and the attendant problems of declining social, financial resources, and poorer overall quality of life. Depression can arise from some HIV medications and even from the virus itself. Regardless of the source, trauma and its partner, depression, are such significant factors in the health and well-being of people living with and at high risk for HIV/AIDS, it should be always be assessed for prevention and treatment planning.

Trauma

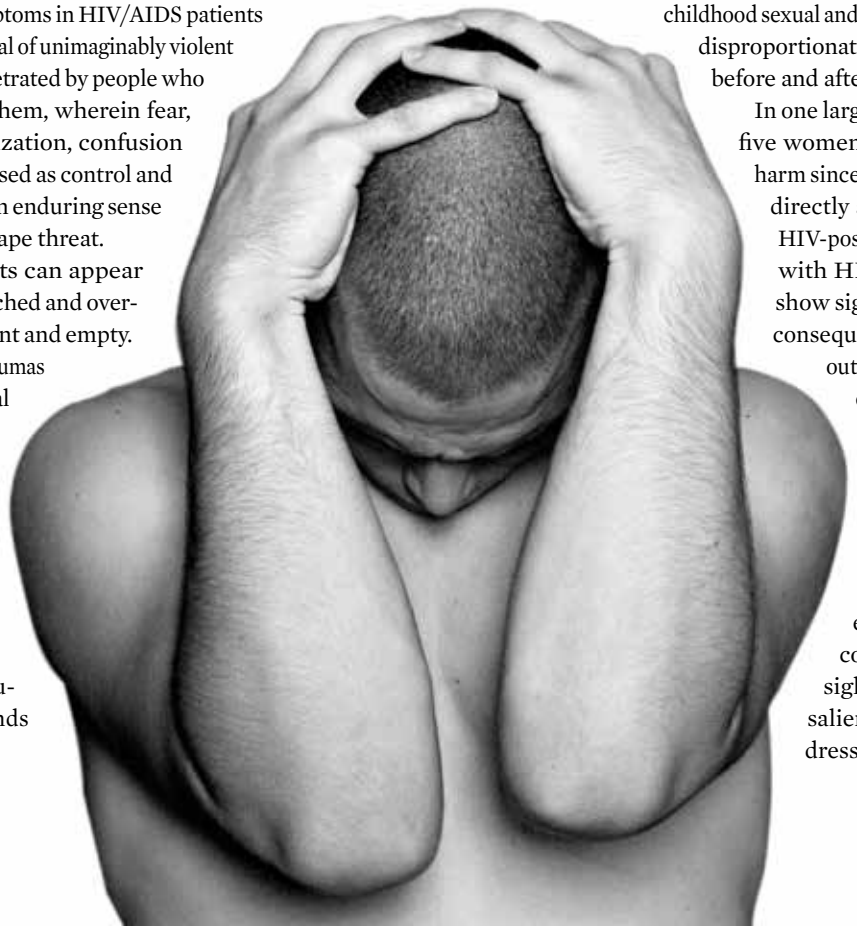
The term "trauma" is generally reserved for severe stress directly connected to one or more major life events such as a natural disaster, sexual and physical abuse or assault, severe childhood neglect, or parental drug abuse.

Post Traumatic Stress Disorder (PTSD) is a pervasive stress reaction that co-occurs with at least one other mental disorder.

Many HIV-infected patients live with three or more co-morbidities, particularly depression and substance abuse, with symptoms including a constant sense of environmental threat and an overgeneralization of fear stimuli with hyper-active startle response, hyper-sensitivity, and mistrust in social responses, cognitive distortions, or recklessness or self-destructiveness.

"Complex trauma"[3] occurs when multiple trauma events exert cumulative effects over time. The most difficult trauma symptoms in HIV/AIDS patients often reflect survival of unimaginably violent experiences perpetrated by people who claimed to love them, wherein fear, shame, demoralization, confusion and betrayal are used as control and victims develop an enduring sense of inability to escape threat.

These patients can appear either overly attached and overwhelmed or distant and empty. Severe, complex traumas can limit essential components of self-care, willingness to share sexual history, trust in our offers of concern and service, and the capacity to adapt to new situations and demands in treatment.



Depression

Major depression disorder (MDD) symptoms include hopelessness, a lack of energy (or feeling "weighed down"), and taking little or no pleasure in things that once gave joy for weeks or months on end. Even simple things—like getting dressed or eating—become obstacles.

Depression may seem like an unavoidable reaction to being diagnosed with HIV/AIDS, but MDD is a separate illness with its own etiology and risk profile. Depression, apart from any behavioral components, has been associated with decreased CD4 T lymphocyte counts, increased viral loads and roughly twice the negative health outcomes compared to nondepressed people with HIV.[1]

Vulnerability to Trauma and Depression

Although trauma and depression are not limited to any group, women, individuals in poverty, elders, runaway youth, transgenders, substance abusers (including alcoholics), are most vulnerable to exploitation, multiple trauma events, and to major depressive symptoms. These same groups also face additional challenges in access to care and often have other compromises to their physical and mental health. In a study of 618 HIV-infected youths, having a history two or more stressful life events was associated with almost a three-fold increased risk of immune suppression.[1]

Women account for 20 percent of new HIV infections in the United States, with over three-quarters occurring among black and Latina women. The National HIV/AIDS Strategy, a central guide to federal health planning and policy since 2009, failed to identify the common intersections of violence and trauma in HIV-positive women, although childhood sexual and other forms of abuse disproportionately impacts women before and after HIV diagnosis.

In one large study, over one in five women suffered physical harm since HIV diagnosis, half directly attributed to being HIV-positive.[5] Women living with HIV also commonly show signs of PTSD and its consequent negative health outcomes, and are more often non-compliant.

At the International AIDS Conference in September 2013, the White House released a report officially acknowledging the problem, correcting this oversight, and identifying salient strategies to address it.[6]

The frequency of violence from an intimate partner has been estimated at 55 percent for women living with HIV[7], compared to a national prevalence of 36 percent among women generally[8]. Violence and HIV are also particularly prevalent among transgender women, with 58 percent reporting domestic violence and 28 percent estimated to have HIV[9] .

Assessment and Treatment

Individual trauma responses may vary depending on individual vulnerability and psychological, social and family histories: While some may recover quickly and on their own, others may continue to exhibit PTSD symptoms over a prolonged period of time. Treatments should be tailored to the individual according to his/her presentation and need, taking into consideration all the patient's symptoms and assets as well as the well-informed use of clinical and community resources. Behavioral consultants should be available to conduct or review assessments and help develop treatment plans.

SCREENING/ASSESSMENT—In clinic settings, symptoms like self-neglect, alcohol odor, irritability, or impaired memory are frequently identified by someone other than the physician (e.g., nurse, front office staff, pharmacist), but a clearer basis for referral or treatment is needed than what is provided by these rapid observations.

Standard assessment measures of a patient's adaptive and maladaptive functioning taken repeatedly over time can help in anticipating needs, coping style, provider relationship, as well as in identifying opportunities for interventions.

Patients should be screened at intake; some measures such as the PHQ-2 and PHQ-9 screen for depression, while others, such as the PRIME-MD, screen for other disorders in addition to depression. Following discussion of results with the patient, the provider can determine whether the patient needs urgent intervention, additional specialized mental health evaluations, or another plan. Patients should be continuously be monitored, reassessed annually to determine ongoing need.[10]

Suicide among people with HIV is three-to-five times higher than in their HIV-uninfected counterparts. Clinicians treating HIV-infected patients should become comfortable and competent in recognizing depression and trauma symptoms, as well as being able to screen patients for intent to harm themselves. Suicide risk can be assessed with simple, direct questions and clinics should establish protocols for approaching suicidal patients, including preparation for civil commitment if needed.

TREATMENT—Some patients require individual, group, or family therapy. HIV care practices without such in-house resources should cultivate relationships with agencies or individuals who can provide such treatments and develop the skill of making appropriate referrals.

It is important to understand that referral is an active process and should include follow up to ensure as much as possible that a connection is made. For some patients, a collaborative relationship between the mental health professional and healthcare provider is best, sharing treatment responsibility (e.g., medication, education, symptom management, integrating behavioral goals into the medical care). In some cases, the HIV provider who has established trust may find a traumatized or depressed patient reluctant to start a new relationship and needing time to engage with another caregiver.

Co-existing substance abuse (SA) is often viewed as self-medication, so when looking for trauma and depression, screening for alcohol and drug use also should be conducted. Unsupervised withdrawal can exacerbate PTSD symptoms and psychic pain; conversely, the treatment of PTSD early in SA recovery may lead to relapse. A specialist should, therefore, be part of the intervention plan when any drugs or alcohol are involved.

The interactions of alcohol, domestic violence, and HIV/AIDS demonstrate the need for learning best practices for comprehensive alcohol screening as well as screening for past and present abuse and violence. Such factors emphasize the need for targeted interventions, but only after careful treatment planning, informed partnerships with mental health professionals, training for practice staff, and an integrated team approach.

MEDICATION—Depressed PwHIV are more likely to receive appropriate HIV care if they are treated with antidepressants than if they are not. No particular antidepressant medication is superior for the treatment of depressed HIV-infected patients, but control of PTSD symptoms with long-term medication may make it possible for the patient to participate in psychotherapy. PTSD does not seem to respond to short-term medication and MDD in HIV-disease requires sustained patient adherence for at least six months. Adherence is maximized by more user-friendly regimens, close monitoring, sensitivity to intolerance to the regimen, and appropriate counseling on responses that may trigger patients' sense of retraumatization.[11]

While normally problematic in the general population, side effects actually can be used to counteract the specific difficulties seen in HIV patients. For example, the clinician may want to offer a patient with fatigue an antidepressant that is more stimulating, while patients experiencing insomnia may benefit from a sedating antidepressant, and a wasting patient might benefit from antidepressant fostering weight gain, and anticholinergic side effects may be helpful when patients have diarrhea. There is no evidence that use of antidepressant medication

either suppresses or improves immune system functioning; however some antidepressants have a role in decreasing chronic pain.

TREATMENT GOALS—PTSD should be treated by an experienced mental health professional who may try different treatments to find an appropriate match. Therapy can greatly improve positive coping and reduce depressive symptoms, but the additional social support and self-efficacy provided in medical groups can also diminish isolation and identify resources for change.

Recovery from trauma takes time to modify fear and the false cognitions in traumas and improves self-regulation to new stressors that trap patients in a neurological "trauma vortex".[12]

Several approaches have shown efficacy treating HIV patients with depression and trauma:

- **Cognitive behavioral therapy** consists of techniques that target negative internal dialogue.
- **Skills-building groups** provide psychosocial support to improve quality of life through the use of multi-session curriculum-based groups.
- **Recovery programs** such as 12 Step, have been found useful for substance-using people with HIV. Some such abstinence-based programs may feel too shame-based and re-traumatizating for some patients. In such cases, harm-reduction programs may be better suited, setting smaller and more achievable goals toward substance-abuse reduction and frequently starting with steps to engage in care.
- **Trauma-specific care** is a current best practice of client-centered multi-level techniques incorporating psycho-education and engaging positive affect to generate a sense of personal meaning and optimism about life expectancy and quality with HIV. This standard usually requires a QI process to consider all aspects of a practice, sometimes even parallel trauma in the lives of staff and volunteers that affects services.
- Traumatized patients can cope by splitting staff against each other. **A multi-disciplinary team approach** and integrated care is critical for successful practice with these challenging patients. Medical providers who not only partner with all practice staff, but assure strong communication mechanisms (that include observations of front desk staff) and shared treatment planning are better able to identify, support, or refer clients with mental health barriers like trauma and depression.

Despite the deep wounds seen in these patients, it is important to remember to assess and incorporate the resilience, resources, and strengths that are also within and around each patient and his or her community. (Wells and Jones, 2013).[13] Psychopathology is not the only possible result of trauma experiences or of the social network these patients use.

