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LITERATURE IN BRIEF

Health Issues in Prisons and Jails: Implications for Urban Health

Hammett TM, Harmon MP, Rhodes W. The burden of infectious disease among inmates of and releasees from US correctional facilities, 1997. *Am J Public Health*. 2002;92:1789–1794.

SUMMARY

This study developed national estimates of the burden of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), hepatitis C, and tuberculosis among correctional inmates and releasees during 1997. Data from surveys, surveillance, and other reports were synthesized to develop these estimates. The authors found that, during 1997, 20%–26% of all people living with HIV in the United States, 29%–43% of all those infected with hepatitis C virus, and 40% of all those who had tuberculosis disease that year passed through a correctional facility. The authors concluded that correctional facilities are critical settings for the efficient delivery of prevention and treatment interventions for infectious diseases. Such interventions stand to benefit not only inmates, their families, and partners, but also the public health of the communities to which the inmates return.

COMMENTARY

Once someone is incarcerated in this country, they join the group of people who are, in the words of Hammett et al., "generally marginalized, despised, and politically impotent." The general public and our political leaders tend to think about our health and our public health without considering the incarcerated population. No matter how imprecise these estimates are, they underscore the extremely large number of individuals (about 12 million) who pass through correctional facilities annually, and that these individuals are at high risk for diseases that are potentially fatal and have tremendous public health implications. Much of this is related to the "war on drugs" as it is drug users who constitute most of the increased number of people incarcerated over the last two decades. These high rates of infectious diseases highlight the tremendous opportunities for public health and medical interventions, including screening, prevention, education, treatment, and linkage, that exist in our current criminal justice system. The challenge is how to capitalize on these opportunities.

HIV/AIDS in correctional settings. *AIDS Educ Prev*. 2002;14(suppl B).

SUMMARY

The number of AIDS-related deaths in US prisons and jails has dramatically declined since 1995 due to newer antiretroviral therapies. However, during the same period, the number

of HIV-infected inmates has continued to rise. The AIDS case rate among US prison inmates is five times that of the US general population. This special supplement emerged from a desire to address the complex problem of HIV/AIDS in correctional settings. The introduction describes multiple causes of this problem, including the criminalization of drug addiction, the concentration of individuals engaging in high-risk behaviors, underutilization of harm reduction interventions, limited availability of HIV prevention services, and the competing priorities of safety and security in the correctional setting. This special issue addressed HIV risk factors, HIV among inmates, prevention and treatment interventions, and public policies. The following paragraphs describe articles included in the issue.

Desai et al. (Desai AA, Latta ET, Spaulding A, Rich JD, Flanigan TP. The importance of routine HIV testing in the incarcerated population: the Rhode Island experience. 45–52) described a decade of experience with routine HIV testing of nearly all inmates in the Rhode Island State Correctional Facility. Approximately one third of all positive tests performed in the state were done in the correctional facility, the single largest testing site in the state. Subgroups, including males, African Americans, and injection drug users, were more likely to be diagnosed in the correctional setting than elsewhere, suggesting possible barriers to health care access for these populations.

Krebs and Simmons (Intraprison HIV transmission: an assessment of whether it occurs, how it occurs, and who is at risk, 53–64) cross-linked health department HIV test results with a database of inmates who had been continuously incarcerated since 1978 in an undisclosed southern state. They documented 33 of the original 5,265 inmates (0.6%) who had contracted HIV inside prison.

May and Williams (Acceptability of condom availability in a US jail, 85–91) surveyed inmates and correctional officers in the Washington, DC, Central Detention Facility, where condoms have been available to inmates for nearly a decade. The authors found that the majority of inmates (55%) and correctional officers (64%) supported the availability of condoms in jail. Condom access was unobtrusive to the jail routine, was no threat to security, and was generally accepted by most inmates and correctional officers, and there was no evidence of an increase in sexual activity. The authors suggested that this model could easily be replicated in other institutions.

