August 20, 1998

The Division of STD Prevention has initiated a systematic assessment of the need and feasibility of prevention programs for the viral STDs other than HIV, notably genital herpes and human papillomavirus infection. Enclosed is the report of an external consultants meeting on prevention of genital herpes that was held May 5-6, 1998. The document presents the recommendations of the meeting participants to CDC, not the policy or recommendations of the Division of STD Prevention, or the Center for HIV, STD and TB Prevention, or CDC.

There were a few recommendations for specific prevention activities that CDC was encouraged to implement as soon as practical. These include:

- A campaign to better educate health care providers and the public about genital herpes and its prevention.
- Recommend to health care providers and public health agencies that any serological testing for herpes simplex virus (HSV) infection should employ type-specific assays.
- Promote standards of care that type-specific HSV serological tests should be available to providers and clinics that manage patients with genital herpes or at risk, and that patients should be informed if routine STD evaluation does not include laboratory assessment for HSV.
- Develop guidelines to prevent herpes-related cesarean sections.
- Some consultants advised that CDC recommend that all HIV-infected persons be evaluated for genital herpes, including type-specific serology, but others disagreed.

The main recommendations were for demonstration projects, behavioral and operational research, and other program development activities to inform future strategies to prevent sexual transmission of HSV, neonatal herpes, and herpes-related HIV transmission. Selected topics for these activities include:

- The “real world” performance of the newer type-specific HSV serological tests.
- The psychological and behavioral impact of HSV serological testing on asymptomatic persons.
- Partner management strategies and related behavioral issues.
- The use-effectiveness of antiviral therapy to prevent sexual transmission of HSV.
- Sentinel surveillance for genital and neonatal herpes.
- Strategies to prevent neonatal herpes, including the roles of serological screening, partner management, and antiviral therapy.
- Mathematical modeling of HSV transmission and trends.
- The indirect and intangible costs of genital herpes.

- The effect of antiherpetic chemotherapy on HIV viral load and efficacy in preventing transmission of HIV.

It is not clear that prevention of genital herpes or HPV infection should unfold on a scale or in the style of our prevention programs for the bacterial STDs or HIV/AIDS. Rather, this report and the activities that will stem from it are merely the first steps in a process that will evolve over several years as we critically assess various prevention strategies.

REPORT OF THE GENITAL HERPES PREVENTION CONSULTANTS MEETING

MAY 5-6, 1998

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July 30, 1998

Introduction

Although genital or anorectal infection with herpes simplex virus (HSV) is one of the three most common STDs in the United States (with chlamydial infection and human papillomavirus infection), neither DSTDP nor CDC has established programs or recommendations for the prevention of genital herpes aside from those embodied in the STD Treatment Guidelines. New opportunities that enhance the perceived need and prospects for genital herpes prevention strategies include the rising national prevalence of HSV-2 infection, with 22% of the population $\geq$12 years old infected in the early 1990s; expanding knowledge about the importance of genital herpes in facilitating sexual transmission of HIV and perhaps in exacerbating the progression of HIV disease; the anticipated widespread availability of type-specific serological tests which may be useful for diagnosis, counseling, surveillance, or screening; evidence that antiviral therapy can prevent subclinical shedding of HSV, raising the possibility that chemotherapy may prevent transmission; promising developments in anti-HSV-2 vaccine research; the medical community's and the public's continued and perhaps increasing expectations for prevention recommendations; and improving control of the bacterial STDs, which may create opportunities to address the viral STDs.

Accordingly, DSTDP has initiated activities that will lead to a program and research agenda to address prevention of genital herpes. To this end, 25 external consultants and 21 CDC participants (Appendix 1) met May 5-6, 1998. The meeting was organized around three breakout groups, each of which included experts in genital herpes and the biology of HSV, general STD, epidemiology and surveillance, behavioral science, mathematical modeling, health education, and STD program development and implementation. The three groups focused on five core issues (Appendix 2): Group A addressed 1) the performance and uses of HSV type-specific serological tests; group B discussed 2) the magnitude and burden of genital herpes and 3) prevention of neonatal herpes; and group C addressed 4) prevention of sexual transmission of HSV and 5) interactions between genital herpes and HIV infection. This report is organized around these five core areas, plus two topics that emerged during the meeting: 6) public and provider awareness and knowledge concerning genital herpes and 7) vaccination issues. The discussions from all three breakout groups as well as the plenary sessions are incorporated into each of these sections.