As Levine suggests, "Trauma is like a straightjacket that binds the mind and body in frozen fear. Paradoxically, it is also a portal that can lead us to awakening and freedom."[12]

With our help, some patients could show "post-traumatic growth", the capacity to find meaning rather than depression in their trauma and HIV disease. (Sherr, et. al.) In addition to being victims, these patients are survivors who can teach us much about the healing capacity of the human spirit. HIV

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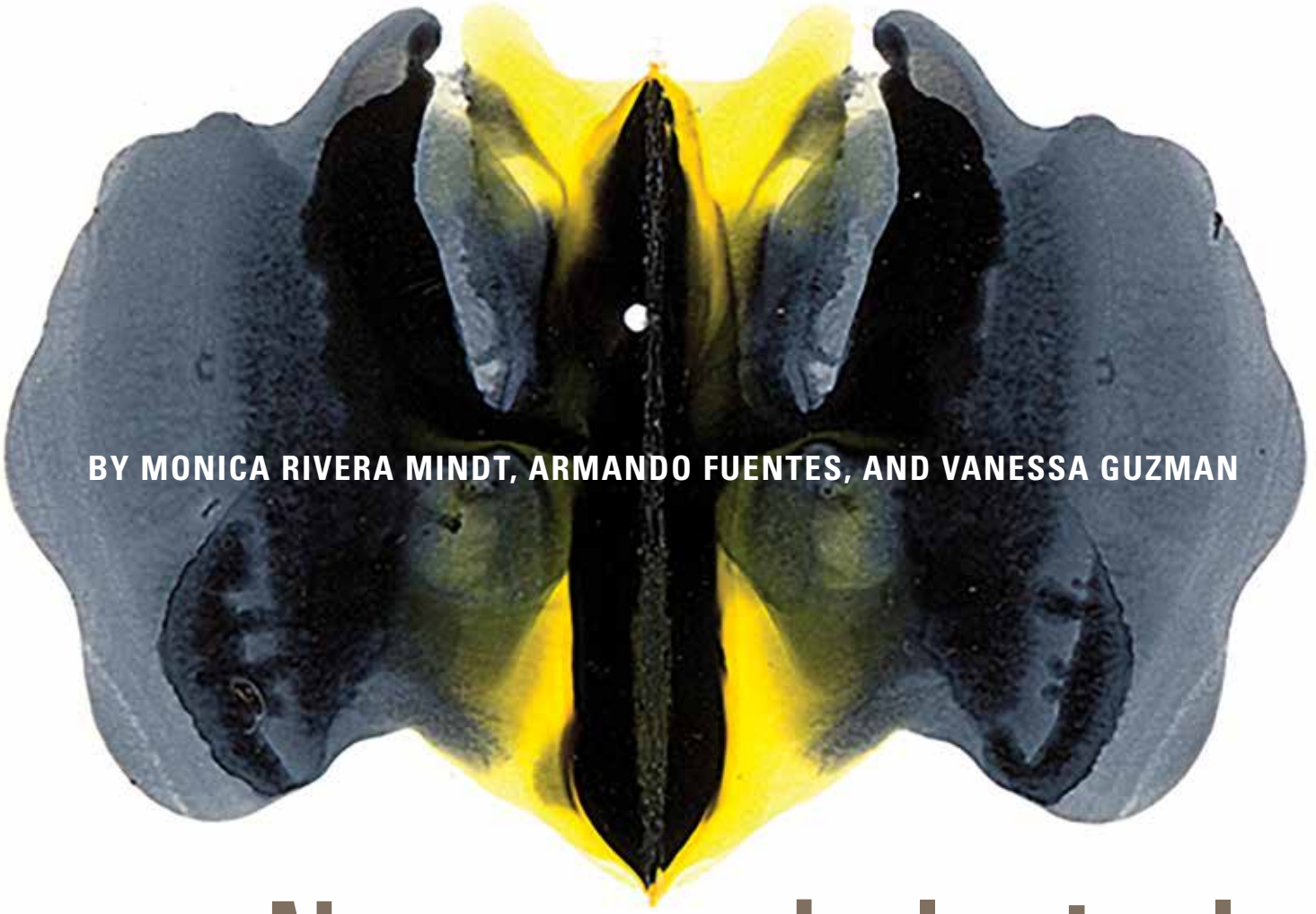

BY MONICA RIVERA MINDT, ARMANDO FUENTES, AND VANESSA GUZMAN

Neuropsychological ASPECTS OF HIV CARE

Neurocognitive and functional screens should be part of routine care

WHILE ADVANCES IN ANTIRETROVIRAL TREATMENT have transformed HIV from a fatal illness to a chronic disease, impairment in neurocognitive functioning persist among people living with HIV. Rooted in the neuropathological impact of the virus on the brain, these neurocognitive difficulties can negatively affect health outcomes, medication adherence, and quality of life for many patients. Neurocognitive impairment in the post-cART era is of increasing concern as individuals live longer and become vulnerable to the physiological ailments associated with aging. Understanding the neurological and behavioral aspects of HIV-Associated Neurocognitive Disorders (HAND) can assist in improving care for this population.

HIV/AIDS and the Brain

HIV has a high affinity for the brain. The virus can enter the central nervous system during the earliest stages of infection. After it crosses the brain blood barrier, HIV infects the brain through infected monocytes and CD4 cells. Neurons are not directly affected; rather, HIV infects microglia and astrocytes, setting off a nueroinflammatory cascade that eventually leads to neuronal dysfunction. Neuroanatomical changes accompany this dysfunction.

HIV differentially affects certain areas of the brain, causing more damage in the basal ganglia, white matter, and frontal lobes. Neuroimaging studies consistently find cerebral atrophy and white matter abnormalities among people living with HIV/AIDS (PLWHA). Atrophy of the caudate nucleus, a region of the basal ganglia, is found in HIV patients[1], although whether these changes occur early in the course of the disease or after the immune system has suffered significant damage remains unknown. Neurochemical and neuroanatomic dysfunction

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within the context of HIV/AIDS is associated with a variety of neurocognitive dysfunction.

HIV-Associated Neurocognitive Disorders

HIV infection can lead to significant neurocognitive compromise, ranging from subtle deficits to pronounced dementia. Specifically, there are three forms of HAND: Asymptomatic Neurocognitive Impairment (ANI), Mild Neurocognitive Disorder (MND), and HIV-Associated Dementia (HAD)[2]. ANI and MND both involve the presence of mild to moderate impairment in at least two neurocognitive areas that are not attributed to comorbid conditions. In ANI, the neurocognitive impairment does not affect everyday functioning. In MND, functional decline is apparent in at least two areas of everyday functioning. HAD requires moderate to severe impairment in at least two neurocognitive areas and substantial functional decline in at least two areas of everyday functioning not attributed to comorbid conditions[3].

In the pre-cART era, rates of HIV-associated global neurocognitive impairment ranged from 30-50 percent, with increased rates at each successive stage of HIV infection. Impairment in neurocognitive domains was generally mild among medically asymptomatic patients as they were found to have fewer ability areas affected. However, the prevalence of HAD among PLWHA was relatively high, up to 15 percent the populations[4].

In the post-cART era, HIV-related CNS manifestations remain prevalent overall. The *CNS HIV Antiretroviral Therapy Effects Research* (CHARTER) study is a large scale, multisite investigation assessing the long term effects of cART on HIV-associated neurocognitive disorders in a diverse group of PLWH. In this sample, Heaton and colleagues found that although the number of individuals with HAD has decreased, the prevalence of HAND remains high. Of the 1,555 participants in the CHARTER cohort, over half (52 percent) demonstrated global neurocognitive impairment, with 33 percent of the cohort meeting criteria for ANI and 13 percent for MND[3]. The prevalence of these milder forms of HAND in this large post-cART era cohort is consistent with pre-cART reports[4]. However, the prevalence of HAD was substantively lower than in the pre-cART era, with only 2 percent of patients meeting criteria for HAD.

In terms of the specific neurocognitive deficits observed in HIV/AIDS, these deficits are consistent with dysfunction and pathology in the frontostriatal circuitry (i.e., frontal lobe and basal ganglia) and white matter. The neurocognitive domains most commonly associated with HIV-related impairment include: attention/working memory; processing speed; executive functioning; learning and memory; and motor functioning[3,5,6]. Moreover, HAND is associated with significant functional impairment, including tasks such as instrumental activities of daily living (IADLs) and medication adherence.

For instance, one large study (N = 267) showed that PLWHA with neurocognitive impairments were significantly less able to perform their IADLs in the areas of shopping, cooking, cleaning, and managing finances, as well as driving, functioning appropriately at work and remembering to take their medications[7]. Similar findings have been observed among Spanish-speaking Latina/o PLWHA[8]. A review of the literature further supports the observation that neurocognitive impairment in PLWH is associated with diminished medication adherence, and this effect is further exacerbated with a complex medication regimen[9].

HAND and cART

The use of cART is associated with reduced incidence of HAD by 40–50 percent[4]. The exact mechanisms underlying their possible advantageous effects on cognition have not been determined. In a longitudinal study of PLWHA with HAND, administration of cART led to up to 41 percent improvement in neurocognitive functioning after 48 weeks of treatment, particularly among those with worse baseline performance[10]. Other findings suggest that PLWHA who live longer due to cART are at increased risk of developing HAD later in life, and only a select group—those who show viral suppression from cART, may experience possible reversal of neurocognitive decline[1].

Considerations for HAND in Special Populations

OLDER PLWHA. As reported by the CDC, the number of older adults (i.e., ages ≥ 50 years) living with HIV has increased over recent years. This is due both to the longer life expectancies of adults already diagnosed with HIV on combined antiretroviral therapy (cART) and to new diagnoses within older adults. Aging in PLWHA is particularly associated with neurocognitive impairment in the areas of processing speed and attention11. Considering the increasing number of older PLWHA, these findings suggest that issues of both neurocognitive and functional abilities should be taken into account when working with this population.

SUBSTANCE USE AND PLWHA. PLWHA with substance disorders may be at increased risk for neurocognitive dysfunction and poorer health outcomes. Rates of illicit substance use (approximately 40 percent according to some estimates) continue to be high among PLWHA. Neurocognitive dysfunction is associated with substance abuse independent of HIV status. Within the context of HIV, the literature on the combined or synergistic effects of HIV and substance use is equivocal. Whereas methamphetamine use among PLWHA is synergistically associated with neurocognitive impairment, recent research suggests substance use history has no additive effect on neurocognitive performance among PLWHA[12,13]. HIV+ substance users demonstrate worse treatment adherence and poorer health outcomes. In fact, substance use is associated with over four times greater risk of failure at treatment adherence compared to non-substance using PLWHA14. These findings suggest that screening for substance use and paying close attention to medication adherence are key considerations for this population.

HAND AND HEALTH DISPARITIES. HIV/AIDS disproportionately affects racial/ ethnic minority communities. In 2011, racial/ethnic minorities accounted for 70 percent of newly diagnosed cases of HIV (primarily African Americans and Latina/os). In addition to these higher rates of infection, some studies suggest elevated rates of neurocognitive impairment (particularly in executive functioning) and HAD among HIV-seropositive Latina/os and African Americans compared to non-minority adults[6,15].

Furthermore, racial/ethnic minority PLWHA have poorer health outcomes than their non-Hispanic White counterparts, including increased mortality rates and quicker progression to an AIDS diagnosis. These health disparities are not limited to HIV. Alzheimer's, dementia, and cardiovascular disease are more prevalent among racial and ethnic minority populations than among non-minority populations. Increased risk of co-morbid disease burden may also be associated with diminished neurocognitive functioning. Health disparities for racial and ethnic minorities highlight the need for continued assessment of neurocognitive functioning in these groups that are significantly affected by HIV.

Implications for Treatment

Brief neurocognitive and functional screens should be part of routine care (see Carey et al., 2004 and the *Patient's Assessment of Own Functioning Inventory,* PAOFI) in order to identify potential neurocognitive impairment and functional complaints. Positive findings may suggest the initiation or alteration in treatment regimen, support with adherence or other health-related behaviors, and/or referral for a more comprehensive neuropsychological evaluation. Such screenings are especially important for special populations, such as older PLWHA, substance users, and racial/ethnic minority patients who may be at increased risk for neurocognitive complications and/or functional impairments such as reduced medication adherence. HIV

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Treating Pain IN OLDER ADULTS Living with HIV/AIDS

HIV Specialists need to become pain treatment experts

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PAIN IS THE MOST SIGNIFICANT DISABILITY in persons living with HIV/AIDS. In spite of improved clinical care and increasingly efficacious antiretroviral therapies, chronic pain remains a persistent, disabling, and life-altering problem for many individuals living with HIV/AIDS.

In the United States, self-reported symptoms of pain in these persons range from 35 to 98 percent, with most pain intensity rated as "moderate" to "severe". While pain is common across the entire HIV spectrum, it is particularly prevalent in persons in end-stage AIDS, many of whom are in palliative care.

Pain in HIV-infected persons is particularly common in those who are depressed or anxious, report histories of verbal, physical, or sexual abuse, and use tobacco or injection drugs. While some studies have found higher rates of pain in persons with lower CD4 cell counts, others have found that as many as 48 percent of HIV-infected persons with undetectable viral loads report being in pain. Every generalist and HIV specialist must, therefore, become expert in diagnosing and treating the multiple forms of pain in patients with HIV.

Pain has been categorized in several ways, such as by chronicity or by assumed source. Chronic pain far surpasses prevalence of acute or terminally-ill forms of pain. While the "neuropathic" label has remained useful in chronic pain diagnosis and management, assumed somatic sources, such as irritated nociceptors near "degenerative joint disease," have not proven very responsive to treatments that are usually effective for acute somatic pain. A paradigm shift in caring for chronic pain as a bio-psycho-social-spiritual dysfunction, rather than a bio-medical one, allows for more significant improvements in function and pain. ►