COMMENTARY

The United States has only 5% of the world's population, yet as the leading incarcerator, we have over a quarter of the world's prisoners. There are approximately 2 million individuals incarcerated, and 12 million are released annually. These numbers are growing, primarily as a direct result of the war on drugs. This population is composed of a disproportionately increased number of racial, ethnic, and minority groups, many from impoverished environments with limited access to health care or even preventive information. The fact that one third of HIV in the state of Rhode Island was diagnosed in the department of corrections highlights the magnitude the problem as well as the missed opportunities for other states.

The documentation of HIV transmission within prisons is clearly important and not unexpected given the concentration of individuals who are infected and engage in high-risk behaviors in single-sex environments with extremely limited access to injection equipment or condoms. However, the jury is still out as to whether incarceration increases or reduces the underlying risk of HIV infection in this high-risk population. There has been much resistance to initiating condom distribution within prisons; however, the description of the program in the District of Columbia shows that it is good common sense. The problem is more complex than simple condom availability as there exists a range of sexual behaviors, including coerced and forced sex, that may not encourage condom use. Furthermore, it is extremely difficult to document the efficacy of condom availability in correctional settings.

Clearly, examples of interventions that lead to screening, diagnosis, treatment, interventions, and linkage to aftercare are tremendously important for preventing infectious diseases. Furthermore, there are parallel opportunities for mental illness and addiction. Interventions

that improve health and public health can also reduce recidivism. In the words of Rapposelli et al. in the *AIDS Education and Prevention* supplement (pp. 103–113), "Continuity of health care is critically important in breaking the cycle of crime, addiction, disease transmission, and recidivism."

National Commission on Correctional Health Care. The health status of soon-to-be-released inmates. Vols. 1 and 2. Available at: www.ncchc.org/pubs_stbr.vol1.html.

SUMMARY

This congressional report by the National Commission on Correctional Health Care describes many of the issues noted in the reviews above, including the increased prevalence of communicable disease, chronic disease, and mental illness among the inmate population. The report highlights the unique opportunities for public health with improved correctional health care and concludes with a description of the barriers to optimal health care and policy recommendations. These recommendations include improved surveillance, utilization of clinical guidelines, immunizations, elimination of barriers to health care, improved correctional health care research, and delivery of care, disease prevention, and prerelease planning.

COMMENTARY

This impressive detailed description of the tremendous opportunities for improved public health in the correctional setting has unfortunately received very little coverage in the lay press. Implementation of the policy recommendations of this report would undoubtedly lead to improved health, improved public health, and probably cost savings. Practitioners in the medical field, public health, and the community should be aware of this report and encourage politicians to follow these policy recommendations for the good of all.

Josiah D. Rich

Child and Adolescent Health Reviews

Powell EC, Tanz RR. Adjusting our view of injury risk: the burden of nonfatal injuries in infancy. *Pediatrics*. 2002;110:792–796.

SUMMARY

To describe the incidence, external cause, and types of nonfatal injuries among infants (younger than 1 year old) treated in US emergency departments (EDs), the authors obtained and analyzed data from the ED component of the National Center for Health Statistics (NCHS) National Hospital Ambulatory Medical Care Survey for 1992–1999. They also used statistics from the National Center for Health Statistics to compare nonfatal injuries to fatal injuries. The estimated rate of injuries was 108.2 per 1,000 infant years; of those injured, about 6% were admitted to the hospital. The mean age was about 7 months. Falls were the cause of almost one third of the injuries (rate 35.1 per 1,000); injuries in the "struck by/against" category were the next most frequent, with 14.2 per 1,000. The motor vehicle traffic injury rate was 8.8 per 1,000, followed in descending frequency by injuries from foreign bodies, cuts, burns, poisonings, and bites or stings. Total injury fatality rate for this age group was 21.3 per 100,000, led by suffocation (mechanical or by food or object inhalation) at 9.6 per 100,000. The ratio of nonfatal falls to fatal falls was 8,789 to 1; for motor vehicle traffic injuries, the ratio was 197 to 1; and for poisonings, it was 1,271 to 1.

COMMENTARY

The need for more and better data on nonfatal injuries in children has long been recognized. This article helps fill that gap. In particular, it calls to our attention that, when 10 of every 100 infants visit an emergency room for an injury, we cannot assume that even babes are safe in their mothers' arms. We should also note that the causes of the babies' injuries are not the same as for their older siblings, and prevention will call for differing interventions.