Specific recommendations are denoted with unnumbered bullets. Within each section or subsection, recommendations for actual prevention activities that should be instituted in the near future are listed first and the bullets are diamond-shaped. Other (round) bullets are recommendations for operational research or other program development activities.

1. Performance and Uses of Type-Specific HSV Serological Tests

Clinical recognition and diagnosis of genital herpes are insensitive due to the frequency of subclinical infection and the insensitivity of virologic testing, especially for healing lesions, and the inability of heretofore widely available serological tests for HSV to differentiate the serological responses to HSV-1 and HSV-2. Several truly type-specific serological tests have been developed, most based on antibody to HSV glycoproteins G1 and G2, which have antigenic specificities to HSV-1 and HSV-2, respectively. Type-specific assays have been available in research settings for about 15 years, but only recently have tests been developed for the commercial market.

A. Availability and Cost

Selected tests currently available in research and commercial settings are listed in Appendix 3. The Western blot has been offered commercially and is widely accepted as the most accurate overall assay but is too cumbersome and expensive for routine use ($95 at the University of Washington), although it is likely to retain a role as a confirmatory assay. The HSV gG type-specific ELISA (Gull Laboratories) and the POCkit-HSV-2 test (Diagnology) are in late stages of clinical testing and are likely to be commercially available in the near future. Their costs are uncertain, but the cost of materials and labor to perform them are likely to be in the range of $8.00 to $40.00 per assay. A few other tests are in various stages of commercial development, whereas others are likely to be available only on a limited basis as research tools.

B. Performance

The Western blot detects antibodies to a large number of HSV antigens and has been shown to have both sensitivity and specificity >99% for symptomatic infections established ≥6 months.* Most other assays detect antibody to single antigens and compared to Western blot are at present less sensitive and/or less specific (Appendix 3). All assays have variable and relatively low sensitivities for infection <6 months' duration.

Substantial discussion addressed the newer tests' specificity, approximating 97-99% compared with Western blot, which has important implications for the use and interpretation of test results in individual patients. For example, in a population with 10% prevalence (as might be expected in some screening settings, such as teen clinics) a test with 95% sensitivity and 98% specificity has a positive predictive value (PPV) of 84%, corresponding to an unacceptable 16% rate of false positive results. Thus, serious concerns were raised about the utility of the newer assays as single tests for screening. A possible approach would be to use a sequential testing scheme, with re-testing all positives with a second assay, a strategy that probably would substantially increase for the cost of screening programs. However, in a population with a 50% prevalence rate the PPV rises to 98%, which may be acceptable for some uses, such as diagnosis of genital ulcer disease or evaluating the sex partners of persons with genital herpes.

Although concerns have been raised that some infected persons may lose antibody to HSV-2 over time ("seroreversion"), there was consensus that this phenomenon is due not to loss of antibody but to a lower sensitivity of antibody detection for some assays, which are operating at or near their limits of detection. However, no studies have determined the natural course of seroreactivity in persons with longstanding subclinical infection or in never-symptomatic infected persons.

There was broad consensus that type-specific serological tests for HSV are useful in the diagnosis of genital ulcer disease (e.g., for patients with recurrent genital lesions in whom viral isolation is impractical or unsuccessful) and for counseling, and that all clinicians who

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* All performance figures are for detection of antibody to HSV-2

manage patients with STD or at risk should have access to such assays when they become generally available at reasonable cost. Nevertheless, several unknowns must be resolved before the full scope of serological testing is known and its role in genital herpes prevention fully defined. These include the "real world" performance of the newer assays, outside research settings; performance of all assays in chronic, subclinical infection, including the natural history of seroreactivity in subclinically infected persons; and the psychological and behavioral responses to being informed of a reactive test, especially in persons with neither clinical nor epidemiologic histories to suggest genital herpes. It was recognized that many patients seeking STD clinical services assume that evaluation routinely includes assessment for all common STDs, including herpes, but that almost no STD clinics and few other providers of STD clinical services routinely offer this service. However, quantitative data are lacking.