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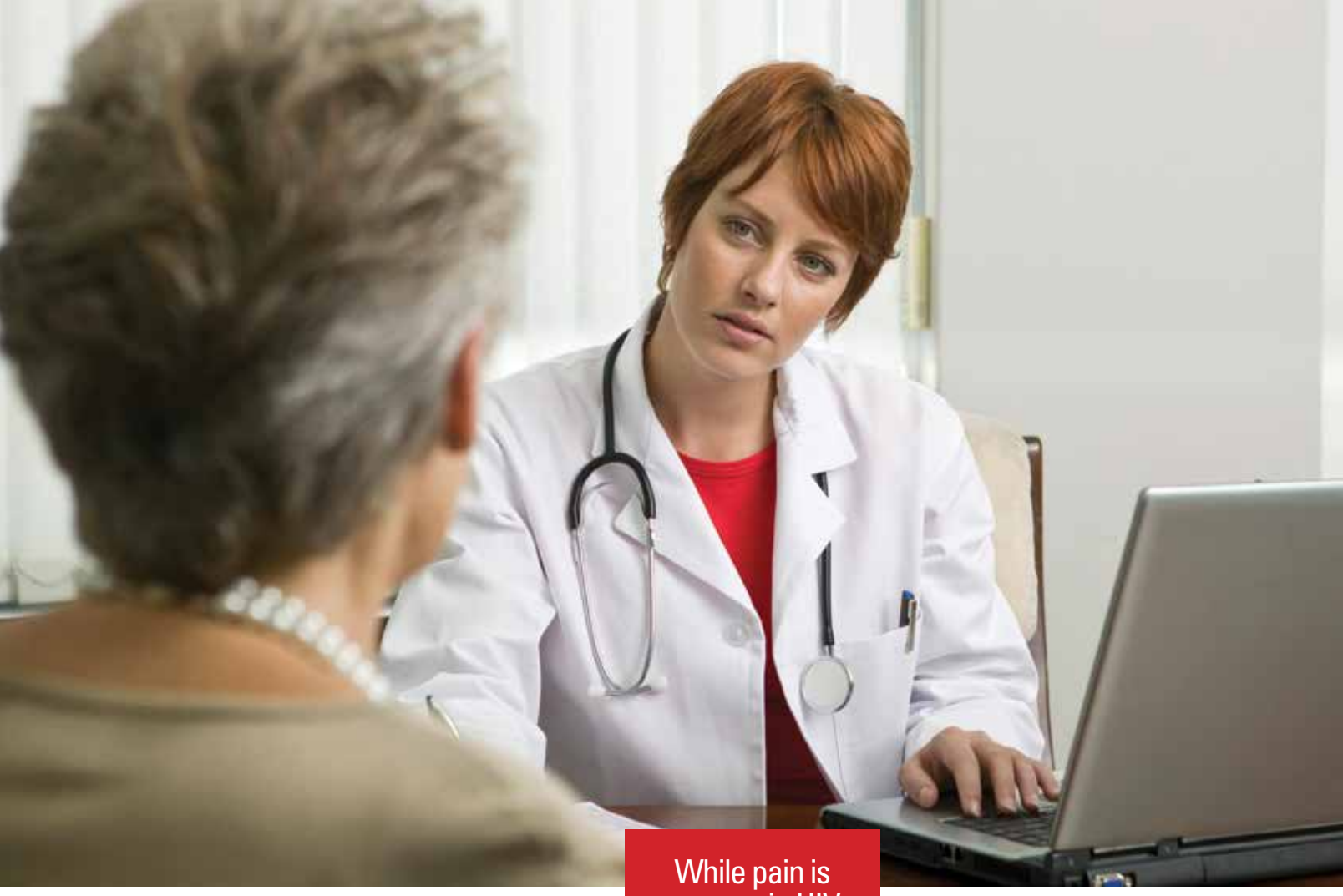

While pain is common in HIV-infected older adults, research reveals that it is often under-treated and poorly managed.

Based on the bio-medical model, the most common types of pain in HIV-infected persons are neurologic pain (e.g., headaches, neuropathies), rheumatologic pain (e.g., arthritis, tendonitis), gastrointestinal pain (e.g., esophageal and abdominal pain), and pelvic and chest pains. In the bio-psycho-social-spiritual framework, HIV-infected persons have inter-related and exacerbated disorders of pain, sleep, energy, and mood. In a longitudinal study with a large and nationally-representative sample of persons living with HIV, worsening pain over time was strongly associated with the onset of panic disorder. Increased pain can also disrupt ongoing friendships and hinder the formation of new social ties, increase financial demands and caregiving burden on family members and friends, and cause greater utilization of health care services.

Overview

Given that 50 percent of HIV-infected persons in the United States in 2015 will be 50 years of age or older, an insufficient amount of research has examined patterns and predictors of pain in adults aging with HIV. Tsao et al. (2007) found that greater age was associated with increased pain in HIV-infected persons both cross-sectionally and at 12-month follow-up. This association was due, in large part, to older HIV-infected persons being more likely to have progressed to AIDS and having more HIV symptoms. In a separate sample, Tsao and colleagues (2011) found that older age was associated with increased physical pain, but lower levels of depressive symptoms and marijuana use.

Havlik and colleagues (2011) assessed common comorbidities and pain sites in almost 1,000 HIV-infected older adults in New York City using a retrospective recall period of the past year. Common comorbidities and causes of pain included: arthritis (31 percent); neuropathy (30 percent); broken bones (9 percent); shingles (8 percent); and migraine headaches (6 percent). Note how most of these conditions are chronic in nature, lasting more than 90 days.

From the bio-psycho-social-spiritual perspective, it becomes clearer how several factors contribute to painful conditions in HIV-infected older adults. First, HIV disease manifestation produces many forms of pain, such as peripheral neuropathies. Second, opportunistic infections may produce painful conditions.

For example, Cryptococcal meningitis can cause severe acute headaches, while Myobacterium avium can cause sub-acute abdominal pain. Third, painful side effects result from many HIV-specific medications. NRTIs (e.g., e.g., Abacavir,

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Lamivudine, Stavudine) often produce headaches and painful sensations in the hands and feet and non-NRTIs (e.g., Delavirdine, Efavirenz) also cause headaches. Protease inhibitors (e.g., Indinavir, Fosamprenavir, Saquinavir) often lead to severe bouts of gastrointestinal pain, headaches, and rashes, while integrase inhibitors (e.g., Raltegravir) often cause headaches, gastrointestinal pain, kidney stones, and fever.

Finally, the onset of painful conditions is common with normal aging, with the incidence of pain more than doubling once an individual surpasses the age of 60. Common painful conditions associated with normal aging include lower back or neck or shoulder pains, due to tendonitis, myo-facial strains, osteoarthritis and "degenerative disc disease."

It is important to note that there is a poor correlation between low back pain and age-related findings on radiologic images such as "degenerative changes." This discrepancy highlights the inadequacy of the bio-medical model. Other less well-defined chronic pain conditions, such as fibromyalgia, may also be present. Fibromyalgia is one of several "Central Sensitization Syndromes," that include multiple forms of chronic pains of the head, abdomen and pelvis.

These later syndromes often have concurrent mood disorders and almost always disrupt sleep. Understanding the mutual reinforcement of undertreated pain and of mental health disorders demonstrates the need to screen for and treat common concurrent problems of PTSD, other anxiety and depressive disorders, as well as not infrequent substance use disorders. Taken together, many AIDS- and non-AIDS-related factors result in acute and chronic pain conditions in persons aging with HIV.

Treatment

While pain is common in HIV-infected older adults, research reveals that it is often under-treated and poorly managed. As with all chronic pain patients, a recent study found that only 2 percent of HIV-infected persons with a chronic pain condition were under the care of a pain specialist.

The lack of trained pain specialists points to the necessity of generalists and of HIV specialists to become expert in caring for patients with chronic pain. Each health care provider should inquire into the acute and chronic pain conditions that their older HIV-infected patients are experiencing at every clinical encounter.

For chronic pain, tools found on the American Chronic Pain Association's website (www.theacpa.org) provide functional, psycho-social assessment options beyond the severely limited "5th Vital Sign" (i.e. the uni-dimensional 0-10 "Pain score"). Unintentionally, this Pain Score may create a false expectation of total pain relief in non-acute pain. These functional assessment tools should be built into the workflow of the clinic to "error proof" the process. The resulting whole patient perspective enables providers to develop individualized pain-management plans within a framework of safe and standardized care

The World Health Organization's "Pain Relief Ladder," originally developed for the treatment of terminally ill cancer pain, was eagerly adopted for use in chronic pain states. It was one of many causes leading to an excessive reliance on Long Term Opioid Therapy (LTOT) for chronic pain. Over 80 percent of opioid prescriptions now are for chronic pains; however, no long term studies exist of LTOT for any chronic pain populations.

Martell and colleagues (2007) calculated no difference in pain with an average of 73mg of Morphine Equivalents Daily (MED; approximately equal to 14 lower dose hydrocodone pills a day) compared to placebo in the most common type of chronic pain, that is low back pain, over a sub-acute to chronic time frame.

Furthermore, numerous, even life threatening complications from opioids are now known, with the CDC declaring an epidemic of accidental overdose deaths from prescription opioids. Sullivan and Ballantyne (2012) appropriately asked "What are we treating" with LTOTs? They reference the facts that patients without HIV, commonly self-medicate psychosocial distress with opioids if they are available, and that those patients who are at highest risk often are on the highest doses of opioids ("adverse selection").

As noted by Tsao (2012), patients may be "Triply diagnosed" with HIV, mental health, and substance use disorders; for these vulnerable individuals it is particularly important not to add to their burdens with misguided attempts of making all the pain go away with opioid escalation.

While awaiting needed research, how can providers help patients with HIV and pain? Here is a new-tiered approach based on moderately effective therapies for non-HIV chronic pain:

STEP 1:

SELF-MANAGEMENT + ACETAMINOPHEN + TOPICAL AGENTS. A thorough bio-psycho-social-spiritual assessment will rule out "red-flags" and will direct treatment of co-morbid conditions if they exist including PTSD or Substance Abuse. Providers should consider offering materials from the ACPA to re-direct patients toward effective self-care. Moderately-effective options include: gradually increased exercises such as walking. Usually patients will need to be encouraged to learn new ways of thinking and behaving to regain function. For these patients, look for on-line or group therapy, such as Cognitive Behavioral Therapy (CBT) for pain.

For medications, the American Geriatric Society recommends acetaminophen as a first line treatment for pain given its analgesic and antipyretic properties. While it does not totally reduce inflammation, commonly associated with arthritis and other inflammatory syndromes in HIV-infected older adults, acetaminophen was equally effective in knee osteoarthritis compared to ibuprofen. Nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin, ibuprofen, and naproxen, should only be used sparingly—if at all—according to the American Rheumatological Society in geriatric patients; but they do recommend topical Diclofenac especially for hand osteoarthritis. Other topical agents can be used (e.g. Capcasian, methyl salicylates, or the more costly Lidocaine patches).

STEP 2:

CAM + ADJUVANT. If pain persists following Step 1, ask about persistent disabling beliefs ("if I hurt, I'm harming myself"...) which benefit from more structured CBT. Inquire about non-opioid preferences for care including Complementary and Alternative Medicine (CAM) therapies. Several forms of CAM can help, both of the "bridging"/"passive" (these types are "done to the patient") variety like massage, spinal manipulation and acupuncture, and of the self-efficacious/"active" varieties like Yoga or the Alexander technique. Adjuvant medications can be considered particularly those affecting the Norepinephrine receptors, such as very low dose Tricyclic Antidepressants or SNRI Antidepressants such as venlafaxine or duloxetine—for both classes, beware the many possible side-effects and contra-indications for these agents in the elderly (even more so with polypharmacy). If sedation is not an issue, and if Central Sensitization Syndrome or Neuropathic pain is present, then trial of gabapentinoid like gabapentin can be used.

STEP 3:

OPIOID TRIAL FOR SEVERE PAIN + PAIN SPECIALIST. A mild opioid in combination with a non-opioid should be considered *IF* the following contra-indications are absent: Substance Use Disorders, unstable Mental Health Disorders, insecure housing, etc. Mild opioids include hydrocodone, tramadol, codeine, or dihydrocodeine. Mild opioids may be efficacious and safe when used as prescribed. According to American Pain Society guidelines, the long-term use of opioids for chronic pain requires appropriate and very frequent monitoring to prevent opioid abuse or dependency. Providers should also appreciate that older adults living with HIV/AIDS may be reluctant to use any opioids to manage their pain (even if recommended by a physician). Excessive doses of these medications can also slow breathing or be lethal. If function does not significantly improve then the opioid trial should be discontinued by weaning off the medication; ceiling dosages for opioids are controversial, but rarely has additional benefit been noted beyond 50 mg MED.

Rates of ART adherence in HIV-infected older adults almost always exceed those of their younger counterparts.

Regarding the use of pharmacological treatments for pain in HIV-infected older adults, research finds that adherence to HIV and non-HIV medications in HIV-infected older adults is quite good. In fact, rates of ART adherence in HIV-infected older adults almost always exceed those of their younger counterparts. A recent meta-analysis found that older age reduced non-adherence to ART by 27 percent in HIV-infected persons (Ghidei et al. 2013). These findings suggest that older persons living with HIV/AIDS may also adhere more consistently to pain relief medications.

Non-pharmacological Treatments

Non-pharmacological treatments (NPTs) as adjuvants for acute and chronic pain in HIV-infected older adults include behavioral, cognitive, and emotional therapies. Although NPTs are most efficacious when paired with analgesic medications, they can be used alone for the management of chronic pain. The selection of the most appropriate NPT adjuvant(s) for the older person aging with HIV depends on the types of pain experienced by the individual, supports available to him or her (e.g., family members and friends), and any pre-existing medical or psychological comorbidities. Common NPTs as pain adjuvants, many of which rely on the body's release of endorphins, distraction, and counter-irritation mechanisms, include:

- **Relaxation techniques.** Relaxation techniques, such as stress management and meditation increase pain tolerance and reduce patients' use of pain medication. Deep Breathing excercises and Progressive Muscle Relaxation are very effective and are available as "Apps" or on-line for free. Mindfulness meditation, a common form of relaxation and stress management, has reduced pain in persons living with headaches, lower back pain, chest pain, and gastrointestinal pain, conditions that impact many older adults living with HIV/AIDS.