Although it is well known that, in every category of childhood injury, the nonfatal injuries vastly exceed fatal ones, the variation in the ratios reported here is a matter of additional interest. Because the most frequent causes of fatal injury are different from those for nonfatal injury, interventions directed to prevention of fatalities may have little effect on improving overall rates of nonfatal injuries. In addition, the actual numbers for fatalities in all categories are quite low, and the tendency to focus resources on preventing fatalities, while understandable, may dilute efforts to deal with the massive problem of nonfatal injuries.

Gotsch K, Annest JL, Holmgreen P, Gilchrist J. Nonfatal choking-related episodes among children—United States, 2001. *MMWR Morb Mortal Wkly Rep*. 2002;51:945–948.

SUMMARY

The source of data for this report was the National Electronic Injury Surveillance System—All Injury Program (NEISS-AIP), which is operated by the US Consumer Product Safety Commission and collects data on initial visits for all types and causes of injuries treated in US EDs from a nationally representative subsample of 66 hospitals. In 2001, children aged 14 years or younger were treated in EDs for choking-related episodes at a rate of 29.9 per 100,000 population. Infants aged younger than 1 year had the highest rates: 140.4 per 100,000. About 10% of all children injured were hospitalized. Of the children, 59.5% were

treated for choking on a food substance, which was candy or gum in 19.0% of all cases. Coins were responsible for 12.7% of episodes. The ratio of nonfatal choking-related episodes to fatal ones was approximately 110 to 1. In 2000, there were 160 children nationally who died from obstruction of the respiratory tract associated with inhaled or ingested foreign bodies. It was recommended that "parents and caregivers should be aware of the types of foods and objects that pose a choking risk for children, become familiar with methods to reduce this risk, and be able to treat choking in children" (p 945).

COMMENTARY

Gotsch et al. provided an example of a relatively infrequent cause of injury, even in those younger than 1 year old. If the rate is calculated to compare with the rates in the first article summarized, choking would be 1.4 per 1,000 compared to 108.2 per 1,000 for all injury causes in infants. With literally dozens of injury causes competing for attention, the situation brings to mind the problem faced in the development of the Healthy People 2010 objectives: 28 focus areas and 467 separate objectives for the nation had the potential for canceling out each other. A solution was to choose "10 leading indicators" from among them. Perhaps we need 10 leading indicators for childhood injury prevention.

That said, it must be acknowledged that the recommended approaches for choking-related injuries (which would probably not make the top 10) are relatively low intensity and for the most part fit fairly easily into general age-specific injury prevention counseling for parents. Teaching all parents and caretakers the Heimlich maneuver for infants is a more challenging initiative and would need to be weighed more carefully.

The relatively recent availability of data from NEISS-AIP promises to broaden and deepen our knowledge of the epidemiology of nonfatal injuries. The gradually spreading use of E codes (i.e., external cause codes) for nonfatal injuries, for emergency department visits, and for hospital discharges is another important development. Improved data will lead to better design and targeting of interventions and ultimately lower injury rates, to the benefit of children, families, and society.

Bishai D, McCauley J, Trifiletti LB, et al. The burden of injury in preschool children in an urban Medicaid managed care organization. *Ambul Pediatr*. 2002;2:279–283.

SUMMARY

This study reviewed all medical claims submitted to a Medicaid managed-care organization (MCO) for 1,732 children aged six years or younger in urban Baltimore, Maryland, between July 1997 and August 1999. *ICD-9* (*International Classification of Diseases, 9th Edition*) codes for burn, poisoning, choking, and blunt/penetrating injuries were identified as were E codes for ED or inpatient claims; E codes were assigned to related outpatient records. Altogether, 796 injuries were recognized, for a rate of 36.5% per year. The median age was 38 months; 92% were African American. The most common causes were falls, being struck by something, and cutting/piercing (68% of all causes). The injury rate for this population was nearly twice the national average. Cost to the MCO for care of these injuries was $396 per covered person-year, which represented 42%–55% of the local capitated rate.