C. Recommendations

1) *Test performance*

- ♦ CDC should more assertively publicize the fact that most HSV serological tests now on the market are not truly type-specific, despite frequent claims to the contrary, and are not useful in diagnosing or screening for genital herpes infection; and that if serological testing is to be used in managing patients with or at risk for genital herpes, type-specific tests should be used **(consensus high, priority high)**.
- CDC should undertake or support studies of "real world" performance of the newer type-specific assays, including studies of the need for confirmatory tests in various settings and the appropriate confirmatory tests to use **(consensus high, priority high)**

2) *Use of HSV type-specific serological tests*

- CDC should conduct or support formative research in a variety of populations and among health care providers to explore the acceptability of serologic testing, responses to test results, content of counseling messages based on the test results, and how to deliver those messages **(consensus high, priority high)**

3) *Serological diagnosis of genital ulcer disease*

- Studies of type-specific serological tests should include assessment of test performance in the diagnosis of genital ulcer disease **(consensus high, priority high)**

4) *Pregnant women*

- CDC should conduct or support demonstration projects that involve serological screening of pregnant women, and perhaps their sex partners, to assess strategies to prevent both neonatal herpes and unnecessary cesarean sections attributable to maternal genital herpes (Section 3, below).

5) *Genital herpes-discordant couples*

- CDC should undertake or support demonstration projects to assess the willingness of partners to know their infection status, the psychological impact of testing, effects on behavior change, effects on relationships, and comparative utility of serological vs clinical/virologic diagnosis of index patients and their partners **(high consensus, high priority)**.

6) *STD clinic populations and patients seeking STD clinical services*

- ♦ CDC should promote standards of care in STD clinics and other facilities where STD services are routinely provided which stipulate that patients should be informed if genital herpes assessment is not included in the clinical evaluation **(consensus high, priority not stated)**.
- ♦ CDC should promote standards of care in STD clinics and other facilities where STD services are routinely provided which stipulate that, at a minimum, type-specific serological tests should be available to patients on request **(consensus high, priority not stated)**.
- ♦ CDC should promote standards of care in STD clinics and other facilities where STD services are routine provided which stipulate that tests to detect HSV (virus, antigens, or DNA) should be available and used routinely in the diagnosis of genital ulcer disease **(consensus high, priority not stated)**.
- CDC should undertake or support demonstration projects to assess the willingness of STD clinic attendees, as well as patients in other settings where STD clinical services are routinely offered (e.g., reproductive health clinics) to know the results of HSV serological tests, psychological impact, behavior change, effects on relationships, and the comparative impacts of serological vs clinical/virologic diagnosis on these variables **(consensus high, priority medium to low)**.
- CDC should assess HSV diagnostic tests offered and approaches to HSV screening and clinical assessment in public STD clinics and other settings where STD clinical services are routinely offered, and should develop guidelines to define the minimal standards for such care **(consensus high, priority not stated)**.

7) *General public*

- Mass screening of the general public is not warranted **(high consensus)**.
- CDC should conduct or support systematic surveys or opinion polls of the public to assess interest and willingness to know HSV serological status **(high consensus, high priority)**.

2. Magnitude and Burden of Genital Herpes

Through the National Health and Nutrition Examination Survey (NHANES), prevalence data for HSV-2 infection in the United States are better than those for any other STD. Nevertheless, poor understanding of the natural history (especially of initially subclinical infection), incidence of complications, and direct and indirect costs of genital herpes makes it difficult to assess societal costs and the cost effectiveness of prevention. Moreover, local and regional data are generally unavailable to program planners, health care providers, or the public. There was consensus that surveillance for genital herpes is warranted, but should begin with sentinel surveillance in targeted populations and settings. Surveillance should determine seroprevalence and seroincidence; clinical incidence and prevalence, with distinction between symptomatic and subclinical infection and among primary, initial non-primary, and recurrent infection; and population-specific results. Issues to be resolved in designing sentinel surveillance include the need for suitable case definitions, the ability to generalize sentinel surveillance data to populations outside those captured in the surveillance system, and resources to extend sentinel systems into ongoing surveillance, if warranted.