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- **Heat and cold therapy.** Cold therapy is most appropriate for acute injuries and to decrease bleeding and chronic back pain. Heat therapy is most efficacious for muscle aches and abdominal pain.
- **Regular physical activity.** Physical activity, such as sports, walking, stretching, dance, or Tai Chi, can reduce chronic pain, particularly in patients with osteoarthritis, fibromyalgia, and peripheral vascular disease.
- **Mental imagery or visualization.** Cognitive NPTs, such as guided imagery and relaxation, can be effective but are largely contingent on a patient's ability to learn relevant skills and maintain discipline and motivation to practice these techniques regularly. Guided imagery and active relaxation can be practiced individually or with a coach and reduce pain primarily by relieving anxiety and reducing muscle tension.
- **Distraction** can reduce the sensation of pain. Methods to distract patients from painful conditions include encouraging them to watch television, play cards, work with their hands, or interact more regularly with family members, friends, or pets.
- **Massage.** Massage offers many therapeutic effects that reduce pain, including release of muscle tension, improved circulation, increased joint mobility, and decreased anxiety.
- **Acupuncture or acupressure.** Several small studies have investigated the efficacy of acupuncture and acupressure to reduce pain. The results of these studies, however, are largely inconclusive given their methodological limitations.
- **Spinal Manipulation.** Also known as spinal manipulative therapy or cervical manipulation, these approaches focus on the relationship between musculoskeletal structure (most frequently the spine) and body function (as coordinated by the nervous system) and how this relationship impacts health preservation and restoration.
- **Alexander Technique.** The Alexander technique instructs individuals to eliminate or reduce unnecessary levels of muscular and mental tension throughout the day. This technique uses an educational approach as opposed to relaxation techniques or forms of exercise. The primary purpose is to help individuals unlearn bad physical habits and achieve a balanced state of rest and posture in which the body is well-aligned
- **Hypnosis.** Hypnosis is a set of techniques that can increase a patient's concentration and responsiveness to suggestions to change his or her thoughts, feelings, behaviors, or physiological state. When conducted correctly by licensed therapists, hypnosis has produced reductions in pain in patients with headache, backache, burns, fibromyalgia, carcinoma-related pain, temporal mandibular disorder pain, and rheumatoid arthritis. In fact, a meta-analysis by Montgomery and colleagues (2000) that examined 18 published studies found that hypnotic techniques produced pain reductions in 75 percent of clinical and experimental participants.

Regarding the use of NPTs, Tsao et al. (2005) found that older persons living with HIV/AIDS were less likely than their younger counterparts to use NPTs to manage pain. As such, persons aging with HIV may be hesitant to use adjuvant therapies typically thought of as complementary or alternative medicines (CAMs).

Conclusion

Highly personalized and multi-disciplinary pain relief treatment approaches that take into consideration the bio-psycho-social-spiritual perspective of pain have the greatest potential to alleviate physical pain while concurrently addressing and mitigating the complex psychosocial sequelae common in persons with chronic pain conditions. As the number of older adults living with HIV/AIDS continues to increase, it will be all the more important for providers to assess for painful conditions in this population and develop age-appropriate and individualized treatments that can decrease pain and improve quality of life in this emotionally-vulnerable group. HIV

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Management of Substance Abuse in HIV Care

For the triply diagnosed, comprehensive approach is needed

BY RAMANI DURVASULA, PH.D. AND THEODORE MILLER, B.A.

SUBSTANCE USE AND ABUSE are common among HIV positive individuals, with nearly 50 percent of persons living with HIV/AIDS reporting current or past histories of drug or alcohol use diagnoses[1]. Rates of lifetime and/or current substance use, abuse, and dependence are high in HIV seropositive cohorts.

Among HIV-positive individuals, 10-28 percent have co-occurring psychiatric and substance abuse disorders[2]. Substance use is associated with key health behaviors and outcomes, including non-adherence, immunosuppression, increased sexual risk behaviors, and increased burdens on health care systems. In addition, it represents both a direct and indirect vector of transmission that occur through sharing contaminated injection equipment and increased likelihood of riskier sexual behaviors resulting from decreased inhibitions, poorer affect regulation, and increased sexual arousal.

Persons living with HIV/AIDS tend to underutilize substance use treatment[3], and this can be more pronounced in certain HIV seropositive subgroups including gay and bisexual men and transgenders[3]. Integrated care, particularly substance abuse treatment, is important in identifying and monitoring patients within this high-risk population who present with 'triply' diagnosed conditions of HIV, substance abuse, and psychiatric comorbidities[4]. ►

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The triply diagnosed condition severely affects the patients' quality of life and can exacerbate preexisting conditions. In addition, the portal of substance abuse treatment has ramifications for both HIV care and for prevention, as help-seeking for a substance abuse diagnosis may represent an opportunity for testing, education, and connection to primary care.

Substance Abuse and Risk

Increased sexual risk taking is observed in HIV seropositive individuals engaged in substance use. Stimulant and alcohol use is associated with increased sexual risk behavior[5] and empirical research has suggested that drug use, psychiatric symptomatology, and sexual risk behaviors operate synergistically. In addition, drug use and sexual risk patterns vary across groups as a function of ethnicity, gender and sexual orientation, which can place different groups at differential risk[6].

Standard integration of HIV testing into substance abuse treatment is an essential prevention tool. Substance abuse treatment services represent a rich opportunity to reduce incident infections by addressing injection drug use as well as other HIV risk behaviors.

Substance Abuse Treatment

Substance abuse treatment of HIV positive persons optimally occurs on a continuum of (1) individuals becoming aware of their HIV status, (2) engaging in HIV, psychiatric and substance abuse related care, (3) avoidance of relapse and continued adherence to treatment with the recognition that these steps can be bidirectional[7], and lapses and setbacks in psychiatric symptomatology, drug use and adherence behaviors should be prepared for and expected. Health care providers administering substance abuse treatment, psychiatric care, and HIV services vary in education, training, opinion, attitude, and experience, resulting in varied treatment approaches and outcomes.

The body of literature directly addressing the provision of substance abuse treatment to HIV infected individuals is limited. Because substance abuse treatment often occurs concurrently with medical care, determining the impact of substance abuse treatment in itself may be a challenge.

Methadone maintenance programs have been shown to be effective treatments for opioid dependent persons living with HIV/AIDS, and have shown additional utility in providing medical management and psychiatric care, in slowing disease progression, and in mitigating risk behaviors.

The use of pharmacologic treatments for opioid, alcohol and tobacco use and abuse including methadone, buprenorphine, naltrexone, disulfiram, varenicline, buproprion, and nicotine-replacement products have received variable attention in the HIV literature; potential interactions among pharmacologic products used to manage substance use, psychiatric medications and HIV medications exist. The use of pharmacologic management in triply diagnosed patients, while often an important first line intervention, may therefore raise additional challenges[8].

Approaches such as methadone maintenance also highlight the role of Directly Observed Therapy (DOT) in triply diagnosed individuals. DOT is typically employed in settings such as methadone maintenance, day treatment, and incarceration. It has not consistently been found to improve health outcomes (i.e., increased CD4 count and decreased HIV viral load) or improve medication adherence. The quality of findings has been context dependent with less consistency and efficacy with incarcerated populations. Although DOT is not practical for most clients, the key ingredients of DOT—structure, support, and routine—may be ingredients that facilitate its success as an intervention, and to the degree possible should be built into all integrated care.

Research on cognitive behavioral treatment models for substance abuse treatment in HIV infected samples has suggested reductions in alcohol use,

withdrawal and dependence symptoms, functional impairment, and depressive symptoms. However results often are variable and may not generalize to treatment for other drugs of abuse. These models typically rely on traditional cognitive behavioral techniques in conjunction with behavioral tools, such as contingency management and behavioral activation. Shoptaw et al.[9] compared Gay Specific Cognitive Behavioral Therapy (GCBT) and Gay Specific Social Support Therapy (GSST). The GCBT model focused on building skills such as identifying relapse triggers, interrupting cravings for drug use, and return to abstinence, whereas the GSST integrated elements of peer-driven social model counseling and HIV health education/reduction groups. Participants in both conditions showed a two-fold decrease in substance use and sexual risk behaviors, but among those using methamphetamine, GCBT was more useful in sustaining reduction in use.

Cognitive behavioral interventions with HIV infected substance using cohorts also have shown differential impacts on behaviors such as adherence, with some studies revealing improvements in depression, but not adherence[10]. Substance use treatment itself has been recommended as a useful adherence intervention tool, with the transition from using to non-use of drugs being associated with improved adherence. However, participation in substance use treatment has been associated with greater access to HAART, but has not been found to lead consistently to greater adherence.

The Transtheoretical Model11 posits ordered stages of behavioral change along a continuum of motivational readiness to change a problem behavior; transitions from one stage to another constitute the processes of change.

An intervention based on the Transtheoretical Model used a continuum of care to match clients' differential states of readiness for change11. The intervention focused on establishment of the therapeutic relationship, individual client assessment, client education about triple diagnosis, motivational enhancement and goal setting. The intermediate phase of treatment included shoring up coping skills, building social support, engaging in meaningful activities, developing a consistent sense of self and addressing grief and loss issues. The final phase of treatment was centered on maintenance of change and preparing for setbacks. Both individual and group treatments were employed, as well as psychopharmacology as needed. This intervention resulted in decreases in substance use and psychiatric symptoms.

Lower cost interventions delivered by video have shown outcomes for improvements in adherence and frequency of drug use on par with those obtained through Motivational Interviewing (MI)[13], an intervention closely related to the Transtheoretical Model. Ingersoll et al.[12] developed a six-session motivational interviewing and feedback and skills building program, which they compared to video information plus debriefing intervention (which was largely educational in nature, using a sample of HIV seropositive crack cocaine users who reported poor medication adherence.

Both MI and the video information sessions increased adherence and decreased problems due to drug use and number of days of crack cocaine use, highlighting the potential utility of lower-cost interventions such as video training, which may work well with subgroups of HIV seropositive drug users. MI has also been integrated into methadone maintenance programs and has resulted in less risky sex in these cohorts.

Integrated care is important in identifying and monitoring patients within this high-risk population.

Contextualized treatment programs such as the Structural Ecosystems Therapy employed by Feaster et al.[13] focus on the social environment, facilitating of adaptive interactions, and reduction of maladaptive interactions between HIV seropositive women and systems, including families, health care, and community organizations.

In managing ongoing recovery, addressing the structural environment is a key element, and, especially for women, the presence of substance using network members, particularly intimate partners, significantly increases the probability of relapse. This intervention, conducted with 126 HIV+ women in recovery, resulted in decreases in the proportion of women living with an active substance user and greater drug treatment utilization, though significant gains were not made with medication adherence. In managing ongoing recovery, addressing the structural environment is a key element, especially for women, because the presence of substance-using network members, particularly intimate partners, significantly increases the probability of relapse.

Given the higher rates of personality disorders, including borderline personality disorder (BPD) in HIV infected samples, treatment models such as dialectical behavior therapy (DBT) that have shown utility for symptom management in BPD, may have utility for management of triply diagnosed individuals with BPD[14].

This adaptation involves opening up the framework of DBT to specifically address targets such as adherence and mindfulness in HIV specific contexts. DBT uses a four-stage system that entails pretreatment targets and commitment to therapy, The first stage targets stability, connection and safety; the second stage targets exposure and emotional processing of the past, and third stage targets individual goals. While few outcome data exist, this technique has promising outcomes for a psychiatric risk group that is likely at higher vulnerability for triple diagnosis.

Particularly in the triply diagnosed, integrated care models[4] may provide the best means of simultaneously addressing multiple clinical issues. In one study examining an integrated care model that coordinated AIDS service agencies, case management, primary care and substance abuse treatment, participants had more medical visits than those not in

the program, although participants had lower CD4 counts. It is likely that the participants were sicker, as evidenced by their frequency of care and immune functioning, but within an integrated care model. Thus, the opportunity to connect medical visits to case management, substance use treatment, and mental health care may more efficiently target the needs of more medically ill clients.

Cultural Factors and Intersectionality

Disparities stemming from ethnicity, sexual orientation, socioeconomic status and gender highlight the importance of culturally responsive treatment programs.

The intersectionality of these variables can raise even greater challenges. For example ethnic minority women may require very different treatment approaches from Caucasian gay men. Focus group studies with African American men highlight the utility of extant community structures such as Black churches, fostering open dialogue about sexual behavior and drug use, and capacity building for families[15].

Halkitis[6] also cites the interaction between person and environment when highlighting sensitive issues, such as bathhouses as venues for prevention messages for gay men. Because many interventions, particularly adherence interventions, are individually targeted, they also may be less useful with ethnic minority or low income individuals as these models often overlook issues such as poverty, community and family.

Hybrid programs that address contextual factors such as stigma, discrimination, oppression and economic factors, while also addressing the unique needs of the individual (e.g. mental health history, medical status), may be challenging to construct, but they are necessary to address the environment interactions that can delimit the efficiency of intervention programs.

Recommendations

- The complexity of clinical needs among triply diagnosed individuals and persons living with HIV/AIDS who require substance abuse treatment highlights the importance of comprehensive, integrated, continuous, and culturally responsive treatment services that target primary care, ancillary services, substance abuse treatment, mental health care and behavioral health. Integrated care systems must focus beyond just mitigation of substance use and psychiatric symptoms, but also must address issues such as sexual risk, self-care, and adherence.
- Treatment programs that provide services to both HIV seropositive and seronegative cohorts can serve as portals of prevention, and HIV testing and prevention messages should be standard of care in substance abuse treatment programs.
- The goal of fast track abstinence in these populations may be untenable. Other clinical issues including physical/medical symptoms, mood symptoms, psychosocial factors, burdens due to economic factors mean that achieving sobriety is a marathon and not a sprint; clinical goals will be driven by biological, psychological, and social exigencies. HIV

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Transgender Issues in HIV

Providers need accurate, current information to provide optimal care

BY JAE SEVELIUS, PH.D.

AS AWARENESS ABOUT THE EXISTENCE OF TRANSGENDER PEOPLE GROWS in mainstream consciousness, so does our knowledge about their unique strengths, needs, and vulnerabilities. Providers of HIV care need accurate and current information about transgender people living with HIV, including potential barriers and facilitators to engagement and retention, as well as strategies for optimizing HIV care and treatment for transgender patients. ►

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Terminology

'Transgender' is an umbrella term for individuals whose gender identity differs from the sex they were assigned at birth.

'Transgender women', sometimes referred to as 'male-to-female' (or 'MTF') are individuals who were assigned male sex at birth, but who identify as women or as transgender women.

Similarly, 'transgender men' ('female-to-male' or 'FTM') were assigned female sex at birth, but identify as men or as transgender men. Some transgender people do not identify within the male/female binary at all.