COMMENTARY

Although economic analyses of the burden of injuries are plentiful, this may be the first study that relates the cost of injury per covered child to the capitation rate in managed care. The finding that injury costs for children accounted for almost half the capitation income

they generated in one MCO serving inner-city children should motivate other MCOs to undertake this kind of analysis. If their results are similar, self-interest alone would dictate giving more emphasis to cost-effective injury prevention strategies. This is one situation for which the operation of managed care might conform to the original concept of "health maintenance."

The data presented in this paper remind us yet again of the problem of health disparities, of which injuries unfortunately are no exception. Another point noted by the authors is the lack of E code use in outpatient claims—one more gap in data collection for nonfatal injuries. Variation by age group for causes of injury is another important consideration in data collection and analysis. This relatively small series, of necessity, lumps together its entire sample of children to 6 years old. But other authors (Agran PF, Winn D, Anderson C, Trent R, Walton-Haynes L). Rates of pediatric and adolescent injuries by year of age, *Pediatrics*, 2001;108. Available at: www.pediatrics.org/cgi/content/full/108/3/e45) have convincingly suggested that the age of highest risk for various causes of injury will not be recognized if conventional age groupings are used; consequently, the opportunity for appropriate interventions specific to the year of age may be missed.

Pollack H, Frohna J. Infant sleep placement after the Back to Sleep campaign. *Pediatrics*. 2002;109:608–613.

FOLLOW-UP NOTE

Last quarter's Child and Adolescent Health Reviews summarized the article by Pollack and Frohna, which showed significant disparities for African Americans in percentage of infants put to sleep in the prone position. A recent case-control study of sudden infant death syndrome (SIDS) in a predominantly African American population (Hauck FR, Moore CM, Herman HM, et al. The contribution of prone sleeping position to the racial disparity in sudden infant death syndrome: the Chicago infant mortality study. *Pediatrics*. 2002;110: 772–780) shows the higher rates of SIDS among blacks in Chicago were partly explained by prone sleeping position and the fact that mothers of SIDS infants were significantly less often advised by health providers about how to position the infant for sleep than were controls. For African American mothers, both cases and controls, 25% reported being told to use the prone position compared to 7% of those who were not African Americans. Over 94% of all mothers reported following medical advice. Clearly, the need for further diffusion of information about preferred infant sleep position applies especially to medical personnel who care for African American mothers and infants.

Katherine S. Lobach

HIV/AIDS Reviews

Nelson M, Portsmouth S, Stebbing J, et al. An open-label study of tenofovir in HIV-1 and hepatitis B virus co-infected individuals. *AIDS*. 2003;17:F7–F10.

SUMMARY

Although the antiretroviral activity of the nucleotide analogue tenofovir is now well documented, in preliminary studies the drug has also been shown to have activity against the hepatitis B virus (HBV). In this comparatively small, proof-of-principle trial, the investigators sought to examine the specific activity of tenofovir against HBV infection in patients also co-infected with human immunodeficiency virus (HIV). They chose to study 20 co-infected patients (median age 43 years) who were already receiving various combinations of standard-of-care antiretroviral medications for HIV, 15 of whom were also 3TC (lamivudine) experienced for a median period of 138 weeks. Of the 15 patients with 3TC treatment experience, 11 had HBV mutations at baseline known to be associated with significant 3TC resistance. All 20 participants had evidence of active HBV infection, as demonstrated by HBeAg (hepatitis B e antigen) positivity; the majority also had measurable HBV viral loads at a median baseline level of 181.5 million genome equivalents (Geq) per milliliter.

After the first 24 weeks of daily treatment with tenofovir at a dose of 245 mg orally, a median 4-log reduction in HBV viral load was observed. During this time, there was also a median decrease in serum ALT (alanine aminotransferase) from a baseline level of 96 IU/mL to a level of 43 IU/mL; 46% of patients actually experienced normalization of their ALT levels during this time. Whereas only 5 of 20 patients had an undetectable HBV viral load at week 4, by week 52 this number had risen to 13 of 20. Of note, 2 patients had seroconverted to hepatitis B e antibody positivity by week 24; by week 52, this number had risen to 5, including 3 patients who had evidence of 3TC resistance at baseline. In fact, the slope of decline in HBV viral load appeared to be more rapid in those individuals with baseline evidence of 3TC resistance than it did in those without baseline mutations. The median HIV viral load remained below 50 copies/mL throughout the trial.