Estimates for the direct medical costs attributable to genital herpes were presented and discussed. Inherent difficulties in estimating such costs include the limitations of administrative

databases (e.g., underdiagnosis and intentional miscoding to preserve confidentiality) and of pharmacy sales data. Although efforts are underway to refine these figures, even when the uncertainties are considered it seems likely that the direct medical costs resulting from genital herpes are relatively small in comparison with other STDs. Accordingly, there was consensus that these costs are unlikely to be a primary determinant of the resources that will be available or of public advocacy for genital herpes prevention. On the other hand, these estimates do not include indirect costs, such as lost wages, lost productivity, or intangible costs, such as pain, emotional burden, and effects on lifestyle, and thus underestimate the true burden of genital herpes.

A. Magnitude of Genital Herpes

- It was recommended that population-based seroprevalence continue to be periodically assessed in future NHANES cycles, and perhaps expanded; and that HSV-1 seroprevalence should be determined and analyzed in the past (NHANES-II and III) and future NHANES cycles **(consensus high, priority high)**.
- CDC should conduct or support demonstration projects of sentinel surveillance for genital herpes **(consensus high, priority high)**.
- CDC should conduct or support mathematical modeling to understand HSV transmission patterns and trends and impact of interventions, while recognizing that refined estimates for some elements of the model (e.g., the risk of transmission per exposure in specified clinical and epidemiological settings) need to be continually reassessed and the models refined accordingly **(consensus and priority uncertain)**

B. Burden and costs of genital herpes

- Further studies of the direct medical costs of genital herpes were felt to carry a **low priority**.
- It was recommended that studies go forward on ways to quantify the indirect and intangible costs attributable to genital herpes (**consensus high, priority high**).

3. Preventing Neonatal Herpes

Although neonatal herpes appears to be infrequent, its severity warrants a better understanding of its incidence and epidemiology. In addition, cesarean section is a serious, costly procedure that is commonly performed to prevent neonatal herpes, but the proportion of cesarean sections attributable to maternal genital herpes is uncertain. Minimally, improved estimates of the number of neonatal herpes cases and of herpes-related cesarean sections should be obtained. Improved data systems are desirable in making such estimates; the lack of an ICD-9 code for neonatal herpes is a specific limitation.

The central recommendation was for demonstration projects in pregnant women to assess strategies to prevent both neonatal herpes and unnecessary herpes-related cesarean sections. The primary strategy for neonatal herpes prevention would be based on preventing initial infection near term, which carries the highest risk for perinatal transmission; the risk of transmission to the newborn from longstanding maternal infection appears to be low. Prevention should emphasize both HSV-1 and -2 and might require testing not only pregnant women, but also the sex partners of seronegative women. Because screening pregnant women would identify many subclinical HSV-2 infections, a possible unintended effect might be an increase in unnecessary cesarean sections. The overall utility of efforts to prevent either neonatal herpes or herpes-related cesarean section might differ substantially according to the background prevalence of HSV infection in the population.

- ♦ CDC should develop guidelines or recommendations to reduce excess cesarean sections due to genital herpes **(consensus and priority not stated)**.
- CDC should explore the feasibility of requesting that states make neonatal herpes a reportable condition nationwide, combined with efforts to improve ancillary data tools (e.g., promoting a specific ICD-9 code for neonatal herpes) **(high consensus, high priority)**.
- CDC should undertake or support meta-analyses of available data on the frequency of HSV shedding at term **(high consensus, high priority)**.
- CDC should support or conduct demonstration projects to evaluate screening strategies

for prevention of both neonatal herpes and unnecessary cesarean sections, conducted in both high- and low-prevalence populations **(high consensus, high priority)**.