Furthermore, current literature is moving away from the MTF and FTM terminology for a variety of reasons; a summary of selected common terms is provided in Table 1. Terminology used to describe transgender identities varies widely by geographic region, age, ethnicity, and other factors. When serving transgender patients, providers can build trust by asking for and using the terminology preferred by each patient and by ensuring that the patient's preferred name and pronoun is recorded in his/her medical record and used by every staff person who interacts with the patient.

Stigma and Discrimination

Transgender people often experience stigma and discrimination, resulting in social marginalization and negative health outcomes. Because their gender identity and/or presentation differs from the sex they were assigned at birth, transgender people challenge society's most basic assumptions about the binary nature of sex and gender and the stability of identity.

The discrimination, rejection, and violence experienced by transgender people are often referred to as 'transphobia'. Just as homophobia negatively affects lesbians and gay men, transphobia affects transgender people in a multitude of deleterious ways. Experiences of discrimination and victimization negatively impact mental health by increasing anxiety, depression, and suicidality.[1-3]

Transphobic discrimination, victimization, and lack of social support consistently are associated with attempted suicide, substance use, dropping out of school, and unprotected sex among transgender youth[4]. Transgender people have shockingly high rates of suicidal ideation and suicide attempts compared to the general population (31 percent vs. 2 percent),1 and often report using substances to cope with the intense stressors associated with the stigma of being transgender.[5]

HIV in Transgender Populations

Transgender women are one of the most highly impacted groups in the HIV epidemic to date, yet they are disproportionately under-researched and underserved by current treatment efforts. Transgender women have 49 times higher odds of HIV infection compared to other groups, a disparity that exists across race, culture, and socioeconomic boundaries.[6] Disparate prevalence rates of HIV are particularly pronounced for African American transgender women when compared with transgender women of other races and ethnicities.[7] Furthermore, HIV+ transgender women have an almost three-fold higher community viral load than non-transgender HIV+ adults in San Francisco (64,160 vs. 22,376),[8] and likely elsewhere. HIV-related mortality and morbidity rates have also been found to be higher among transgender women.[9]

In addition, there is evidence that current efforts to provide effective treatment to transgender women living with HIV are not as successful as with other populations. In the only study of its kind to date, transgender women living with HIV were less likely to be receiving antiretroviral therapy than a control group of non-transgender men and women.[10] Furthermore, transgender women living with HIV who were on antiretroviral therapy demonstrated worse adherence than non-transgender people, reported less confidence in their abilities to integrate treatment regimens into their daily lives, and experienced fewer positive interactions with their healthcare providers.[11]

To date, there are few studies of HIV incidence among transgender men in the literature. Transgender men at risk for HIV are those that report sex with non-transgender men (trans MSM), a subgroup that has only recently begun to receive attention in public health research. The few research studies focused on trans MSM to date have found relatively high levels of reported risk behavior, but lower levels of HIV prevalence (0-3 percent).[12] Some trans men who are on cross sex hormone therapy (i.e. testosterone, or 'T') self-report a link between testosterone use, increased sex drive, increased interest in engaging in sexual activity, and exploration of sexual behaviors that may include sex with non-trans men. For trans men on testosterone, the masculinization of the body may lead to increased access to non-trans MSM partners, and a willingness to take sexual risks that could potentially place trans MSM at risk for STI and HIV infection.

Engagement and Retention in HIV Care

Because transgender women are extremely disproportionately affected by HIV, and because the vast majority of HIV-related research has focused on transgender women, this discussion will focus on what we know about transgender women's experiences with seeking HIV care. Much of this information may be applicable to transgender men as well, but transgender men are likely to face qualitatively different issues as well.

Transgender women living with HIV face culturally unique and substantial challenges to adhering to HIV care and treatment regimens, such as limited access to and avoidance of healthcare due to stigma and past negative experiences, prioritization of gender-related healthcare, and concerns about adverse interactions between antiretroviral therapy and hormone therapy. Issues that affect other marginalized populations, such as mental health issues, substance use, and poverty, are barriers to care among transgender women as well, but additional transgender-specific barriers exist as a result of transphobia, as well as needs for gender affirmation and transition-related healthcare.

Importance of Gender Affirming Health Care

"Gender affirmation" is the process by which individuals feel socially validated in their gender identity through interpersonal

Table 1. Selected common terms used to describe transgender identities

Term	Definition
Transgender	An umbrella term used to describe individuals whose gender identity differs from the sex they were assigned at birth
Trans	Shorthand term for 'transgender'
Transgender woman/Trans woman	Transgender person assigned male at birth, identifies as female
Transgender man/ Trans man	Transgender person assigned female at birth, identifies as male
Transvestite/ Cross-Dresser	A person who dresses in gendered clothing that differs from their own identity for entertainment or sexual purposes but does not necessarily identify as transgender
Genderqueer	Gender nonconforming person, a term increasingly used by youth
Transsexual	A term that is sometimes used to refer to transgender individuals who have undergone medical procedures to affirm their gender; currently a less favored term in trans-related literature

interactions, such as interactions with a healthcare provider. The Model of Gender Affirmation is a transgender-specific model developed to examine the role of gender affirmation in risk-taking, self-care, and healthcare-seeking behavior.[13] It posits that when a transgender woman places a high level of importance on gender affirmation, she will seek out opportunities to receive this affirmation and avoid experiences in which she is not affirmed in her gender.

A gender affirming healthcare experience would include, for example, a transgender patient being called by the correct name and pronoun by all staff throughout the healthcare encounter without unnecessary attention being drawn to her transition status. Gender affirmation also includes having access to and support for transition-related health care, such as hormones and surgeries, as desired by the patient. Evidence of the associations between access to gender affirmation and improved quality of life, mental health, and self-care behaviors among transgender people is growing rapidly.[14,15]

Gender affirmation is of paramount importance to many transgender women at every stage of the HIV care continuum. Transgender sensitivity and knowledge on the part of providers and clinics can be a crucial barrier when absent, and a powerful facilitator when present. Studies have reported that when transgender women do seek healthcare, patients' trust in their provider is compromised when they encounter insensitivity and low levels of knowledge. Diminished trust subsequently impairs patient-provider communication and can affect participants' decisions to initiate and/or adhere to antiretroviral therapy.

Multiple negative experiences can ultimately result in avoidance of healthcare settings altogether. Gender affirming healthcare, however, can support engagement and retention in HIV care among transgender women by increasing patient-provider trust, fostering positive interactions, and supporting a collaborative relationship.

Intake forms should permit transgender patients to identify themselves and their records should correctly identify their preferred name and pronoun to all providers and staff that interact with them. This documentation should be handled as sensitive and confidential health information. This increases trust in the provider and clinic by ensuring that patients are not called by the wrong name and/or pronoun, an experience commonly reported by transgender people as highly detrimental to their health care experience.

Efforts are currently underway to allow for the identification of transgender patients using electronic medical records.[16] In the meantime, clinics should revise local systems to be inclusive and respectful of transgender patients. The UCSF Center of Excellence for Transgender Health's Recommendations for Inclusive Data Collection of Trans People in HIV Prevention, Care, and Services offer guidelines for clinics and have been implemented by agencies across the US.[17]

Currently, few formal medical education programs include transgender-specific medical care in their training of providers. Providers who serve transgender patients should be comfortable with transgender people at all stages of transition. Training providers to conduct thorough yet respectful health assessments, including mental health and sexual health, will help build trust and rapport with transgender patients. In addition, creating a safe clinic space, including respectful front line staff, sends the message that transgender patients are welcome and is more likely to yield positive health care experiences.

Integration of Hormone and Antiretroviral Therapy

Transgender women living with HIV often juggle a variety of demands on their time and energy due to trauma, addiction, and the deleterious effects of transphobia in their day-to-day lives. Once they initiate antiretroviral therapy, transgender women often experience barriers to integrating the regimens into their daily lives.

One method for starting to address this barrier is the integration of hormone therapy and antiretroviral therapy in HIV primary care settings, a strategy that has been employed successfully and recommended by primary care clinics that serve transgender patients.[18]

Seeing the same provider (or at the very least, being seen at the same clinic) for both hormones and antiretroviral therapy may facilitate patient management of their appointments and medications, increase the likelihood that they keep their appointments (augmented by a high level of motivation to adhere to their hormone regimen), and increase trust in their provider.

Several resources are available to guide the provision of hormones for providers who are new to treating transgender patients. The UCSF Center of Excellence for Transgender Health has an online Primary Care Protocol for Transgender Patient Care that provides peer-reviewed guidelines and

additional resources for review.[19] In addition, the World Professional Association for Transgender Health recently revised its Standards of Care document that has long served as a resource for those wishing to increase their expertise and receive guidance in the provision of health care to transgender patients.[20]

Additional Recommendations

- **Increase visibility of transgender people in peer and professional support roles.** Transgender patients often feel most comfortable with outreach and program staff who are also transgender. Transgender staff who already have established relationships with the community that the program seeks to serve can be indispensable in terms of recruitment and retention. In addition, transgender staff who have personal experience with many of the same issues that clients face can offer unparalleled support, guidance, and mentorship. Transgender staff who are openly living with HIV can model disclosure about status to help reduce stigma and can serve as an invaluable resource in peer navigation programs.
- **Attend to transgender-specific needs.** Interventions specific to transgender patients are ideal. Programs such as a transgender-specific portal to a larger health clinic, use of peer health navigators, and transgender-specific clinic hours are exemplar models that have been successful. In areas where it is not possible to create transgender-specific services, explore aspects of existing programs that can be tailored to the transgender community, such as adding a transgender-specific support group to substance abuse treatment programs or housing programs.
- **Maintain current referral resources.** While some areas may not have many transgender-specific referral resources, identifying services that are informed and sensitive can help patients avoid negative experiences in the community. This may also increase the likelihood that they will access support services that may help them stay engaged in their treatment, such as complementary and alternative therapies that help alleviate side effects of HIV medications and spiritual and/or meditation groups that help promote healthy coping strategies. When possible, create a centralized, up-to-date, and comprehensive transgender resource guide that can be given to patients.

Conclusion

Engagement and retention of transgender patients in HIV care and treatment will be optimized by services that are gender affirming and integrate transition-related healthcare needs. Such interventions must fully attend to the social, economic, and psychological context of transgender patients' lives and address the multiple barriers to healthcare engagement, treatment adherence, and empowerment that serve to create, maintain, and deepen HIV-related health disparities, particularly among transgender women living with HIV. HIV

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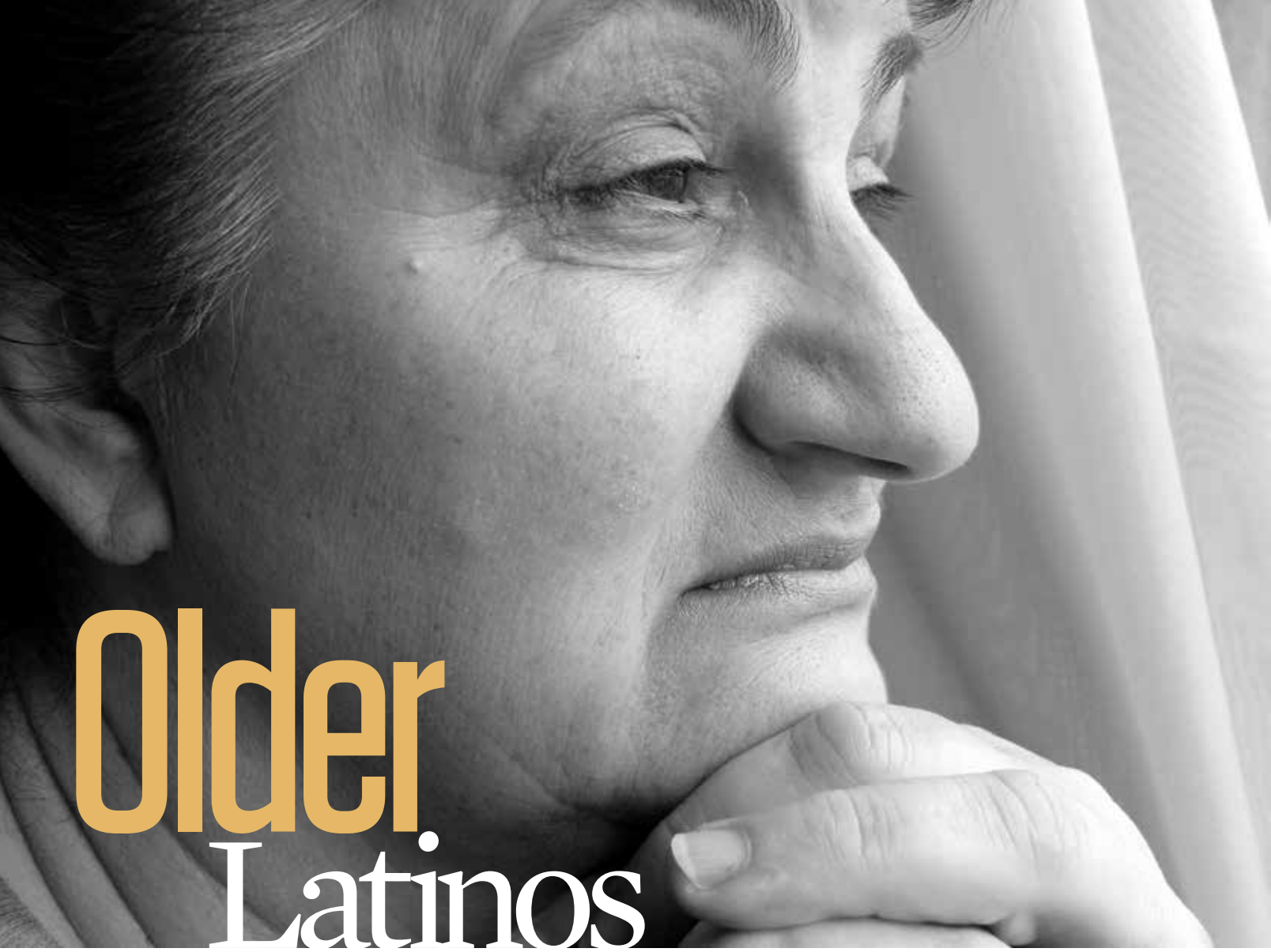

Older Latinos

The double jeopardy of HIV and depression

BY MARK BRENNAN-ING PH.D AND STEPHEN E. KARPIAK PH.D

THE INTERSECTION OF HIV and depression among older Latinos illustrates how social-structural determinants affect health outcomes and well-being in a diverse aging population. Older Latinos in the U.S. reflect a diversity characterized by their nationality, Mexican, Central American, and South American, immigration history, language use, educational and occupational opportunities, and socio-economic status.