COMMENTARY

Until recently, the approved therapies for HBV infection, with or without HIV co-infection, consisted primarily of either daily oral 3TC or subcutaneous treatment with various preparations of recombinant interferon-α. Whereas oral 3TC is generally a well-tolerated drug with very few serious systemic side effects, viral resistance to this agent may develop in many recipients after extended use, principally through emergence of the YMDD mutation in the gene for the HBV DNA polymerase. Interferon-α treatment, in contrast, is associated with a variety of constitutional side effects and the inconvenience of parenteral administration, although tachyphylaxis to the major side effects often develops after a number of weeks of continued therapy. The advent of pegylated interferon-α products, with their enhanced pharmacokinetic properties, appears to have significantly improved the clinical treatment of chronic hepatitis C infection, but whether similar benefits will extend to their potential utility in treating patients with chronic HBV remains to be established.

Adefovir dipivoxil, a nucleotide analogue chemically related to tenofovir, was recently approved in the United States for the treatment of chronic hepatitis B infection when administered at a daily oral dose of 10 mg. At higher doses (generally 60–120 mg per day), this agent also has significant antiretroviral activity, but previously was rejected as a candidate for Food and Drug Administration approval because of a disturbing incidence of significant renal toxicity in earlier trials. Studies evaluating its role in the treatment of HBV in HIV co-infected patients are currently under way, and the preliminary results appear promising. However, at the licensed dose for treating HBV, it has little, if any, antiretroviral activity,

and there remains the obvious concern that its use could engender rapid development of HIV resistance to other agents in its class.

Tenofovir, in contrast, retains potent antiretroviral activity at the usual oral daily dose (generally 300 mg instead of the 245 mg used in this study) and, as this study suggested, may also have substantial anti-HBV activity at the same time with minimal toxicity. If these preliminary findings are validated in larger and longer term trials, they suggest that tenofovir could easily become a preferred agent for the dual treatment of HBV and HIV co-infected patients. However, a usual caveat applies to these considerations: only with longer follow-up will we gain a better sense of whether HBV can develop clinical resistance to the effects of either adefovir dipivoxil or tenofovir after extended therapy.

Gerard L, Galicier L, Boulanger E, et al. Improved survival in HIV-related Hodgkin's lymphoma since the introduction of highly active antiretroviral therapy. *AIDS*. 2003;17: 81–87.

SUMMARY

In this retrospective analysis conducted at a single institution in France, the authors attempted to evaluate the possible effects of the introduction of highly active antiretroviral therapy (HAART) on the long-term survival of HIV-infected patients who developed Hodgkin's lymphoma (HL). They surveyed their institution's experience with histologically proven cases of HL in HIV-infected patients who presented between early 1987 and late 2001. They defined HAART as combination antiretroviral therapy that included a protease inhibitor and/or an NNRTI. Based on the known dates of availability of HAART in France, they categorized their patients as presenting either in the pre-HAART era (1987–1996) or the post-HAART era (1997–2001). HL chemotherapy was not standardized per se, but generally involved conventional regimens (with or without radiotherapy) consisting of MOPP, ABVD, MOPP/ABV, or CHOP.

Of 108 patients presenting with HL, 61 were diagnosed in the pre-HAART era and 47 in the post-HAART era. While other baseline characteristics were generally similar between the two periods, patients in the post-HAART era had a statistically significant longer duration (median of 8 years versus 3 years) of HIV infection and a longer duration of antiretroviral treatment (median of 36 months versus 13 months) before the diagnosis of HL. No significant differences were noted between the two eras in terms of the distribution of HL histology, staging, sites of extranodal involvement, presence of B symptoms, or marrow function. The chemotherapy regimens also did not differ significantly between the two periods, although ABVD usage declined over time. Patients with earlier disease (stages I–III) had a higher complete response (CR) rate in the post-HAART era than did pre-HAART recipients, whereas those with advanced (stage IV) disease fared similarly between the two eras. Of 73 patients achieving a CR, 16 of 38 pre-HAART patients and 6 of 35 post-HAART patients had relapsed at median times of 10.2 months and 10.5 months, respectively. The 2-year cumulative probability of disease-free survival increased from 60.5% to 78.7% between the two eras. Largely due to a decrease in deaths associated with acquired immunodeficiency syndrome (AIDS) rather than HL-related deaths, the overall probability of prolonged survival increased over the years: the median survival time was 19 months in the pre-HAART period versus an undefined (i.e., not yet reached) median in the post-HAART period.