Latinos are disproportionately impacted by HIV. The overall HIV prevalence rate for Latinos is nearly three times the rate for whites. Latinos are the most likely to be classified at Stage 3 (AIDS) at the time of their HIV diagnosis (48 percent), as compared with whites (42 percent) and blacks (39 percent). Only 26 percent of Latinos with HIV achieve the clinical goal of viral suppression.

Due to successful anti-retroviral therapy, by 2015 more than half of those with HIV in the U.S. will be 50 years or older, a proportion that will rise to 70 percent by 2020. The HIV disparity is amplified among older Latinos whose HIV prevalence is five times that of older non-Hispanic whites. In addition these older Latinos have a 44 percent increased risk for major depression and are more likely to present with clinically significant depressive symptoms compared with older whites.

This syndemic of HIV and depression becomes evident when assessing treatment outcomes since the most consistent predictor of HIV treatment non-adherence is depression.

HIV and mental health disparities among older Latinos with HIV arise from a shared set of social-structural determinants, including national origin, education and socio-economic status. Disparities in both HIV prevalence and depression are associated with national origin.

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For example, Puerto Ricans are disproportionately affected by HIV in the U.S. relative to other Latinos, and are at greater risk for depression compared to Mexican- or Cuban-Americans. Lower socioeconomic position is linked to higher rates of HIV infection in Latino communities. Inadequate economic resources increased the risk for depression in this population. Other social determinants of both HIV infection and depression among Latinos include immigration history and acculturation.

These disparities are evidenced in research that we have conducted at the ACRIA Center on HIV and Aging. Reported findings from our landmark Research on Older Adults with HIV (ROAH) study show that older Latinos with HIV were more than three times as likely to be foreign-born (37 percent) and more than five times as likely to have less than high-school educations (27 percent) compared with non-Hispanic whites (11 percent and 5 percent, respectively). These differences in social-structural determinants of health are reflected in study findings that older Latinos with HIV were more likely than non-Hispanic blacks to have an AIDS diagnosis (52 percent and 46 percent, respectively). Further immune system functioning as measured by CD4 t-cell counts, older Latinos had the lowest counts on average (313) compared to non-Hispanic blacks (492) or whites (449). When assessing mental health, older Latinos in the ROAH study evidenced the highest average level of depressive symptoms (CES-D) among the three major racial/ethnic groups. Nearly half of older Latinos (46 percent) met the threshold for severe depressive symptoms compared with 40 percent of non-Hispanic whites and 35 percent of non-Hispanic blacks.

We recently examined the impact of social-structural factors on health disparities between older Latinos and non-Latinos in the ROAH study using an economic decomposition analyses. In these analyses, we examined differences on CD4 counts and depressive symptoms. The analyses also account for the previously mentioned social-structural factors, and included age, education, employment status, and prior AIDS diagnosis.

Even after accounting for these factors, disparities between Latinos and non-Latinos persist regarding immune function and mental health; a phenomenon known as "statistical discrimination." Simply put, statistical discrimination represents an additional degree of health disparity that older HIV-positive Latinos face relative to their non-Latino peers.

It is very likely that this effect was conservatively estimated with the ROAH data since the Latino sample who participated spoke English and we did not see any significant racial/ethnic differences in current use of HIV medications indicating similar levels of access to care. Identifying and addressing the sources of such discrimination is essential to improve treatment outcomes and quality-of-life for older Latinos with HIV. HIV

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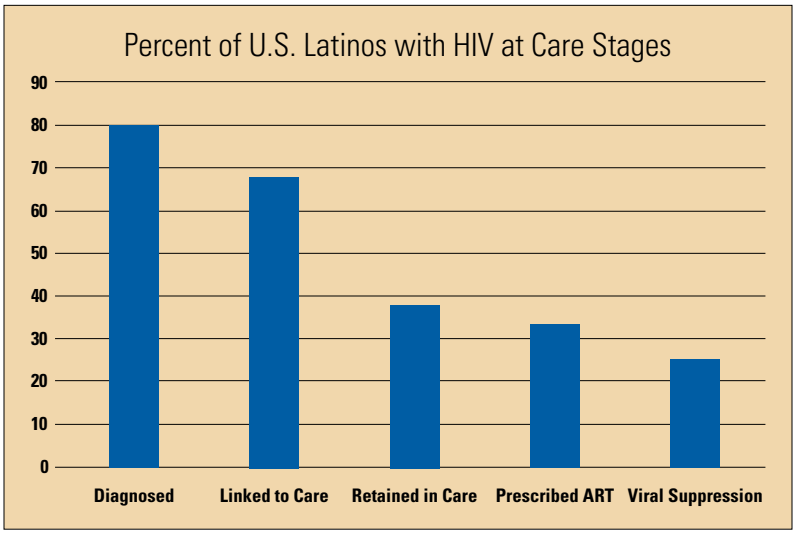
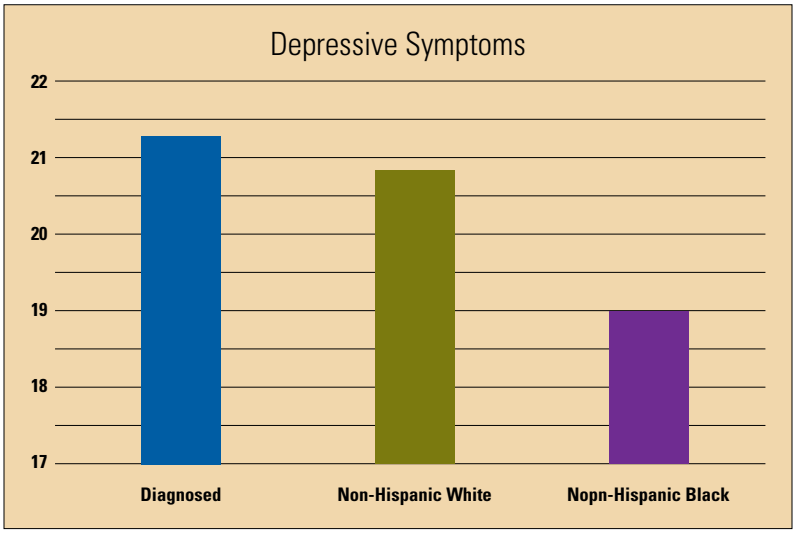
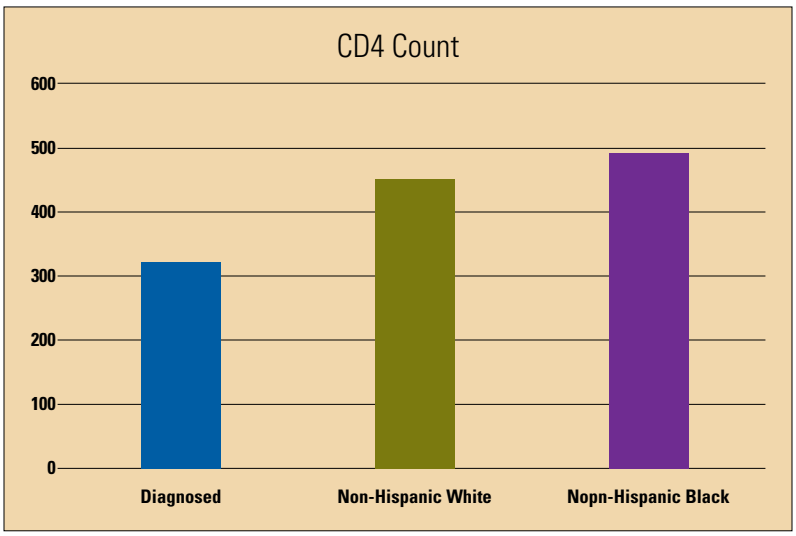
Mark Brennan-Ing, Ph.D, is the Director for Research and Evaluation at the AIDS Community Research Initiative of America in New York City, and an Adjunct Professor at the New York University College of Nursing. Dr. Brennan-Ing's work focuses on mental health, social supports, and resilience among older adults with HIV.







Stephen Karpiak, Ph.D is the Senior Director for Research at ACRIA where he initiated the seminal effort ROAH "Research on Older Adults with HIV" a comprehensive study of 1,000 older adults with HIV/AIDS.

Striking a Balance for Effective Care

Developing an educated, professional empathetic response must be the rule, not the exception

BY DENNIS MYERS, MSN, FNP, AAHIVS

WHAT WOULD YOU TELL a long-term HIV infected client who wants to stop taking his or her antiretroviral medications? The answer to proceed or not can be clinically justified either way.

I must also act in the best interest of the client and "treat that client fairly, equitably and without regards to their race religion, ethnicity, and sexual orientation or health status."

My task as a clinician, especially as an HIV specialist, is to strike a balance between what the client "wants" and what the client "needs." I am ethically bound to first, "do no harm." I must also act in the best interest of the client and "treat that client fairly, equitably and without regards to their race religion, ethnicity, and sexual orientation or health status." I must do this while respecting the client as an individual who is capable of participating in his or her own care and who is capable of making sane, rational choices about their health care needs.

HIV disease remains a very complicated disease to control, and clients living with HIV/AIDS get very little respect for their long term survival abilities. John Mack was such a person and his case is an example of why my work matters.

When I inherited John from another provider, his ability to control his HIV was already compromised by a geno-pheno type that left him few choices to boost his immune system. Diagnosed in the late 80's when HIV was "new," he enrolled in multiple single drug trials just to survive.

John paid the price. His CD4 never rose past 96; his viral load never got lower than 15,000 copies. His physical health progressively spiraled downwards. Mentally, he never gave up, always believing that I could and would come up with a new treatment or regimen combo to keep him going. For 10 years, we worked as a team. But then, his throat carpeted with thrush, losing weight, fatigued and with a CD4 of 2, he finally asked me to stop.

HIV disease is not a socially acceptable or a politically correct disease. Being forced to choose every day between medications, food, housing or transportation is nothing new for the chronically ill. These decisions are less likely to be resolved equitably if you add the stigma of being HIV positive.

Chronic pain is rampant and unrelenting among long-term HIV survivors. Chronic pain prevents gainful employment. Chronic depression sets in. Suicide can be considered a source of relief. Hopelessness rules. Fatigue sets in. Hope for a peaceful resolution wanes with each setback or rejection. The daily grind of pills, side effects, fear of being "outed" as someone who "has AIDS" forces the client to yell STOP. Fortunately John never lacked for support or good insurance. His body quit before he did.

An HIV client is not stupid. That does not mean the consequences of his or her decisions cannot be fatal. As their clinician, I must call upon all of the wisdom and skill that I possess, and then some, to help guide the right decisions. My only remedy is to provide up-to-date, clinically correct and socially viable information and support in a professionally objective manner that will enable clients to choose their fate with dignity and understanding. Anything less is unethical.

An HIV positive person's choices may not be ours. His or her life may not be like ours. Developing an educated, professional empathetic response must be the rule, not the exception when dealing with an HIV positive client. The decisions and challenges will not get any easier in the near future as our population ages. One may be forced to "take a road less traveled" when dealing with HIV positive clients. But in the end, a positive difference can be made. That is why our work matters. HIV

ABOUT THE AUTHOR:

Dr. Dennis Myers is a board certified family nurse practitioner practicing since 1996. He provides a full range of primary care services to teens and adults at the Evansville Multi-Specialty Clinic in Evansville Indiana. He specializes in treating HIV and Hepatitis C infections including those who are dual infected with HIV and Hepatitis C.

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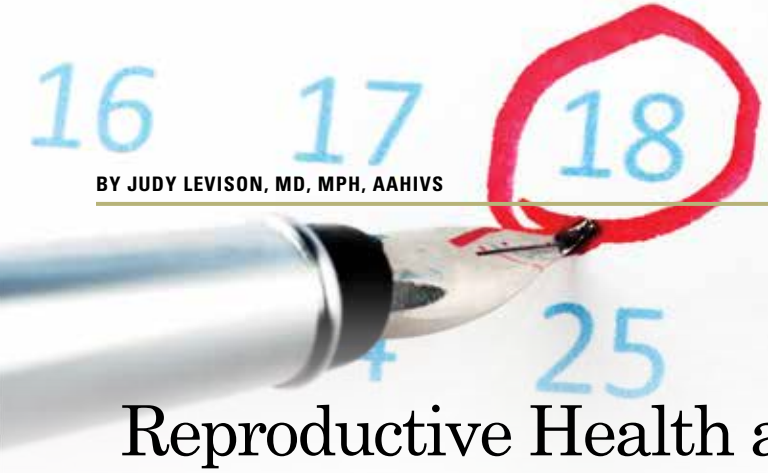
BY JUDY LEVISON, MD, MPH, AAHIVS



Reproductive Health and Preconception Care for Women and Men

What HIV providers should know

THE LARGEST GROUP OF INDIVIDUALS diagnosed with HIV annually in the United States are ages 25-34 and thus in the peak years of reproduction.[1,2] HIV positivity does not prevent women and men from desiring pregnancy.[3] After all, with the availability of antiretroviral therapy, we expect longevity among those with HIV to be 72 to 75 years of age[4] and transmission of HIV from mother to child to be under 1-2 percent.[5]

Preconception care (preparing and planning for a healthy pregnancy) seeks to improve the wellbeing of women and men before conception using interventions that can identify and modify medical, behavioral, and social risks to health and pregnancy-related outcomes through prevention and management.[6]

Moreover, preconception care can reduce the risk of adverse outcomes for the woman, fetus, or neonate by optimizing the woman's health and knowledge before planning and conceiving a pregnancy[7] and engage men in pregnancy planning.[8] As a component of HIV management, preconception care helps patients avoid unintended pregnancy; reduce the risk of viral transmission to partners; implement safer conception options, particularly for serodiscordant couples; and prevent perinatal transmission of HIV.[9]

In the Women's Interagency HIV Study, more than 30 percent of participants reported not using any form of contraception.[10] Underuse of highly effective contraception and barriers leaves women with HIV at risk for unintended pregnancy and men and women at risk for disease transmission.

Also, increasing numbers of men who have sex with men are desiring to father pregnancies. For these reasons, all sexually active HIV-infected women and men of reproductive age (regardless of sexual orientation) should receive preconception counseling to help them achieve their reproductive goals, while minimizing transmission to partners and infants.

HIV providers need to know whether their patients want to prevent conception or bear children.[11] The Women Living Positive Survey found that 70 percent of HIV-infected women in the United States considered family planning an important part of their HIV care, yet 55 percent of survey participants had never discussed gender-specific HIV treatment issues with their HIV providers. Among women who had been or were pregnant at the time of the survey, 57 percent had not engaged in pre-pregnancy discussions with their HIV provider about the most appropriate HIV regimens.[12]

In a qualitative study of HIV-positive women, only 25 percent reported discussing their childbearing goals with their HIV provider.[13] When conversations are initiated, they are usually initiated by patients.[14]

HIV providers may not integrate preconception care into overall HIV management for a number of reasons including lack of comfort or knowledge about preconception counseling or contraception; competing priorities and more immediate concerns related to care of HIV and comorbidities; time constraints; reluctance to discuss fertility and reproduction;[14] an assumption that HIV-infected women do not want to become pregnant; an expectation that the subject will be addressed by other health care providers such as obstetri-

Practice Support Tools: Electronic Medical Record Template. For example:

- Have you ever been pregnant? When?
- Are you interested in having a child/another child?
- When do you wish to conceive?
  - Currently?
  - 6 months to 1 year?
  - 1 to 2 years?
  - >2 years?
- Are you currently using condoms?
- Are you currently using a contraceptive other than condoms?
  - If "yes," what method?
  - If "no," are you seeking pregnancy?
- Would you like information on planning a safe pregnancy that may reduce the risk of HIV transmission to your partner and your baby?

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Components of preconception counseling for women living with HIV
[Adapted from Hoyt 2012]

Current and future wishes and plans to have children by woman, her partner, and family and desired timing of pregnancy
Contraceptive options (for women who do not wish to become pregnant or who wish to delay pregnancy for better birth spacing or while health or non-health-related issues are managed)
Effect of HIV and antiretroviral drugs on pregnancy course and outcomes
Effect of non-HIV-related medical, social, and other factors on pregnancy and pregnancy outcome
Optimization of maternal health status and timing of pregnancy
Counseling on safer sexual practices and healthy living generally (smoking cessation, eliminating alcohol, discontinuing drug use)
Options for conception that decrease risk of HIV transmission to an HIV-uninfected partner
Perinatal HIV transmission and prevention of mother-to-child transmission: the role of antiretrovirals for mother and baby, mode of delivery, avoidance of breastfeeding, infant antiretroviral prophylaxis

cians/gynecologists; and an assumption that men who have sex with men do not need to receive preconception counseling. Nevertheless, preconception care remains an integral element of HIV management and may help patients in their reproductive decision making.[15]

What can HIV providers do?

Preconception care allows individuals with HIV to make the most informed reproductive choices while correcting misconceptions and increasing awareness of new conception options. Through effective communication with patients, HIV providers can identify those who desire or do not desire children and either provide counseling directly or refer them to preconception services to ensure safer childbearing or contraception.

Preconception counseling is most effective when both partners are present so couples can participate in the decision-making process. Preconception issues may differ for seroconcordant couples and serodiscordant couples, including conception options and HIV transmission prevention when attempting conception.[16]

Specifically, methods available to HIV-infected women in serodiscordant relationships include: 1) having an undetectable viral load, 2) using ovulation predictor kits to identify the most fertile day in each month, and 3) doing home insemination (partner ejaculates into cup or condom, semen is placed in a needleless syringe, and syringe is used to deposit semen in vagina) or having unprotected intercourse just on the peri-ovulatory day.

For HIV-infected men with HIV-uninfected female partners, recommended methods are: 1) having an undetectable viral load, 2) having the female partner use ovulation predictor kits to identify the most fertile day in each month, 3) once-a-month sperm washing followed by vaginal or intrauterine insemination or once monthly unprotected intercourse, and 4) consideration of preexposure prophylaxis (PrEP) for the HIV-uninfected woman.[17]

In addition, preconception counseling is important for all single men and for male couples who are considering fatherhood, particularly when the sperm donor is HIV-infected. Lastly, if both partners are HIV-infected and attempting conception, there is a theoretical risk of superinfection with a second viral strain. At a minimum, both partners should have an undetectable viral load; if they usually use condoms, they may consider using ovulation predictor tests and having once a month unprotected intercourse.

Preconception counseling

Every provider-patient interaction presents an opportunity to discuss reproductive health in the context of HIV infection, including preconception care, safer conception, and contraception. It is never too early to begin these discussions, which ideally should begin at the time of the first visit.

Ongoing discussions about reproductive issues and intentions at every visit can prevent missed opportunities to educate and offer guidance to those with childbearing interests and help those without such an interest to avoid unintended pregnancies.[14]

What issues should be discussed?

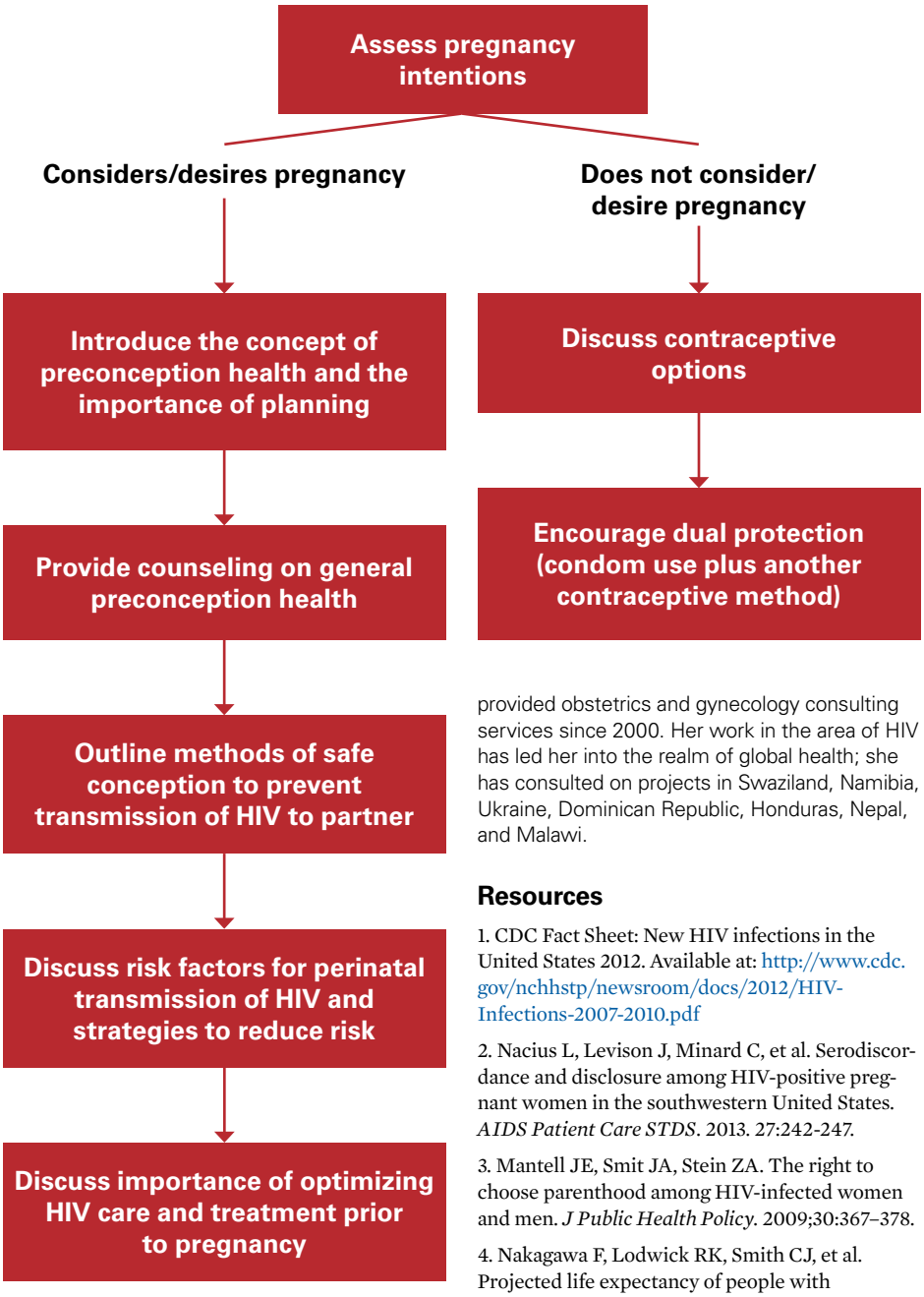
Preconception counseling should address a number of topics, including the impact of pregnancy on HIV and the impact of HIV on pregnancy, risk factors for mother-to-child transmission and strategies to reduce those risks (e.g., antiretroviral medication, Cesarian section if the viral load is high, avoidance of breastfeeding), the risks and benefits of HIV-related medications, disclosure of HIV diagnosis, and safer conception options.

In addition, provider checklists have been developed to address fertility issues in the context of HIV (i.e., the desire to conceive and the desire to prevent pregnancy). These tools can also be used to review current medications, some of which are contraindicated in women trying to conceive (e.g., efavirenz, statins, ribavirin, tetracyclines).[18]

Conclusion

Contraception and pregnancy desires change over time. Just because an HIV-infected patient did not desire pregnancy last year does not tell you what he or she wants currently, so providers should not assume that pregnancy is not a consideration for their HIV-infected patients. It is always best for couples to conceive with the knowledge of safe options and the support of their HIV provider. HIV

Preconception health counseling [Adapted from: F-XB Center: Preconception counseling for women living with HIV infection. 2012.]



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Coming of Age with HIV

JESSICA, an engaging 17-year-old, perinatally-infected with HIV, who has been a patient in the Pediatric and Adolescent HIV Clinic since birth, becomes tearful when discussing plans for future care in the Adult HIV Center. ▸

BY JOSEPH S. CERVIA, MD, MBA, FACP, FAAP, FIDSA, AAHIVS

Attending clinic with her maternal grandmother since her mother's death when she was just an infant, both consider the clinic team as members of their extended family. Like many of her peers, Jessica has had a challenging course of illness, marked by treatment with numerous antiretroviral agents, at times with incomplete adherence. Nevertheless, she has had undetectable viral loads for the past 18 months on tenofovir, emtricitabine, and ritonavir-boosted lopinavir, with CD4+ over 350 cells/μL.

The pediatric team has been working with Jessica on a planned transition to the Adult Center for the past year. She has been making great progress, with a mature understanding of her illness. Jessica makes appointments with the assistance of her grandmother, although recently she has been missing them frequently without calling, or she has been arriving late.

Jessica has had several boyfriends, but denies sexual activity. She expresses great distress at the thought of discussing her HIV infection with friends, and has been treated for depression and anxiety by the team child psychiatrist with daily escitalopram and alprazolam.

Across the waiting room sits Andre, a reserved and artistic 21-year-old gay man who has been a patient in the Pediatric and Adolescent HIV Clinic since testing positive for HIV after some injection drug use and high-risk sexual encounters three years ago. He has remained clinically asymptomatic, with CD4+ lymphocyte counts just below 500 cells/μL, and recently commenced antiretroviral therapy.

Andre has developed trusting relationships with the care team, but has not disclosed his sexual orientation or HIV status to his parents and family, and remains reluctant to do so. While he admits occasional use of marijuana and alcohol, Andre has been free of injection drug use and consistent in making and keeping appointments over the past year. Andre has just been offered a graduate fellowship in film at an out-of-state university, but expresses reservations about transitioning his care to an adult provider at this time.

Adolescence always has been appropriately regarded as a turbulent time, characterized by innumerable challenges. Yet for Jessica, Andre, and the over 25,000 other HIV-infected U.S. youth aged 13-24 that will require transition to adult care within the next decade, another set of formidable trials awaits. According to Connie Colter, CPNP, who cares for children and adolescents in the Pediatric Immunology Center at Cohen Children's Hospital in New York, "For teens with HIV infection, the transition process can invoke an entire range of emotions and responses, affecting not only the emerging young adult, but also their providers."

While perinatal HIV infections have decreased dramatically over the past two decades, the use of combination antiretroviral therapy (cART) has markedly reduced mortality among children and adolescents infected with HIV-1. As a result, many perinatally-infected youth are surviving to adulthood. In addition, it is now estimated that 13 percent of all new infections are occurring in young persons aged 13-24. In that age group, male-to-male sexual contact is the leading risk factor for transmission.