During the overall study period, 42 patients were receiving HAART (commencing either before or concomitant with their treatment for HL), and 66 were not. Whereas the CR rate did not differ statistically between the two groups, those on HAART had a higher probability of prolonged survival than those not receiving HAART: a median not yet reached versus a median of 20 months, respectively. In those patients achieving a CR, the disease-

free survival was also significantly longer in those on HAART versus those not receiving HAART.

COMMENTARY

Despite dramatic decreases in death and the incidence of AIDS-defining events for which the advent of HAART is responsible, there is little evidence that these medications have had a favorable impact on the occurrence of lymphomas of various types in HIV-infected patients. Indeed, as a relative percentage of AIDS-associated deaths in the developed world, the impact of lymphoma has likely increased as the incidence of other, more preventable or treatable conditions has declined over time. In this retrospective analysis by a group at the Hôpital Saint-Louis in Paris, patients continued to present with histologically confirmed Hodgkin's lymphoma despite the use of HAART and the ability in many cases to achieve effective viral suppression with these drugs. However, although neither the histologic subtypes of the HL nor the use of various combination chemotherapy regimens against HL appeared to change substantially over the past 15 years, the survival of HIV-infected patients diagnosed with HL nonetheless improved significantly in the "post-HAART" (perhaps more aptly titled the "peri-HAART") period. Not surprisingly, this improved survival did not appear to be due to major improvements in the chemotherapeutic response of HL or a decline in HL-related deaths, but rather was associated with a significant decrease in the incidence of other AIDS-associated deaths. In other words, HAART appeared to prevent patients from succumbing to other opportunistic conditions either while their HL was being successfully treated or during the posttreatment period. That it did so with little apparent treatment-limiting toxicity argues strongly against the once-conventional notion of interrupting HAART while intensive combination chemotherapy against HL is being pursued. Especially in an era when several supportive or adjunctive medications to reduce marrow toxicity, such as the various colony-stimulating factors, are now readily available, this approach would seem even more compelling. Similar findings are also emerging from studies of the treatment of non-Hodgkin's lymphoma afflicting HIV-infected patients.

Joly V, Flandre P, Meiffredy V, et al. Increased risk of lipoatrophy under stavudine in HIV-1-infected patients: results of a substudy from a comparative trial. *AIDS*. 2002;16: 2447–2454.

SUMMARY

In a randomized, open-label, multicenter trial called NOVAVIR, investigators evaluated the comparative safety and efficacy of zidovudine (ZDV) versus stavudine (D4T) when administered in combination with lamivudine (3TC) and indinavir. In this article by Joly et al., they examined specifically the comparative effects of either zidovudine or stavudine on the incidence and type of lipodystrophy seen in these HAART-treated patients. Patients pretreated with nucleoside analogues, but naive to lamivudine, stavudine, and protease inhibitors, were randomly assigned to receive either ZDV/3TC/indinavir or D4T/3TC/indinavir at the conventional licensed doses for an extended observational period totaling 30 months. At the end of 30 months, the patients were evaluated cross-sectionally for the signs and symptoms of lipodystrophy.

Of 170 originally enrolled, 101 patients were evaluated for lipodystrophy at month 30; these patients were 47 D4T recipients and 54 ZDV recipients. The baseline characteristics did not differ between the two groups, and by month 30, viral suppression to less than 500 copies/mL was achieved by 76% and 78% of patients in the D4T and ZDV arms, respectively. The median CD4 cell counts at month 30 had risen to above 500 cells/μL in both