Hard to Let Go

Regardless of mode of transmission, many youth coming of age with HIV infection in the United States have become accustomed to family-centered, youth-friendly, multidisciplinary primary care with integrated HIV subspecialty services offered by teams that may include pediatricians, pediatric nurse practitioners, nurses, social work case managers, child life therapists, psychologists, nutritionists, chaplains, and other dedicated caregivers.

These team members often have developed long-standing and intimate bonds with patients and family members. Ironically, it is the very strength of these bonds, which have been forged by shared struggle against poverty, social stigmatization, drug use, and often the concurrent illness and death of multiple family members, that may render transitioning all the more painful and difficult for all concerned.

Like Jessica, many perinatally-infected youth describe leaving their pediatric care team as similar to the loss of a family member. Like Andre, behaviorally-infected youth may experience similar feelings, particularly those who may have disclosed their diagnosis to few others besides the adolescent care team. Compounding the challenges posed by such feelings, pediatric care providers also may have difficulty letting go of their long-term patients.

"Young people don't want to have to 'tell their story' with someone else," explains Coulter. "They are anxious that their new providers won't spend the same type and amount of time with them, or won't be as accessible by phone, email, or text. There is also uneasiness with presenting in an unfamiliar waiting room, where other clients may be perceived as judging them."

Joseph McGowan, MD, AAHIVS, director of the Center for AIDS Research and Treatment at North Shore University Hospital and chair of the New York/New Jersey Chapter of the AAHIVM, agrees that setting up an environment that is welcoming and non-threatening is of great importance.

"The adult clinic is much larger than those of pediatric/adolescent programs and, especially for perinatally infected youth, it is like leaving the comforts of home," states McGowan. "This is also a time when young adults are required to take on more responsibility to plan for their future, and develop independence. Socially they must deal with developing relationships and sexuality which can be difficult due to their HIV status. It may seem destabilizing on several fronts."

Transitioning

It is never too early to begin preparing for care transitions. As most transitions in HIV care occur between ages 21-24, it is important to develop a transition plan several years prior, and to update it regularly.

"While we aspire to begin the process in early adolescence, the relevance of the event that will occur in what they perceive to be the 'not very near' future to what is currently on the teen's radar often prohibits meaningful discussion about the actual transfer of care," cautions Colter.

"Age-appropriate preparation and engagement in the transition process requires the focus to be on the achievement of meaningful life skills such as working with a younger teen to master the concepts of knowing basic disease-related terminology (e.g. T-cells, viral load)," she adds, "understanding facts about their own personal health history, and reciting the names and administration schedule for their medications as an early step which additional skills and knowledge can be built upon."

McGowan agrees, "I think it is very important that pediatric HIV care providers spend more

time truly educating infected youth about what it means to have HIV or AIDS. This foundation from early age may make it easier for them to put this infection into proper context, support adherence and improve long term success."

Successful transitioning requires that caregivers ensure that HIV-infected youth understand their illness and offer training and practice in skills necessary for actively participating in their adult care. This includes knowing when and how to seek care, identify and describe symptoms, schedule appointments, arrive on time, and request necessary prescriptions and refills. Also, in negotiating care within complex, changing and often confusing payment systems, young people must also understand how to evaluate, select, obtain, and renew health insurance, understand entitlements and how to access them, and actively collaborate with a case manager.

Colter emphasizes the importance of a "crossover" member of the health care team, who can attend office hours at the youth's current care site, meeting multiple times with the transitioning youth during the year prior to the anticipated date of transition, and then serving as the familiar face at the time that the young adult appears at the adult center for their initial visit. Supportive mental health services that provide anticipatory guidance and continuity also are helpful preparation and followup of youth in transition.

Referring pediatric providers should identify adult providers and care teams experienced with transitioning HIV-infected adolescents and young adults who are willing to communicate, collaborate, and accept the patient's health insurance.

Indeed, socioeconomic factors and the availability of continuous health insurance coverage prove substantial hurdles for many young people. HIV-infected adolescents and young adults are less likely to have health insurance than other age groups, more likely to experience poverty than their uninfected counterparts, and are more likely to experience delays in accessing an adult provider due to difficulty navigating an insurance referral system. Young people like Andre may be less likely to access care due to disclosure issues with parental primary health insurance beneficiaries.

Disclosure is particularly problematic given the continued social stigma associated with HIV. Many HIV-infected adolescents and young adults report experiencing rejection, violence, or discrimination. The majority young adults with perinatally-acquired HIV participating in one recent survey have struggled with disclosure of their HIV status in intimate partner relationships. Concerns about stigma and disclosure are prevalent in both perinatally and behaviorally infected youth and among their providers. This often is an important issue underlying delays in transition as pediatric/adolescent HIV care may be perceived as more likely to afford anonymity.

Adult providers should become knowledgeable about the challenges of transitioning and how these pertain to individual patients. They would be well-advised to meet with patients and family members before the change in care, and communicate with pediatric providers, assigning one staff member as a liaison or point of contact.

Adult care settings should have an orientation plan in place, addressing all anticipated needs. McGowan recommends a pre-visit tour of the adult program to become familiar with the physical space and meet the care team before the first visit, when the young person can feel at ease, while also making certain that the entire staff is aware that a transitioning young adult is scheduled for his or her first visit.

He also emphasizes the importance of complete sharing of records from the earliest visits (especially including all resistance tests), and developing an individualized assessment and care plan that includes: health literacy (understanding of the disease process, the role of treatment and need for adherence), beliefs in treatment efficacy, social support, sexual risk behavior, substance use, mental health, housing and economic stability, and linkages to community-based care.

All agree on the importance of close collaboration in ensuring successful transition. Colter expresses the wish that adult care providers understand that, "Patients in transition are anxious to know that the new provider will listen to them, and understand that their lives have been full of challenges, losses, fear of rejection, and multiple other events and emotions that those patients who acquired HIV in adulthood may have never experienced. They have been under their guardians' wings, and are in the midst of achieving their own independence while simultaneously going through the transition process. It is difficult for many to venture out on their own, and difficult for the families to relinquish oversight and participation in their care."

Optimally, the transition plan should be implemented when the youth demonstrates an understanding of the disease and its management, the ability to make and keep appointments, knowledge of when and how to seek medical care for symptoms or emergencies, and is clinically and psychosocially stable.

However, even with attention to detail in managing transitions, the road at first is often bumpy. "Patients, especially perinatally-infected young adults who have been seen within the same setting by the same team of providers, are notorious for crafting ways to procrastinate and delay the final visit with their youth providers," Coulter explains. "Some suddenly develop adherence problems, or report that they need a gynecologic exam, or simply become too busy to show up for repeatedly rescheduled pre-transition visits."

McGowan adds, "There is some fear and frustration. We had one young woman come for a visit and then return to her adolescent program again before she would come back. She felt a bit overwhelmed. Now, she is very comfortable, has a job, has a stable relationship, and is thriving." HIV

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BY CYNTHIA ISTA, RN

The Role of Acupuncture in the Treatment of Symptoms and Substance Abuse in HIV/AIDS Patients

HUMAN IMMUNODEFICIENCY VIRUS (HIV) and Acquired immunodeficiency syndrome (AIDS) carry a heavy burden for patients. From compromised immune systems to a plethora of symptoms related to both the diseases and often resulting from the treatments as well, it can be an overwhelming situation for patients and providers. But acupuncture can offer some relief without adverse side effects.

As you no doubt are aware, acupuncture is a form of Traditional Chinese Medicine (TCM) dating back over 5,000 years. It is an invasive procedure that uses thin solid and sterile disposable needles to access particular points along channels that run throughout the entire body. These channels carry the body's vital energy or "Qi" (pronounced chee).

The practice of acupuncture is performed by Licensed Acupuncturists who complete four to six years of graduate studies, obtaining a master's degree or doctorate. The profession is regulated by state licensing boards (often the same medical boards that license MD's), as well as the National Certification Commission for Acupuncture and Oriental Medicine.

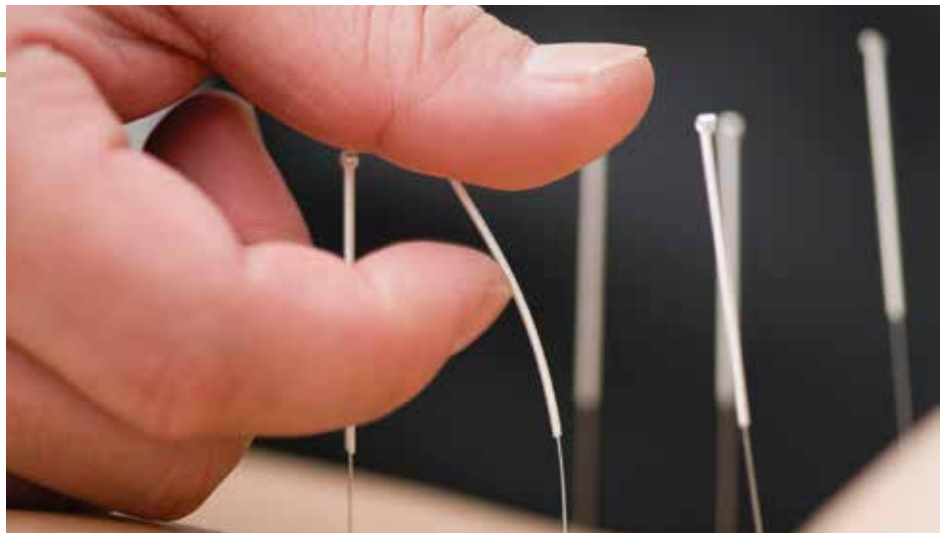
According to TCM Theory, symptoms and illnesses are a result of Qi becoming blocked, deficient, excessive or stagnant. This in turn may affect the Yin and Yang (ways of describing clinical patterns), organs, blood and/or body fluids. These changes can result from injury (i.e. trauma, surgery), nutrition, weather (i.e. heat stroke, cold, damp, dehydration etc.), emotions (stress, psychological issues, anger etc.), and/or heredity factors. When one or more of these events remains in an excessive or deficient state for months to years, the body goes out of balance and symptoms begin to manifest. A healthy person, in contrast, exhibits a balanced state, resulting in a strong immune system that is able to prevent or resist disease.

Practical Applications

TCM offers an individualized approach to diagnosis and treatment of symptoms. The practitioner's in-depth assessment of each client includes diagnosis by looking: assessing the patient's spirit, body, demeanor, head/face, eyes, nose, ears, mouth, lips, teeth, gums, throat, limbs, skin, tongue, and channels. It includes diagnosis by hearing and smelling: listening to the voice, breathing, cough, borborygmi, breath, and body odor. There is also diagnosis by asking: chills, fever, sweating, thorax/abdomen, food/taste, sleep, ears/eyes, thirst/drink, pain, women's/children's issues. Finally, diagnosis includes feeling: palpating pulses, skin, limbs, hands, chest, abdomen and acupoints (Maciocia, 1989).

From this information, patterns and imbalances are identified and treatment using acupuncture, herbs, nutrition, massage, meditation, and/or exercise is implemented.

Why does one person diagnosed with HIV develop AIDS



and another may not? According to TCM, the answer lies within the person's state of health. TCM strengthens the person's internal environment by addressing imbalances. This promotes a coexistence with HIV/AIDS and diminishes or eliminates the impact of debilitating symptoms without adverse effects (Shattuck, 1994).

Acupuncture also is effective in treating emotional issues, such as anxiety, depression, and stress, substance abuse, nausea, poor appetite, diarrhea (Chang & Sommers, 2011 September), headache, fatigue, night sweats, insomnia, neuropathies (Franconi, Manni, Schroder, Marcheti, & and Robinson, 2013), and much more.

Western medical models devote much attention to the disease organism, finding ways to eradicate it. TCM looks for ways to return the person to homeostasis. It is a nice combination, and increasingly we see TCM practitioners working alongside their Western medical counterparts to provide patients with every advantage to improve their quality of life.

Substance Abuse

IV drug use (IVDU) is a major route of transmission of HIV infection and while decreasing substance abuse is difficult, acupuncture has been found to be effective in helping to diminish withdrawal symptoms.

One study of acupuncture and opioid agonist treatment found this combination to be more effective than medication alone and subsequent relapses were lower (Liu, Shi, Epstein, Bao, & Lu, 2009 June).

Additionally, acupuncture may be considered a safe inexpensive way to treat pregnant women exposed to opiates (Janssen, Demorest, Kelly, Thiessen, & Abrahms, 2012). Another study using transcutaneous electrical stimulation on acupoints found it accelerated the production and release of neuropeptides in the central nervous system that interact with different opioid receptors to ease pain and withdrawal symptoms (Meade & Lukas, 2010 January).

The most effective way to help substance abuse patients detox with acupuncture is through community clinics. Janssen et al, 2005, studied the use of acupuncture for substance abuse in 261 individuals in downtown Eastside Vancouver. The area has an estimated 4,000 people with drug addictions in an area of approximately 10 city blocks. Their research indicated 30 percent were infected with HIV and approximately 90 percent were positive for hepatitis C. Reductions in the severity of withdrawal symptoms with acupuncture were statistically significant. These symptoms included a decrease in shakes, stomach cramps, hallucinations, muddle headedness, insomnia, muscle aches, sweats, suicidal thoughts and heart palpitations.

Conclusion

With thorough assessment and diagnosis, TCM provides individualized plans to help restore balance within the person. Acupuncture has demonstrated promising outcomes in the treatment of symptoms related to the diagnosis and Western medical treatments of HIV/AIDS; as well as improving subsequent quality of life issues for this population.. HIV

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