groups. At this evaluation, there were no significant differences between the two arms in fasting cholesterol, triglyceride, or glucose levels. However, more patients (7 versus 1) in the D4T arm were receiving lipid-lowering agents than in the ZDV arm. In assessing body shape changes, the investigators labeled 23 patients with lipoatrophy alone, 11 with lipohypertrophy, and 33 with mixed lipodystrophy. There was no difference in the proportion of patients having signs of central adiposity (i.e., buffalo neck or increased neck size, increased breast size, increased abdominal girth or thickness). However, more D4T than ZDV recipients had evidence of peripheral fat loss, such as facial atrophy (48% versus 22%, respectively), lower limb atrophy (49% versus 22%, respectively), buttock atrophy (47% versus 20%, respectively), or venomegaly (57% versus 24%, respectively). Only 30% of D4T recipients did not manifest clinical signs of lipoatrophy, compared with 57% of ZDV recipients. By multivariate analyses, older age and female gender were independently associated with a higher risk of lipohypertrophy, whereas use of D4T, prior exposure to didanosine, and lower CD4 cell count at study entry were independently associated with a greater risk of developing lipoatrophy.

COMMENTARY

Several studies, including this one, have suggested that the risk of developing clinical signs of lipodystrophy while on HAART cannot always be attributed to the use of protease inhibitors alone. Previous studies have implicated D4T in particular as one of the agents most likely to be associated with a higher risk of peripheral fat depletion, or lipoatrophy, in long-term recipients. In this substudy of a larger trial comparing the efficacy of ZDV versus D4T in nucleoside-experienced patients, the investigators were able to demonstrate simple, but clear, differences in the incidence of central fat accumulation versus peripheral and facial fat loss despite the ongoing absence of a universally recognized or consensus definition of what constitutes the HAART-associated "lipodystrophy syndrome."

As suspected from earlier trials, incorporation of D4T into HAART regimens is associated with a significant increase in the risk of developing substantial body fat changes involving the face and extremities; this can be cosmetically disfiguring. While D4T may generally be better tolerated than ZDV in terms of acute or short-term side effects, these data add to the growing list of potential toxicities associated with long-term exposure to the so-called (D) drugs (ddI and D4T) within the broader category of nucleoside analogues. The effects of these altered fat patterns on self-image and quality of life can be substantial and are not always readily reversible by switching to other agents. Newer antiretroviral drugs of equal or greater potency but lacking this serious drawback continue to be needed.

Richard T. Davey Jr.

Bovine Spongiform Encephalopathy Becomes More Complicated

Asante EA, Linehan JM, Desbruslais M, et al. BSE prions propagate as either variant CJD-like or sporadic CJD-like prior strains in transgenic mice expressing human prion protein. *EMBO J.* 2002;21:6358–6366.

SUMMARY

The human form of bovine spongiform encephalopathy (BSE; "mad cow disease") is designated variant Creutzfeld-Jakob disease (vCJD) and is considered biologically and epidemiologically distinct from the classical "sporadic" CJD that has been described for almost 100 years. Transgenic mice have been produced that allow better examination of the nature of the species barrier, if any, between the disease of livestock and human disease, a question of paramount importance in assessing the risks not only from beef, but also from sheep, deer, swine, and other animals used for food by humans. This article reported results from experiments that passed BSE and vCJD material into susceptible transgenic mice. As expected, both BSE and vCJD succeeded in infecting the mice with prion proteins typical of vCJD, but surprisingly, BSE inoculation also produced prions typical of classical CJD, raising the possibility that current methods of distinguishing BSE from sporadic (non-BSE) disease is problematic, and that more than one foodborne prion strain might infect humans, a new finding.

COMMENTARY

Intensive study of the biology of BSE and its relation to human vCJD has been conducted for more than a decade, and while much progress has been made, unpleasant surprises are still to be expected. This article presented one of these surprising and worrisome turns of events. To date, only one type of aberrant foodborne prion protein (the type 4 strain) had been shown to infect humans, and infection with that type has been considered characteristic of CJD acquired from eating beef. This article holds out the possibility that some cases thought to be of sporadic CJD might actually be foodborne. Clearly, the question of species barriers, what causes them, and under what conditions they are breached has a bearing on the integrity of the food supply. Given the uncertainties, any complacency about the safety of the US food supply with respect to spongiform encephalopathy is unwarranted.

Health in the Big City

Frumkin H. Urban sprawl and public health. *Public Health Rep.* 2002;117:201–217.

SUMMARY

The development of efficient modes of transportation, especially the automobile with its publicly financed highway network, has made it possible for people to live at some distance from where they work in the urban center and, in many instances, has produced miniurban satellite centers to service the new residential neighborhoods. The result is the familiar phenomenon of *urban sprawl*, the extension of the urban to the suburban areas, where now one of every two Americans lives. This extension, crossing as it does city and town boundaries and sometimes even state and national borders, has occurred with little or no planning and has produced complicated patterns of land use, economic development, and social arrangements. Along with this have come public health consequences, from air pollution, motor

vehicle injury, violence, urban heat islands, and many others, including the physical, psychological, and social consequences of a more sedentary lifestyle.

In this wide-ranging survey, the author aimed to reclaim urban design as a public health problem, presenting a framework for public health professionals to use and encouraging them to weigh in on problems of urban design and development. The author noted that many of the health burdens fall unequally on the population, with the poorest and most vulnerable once again bearing the brunt.

COMMENTARY

It is heartening to see a reawakening of interest in the "built environment" as a major factor influencing the health and well-being of the community. It is no coincidence that the author is Professor of Environmental and Occupational Health at the Emory School of Public Health in Atlanta, Georgia, a city exhibiting one of the most spectacular and egregious examples of urban sprawl in the United States. In one of its dimensions, for example, Atlanta measures 115 miles across. Our understanding of the complicated way urban design affects health is still primitive, but there are enough obvious examples (such as urban heat islands and motor vehicle pollution) to show that it is not trivial. The new awareness of the dramatic prevalence of obesity in this country will further focus attention on those factors in urban design that act to increase this problem. This is an article worth reading and pondering.

Chronic Carbon Monoxide

Devine SA, Kirkley SM, Palumbo CL, White RF. MRI and neuropsychological correlates of carbon monoxide exposure: a case report. *Environ Health Perspect.* 2002;110:1051–1055.

SUMMARY

This is a case report of a 45-year-old, white, college-educated woman referred by her neurologist after a reported 1-year chronic exposure to carbon monoxide in a restaurant kitchen. The patient had exhibited changes in behavior and cognition prior to the discovery of a leak that was then repaired by the gas utility. The utility confirmed "high" (unspecified) levels of carbon monoxide in her workplace. Exposure ceased from that point.

The patient's carboxyhemoglobin levels 5 days after repair of the leak were reported to be normal. She had been complaining of symptoms for at least a year, and communications with the insurance company were consistent with this length of exposure. She reported flu-like symptoms, problems with balance, headaches, exhaustion, problems with mentation and speaking, paresthesias in both thighs, and pain in her face, among other diverse symptoms. Most symptoms resolved after exposure ceased, with the exception of some residual problems in reading, writing, and speaking. Routine magnetic resonance imaging (MRI) and neurological exam were reported as normal, but follow-up neuropsychological testing revealed evidence consistent with mild frontal or subcortical dysfunction and blind review of the MRI by neuroimaging specialists identified multiple bilateral lesions in the basal ganglia.

COMMENTARY

Exposure to carbon monoxide, a product of incomplete combustion, is ubiquitous, but usually is not severe enough to be clinically significant. However, faulty heating systems or exposure to internal combustion engines in enclosed spaces can produce fatal exposures that usually make the evening news. This case report reminds us that chronic exposures to lower

levels can also be of clinical importance, and the nonspecificity of the symptoms means such exposures may go unrecognized. This case report contains a valuable review of the literature on chronic carbon monoxide poisoning and notes that symptoms can often be episodic, with asymptomatic periods punctuated by symptomatic ones. Often, symptoms of acute exposures are delayed. Blood carboxyhemoglobin, because of its short half-life (4–5 hours in room air), may not be helpful in diagnosis. Brain MRI and neuropsychological testing may be useful, but are similarly nonspecific, and the small lesions on MRI may easily be overlooked.

Chronic carbon monoxide poisoning remains a diagnostic problem with a true prevalence that is unknown. Like many other conditions, the essential element in diagnosis is to consider it in the differential and then to apply a variety of diagnostic modalities with full understanding of their limitations. This article contains many valuable references that would be helpful in working up such a suspected case.

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