- Partner-screening vs abstinence near term should be evaluated and compared as neonatal herpes prevention strategies **(high consensus, high priority)**.
- Mathematical modeling should be used to analyze the potential efficacy and cost effectiveness of strategies to prevent neonatal herpes and herpes-related cesarean sections **(high consensus, high priority)**.
- CDC should support demonstration projects of active surveillance for neonatal herpes **(high consensus, high priority)**.
- CDC should undertake or support research to determine the role of suppressive antiherpetic chemotherapy in preventing excess cesarean sections **(consensus and priority not stated)**.

4. Preventing Sexual Transmission of HSV

The discussions addressed epidemiologic and biomedical issues, behavior change, and professional education. The consultants recognized that most sexual transmission of HSV occurs during subclinical viral shedding; that HSV-1 prevalence in a population affects the transmission and clinical manifestations of HSV-2 infection; that both male and female condoms are likely to reduce the likelihood of transmission, but quantitative data are lacking on the actual protective effect; that the female condom may be more effective in preventing HSV transmission than the male condom, because the female condom covers a greater surface area of potentially infected susceptible tissues; that antiviral therapy reduces subclinical shedding but does not eliminate it, and the effect on transmission is not yet known; that complex prevention messages and strategies will be required in addition to condom promotion and antiviral therapy; and that both patient and clinician knowledge are poor concerning the epidemiology, clinical manifestations, transmission, and prevention of genital herpes. Low-prevalence, high incidence groups (e.g., adolescents and persons recently initiating sexual activity) were felt to represent ideal populations for the study of the effectiveness of a variety of interventions to prevent genital herpes; the results are likely to be broadly applicable to other populations in which incident infection is more difficult to measure.

It was acknowledged that because the strategies to prevent transmission of other causes of sexual and reproductive morbidity (HIV, bacterial STDs, pregnancy) are insufficient to completely prevent HSV transmission, and that condoms are not fully protective, additional herpes-specific prevention messages will be required. There was consensus that a national genital herpes education campaign should be undertaken as soon as possible. The specific goals of such a campaign were not delineated, but examples include promotion of male and female condom use, combined with recognition that protection is incomplete; information about the potential utility of the female condom; and the fact that subclinical viral shedding is common and accounts for most episodes of HSV transmission to sex partners.

A. <u>Epidemiology and biomedical issues</u>

- It was recommended that existing data on transmission risks (e.g., among HSV-discordant couples in HSV vaccine trials) be promptly analyzed to assess the determinants of transmission, such as symptom status, specific sexual practices (e.g., anal vs vaginal intercourse), prior HSV-1 infection, age, duration of infection, antiviral therapy, hormonal status, and co-infection with HIV **(high consensus, high priority)**.
- Because of probable effects of chronic HSV-1 infection on HSV-2 transmission

efficiency, it was recommended that the existing NHANES-III data on HSV-1 seroprevalence be analyzed and compared with data from NHANES-II and other available data bases **(high consensus, high priority)**.

- Studies should be undertaken or supported by CDC to determine the *efficacy* of male and female condoms in preventing genital herpes **(consensus high, priority high)**; studies of *use-effectiveness* also are desirable, but with **low priority** because of uncertainties about the ability to design and conduct the necessary research .

- It was recommended that CDC undertake or support demonstration projects among adolescents and other low prevalence/high incidence populations to assess the efficacy of male and female condoms, antiviral chemotherapy, partner communication/negotiation, and other strategies to prevent sexual transmission of HSV **(consensus high, priority high)**.

B. Behavior change and professional education

- ♦ A national campaign to enhance awareness of genital herpes, integrated with more general STD-prevention campaigns and messages, should be undertaken **(consensus high, priority high)**.

- CDC should support or conduct operational research in various populations on ways to communicate complex prevention messages to populations, including symptom recognition, abstinence during symptoms, and the threshold of symptom recognition and health care-seeking behavior **(consensus high, priority not stated)**.

- The most effective model(s) for testing persons at risk for HSV antibody and counseling them about their HSV serostatus is unknown, and undoubtedly will vary with symptoms, socioeconomic status, literacy, and other factors. It was recommended that these issues, and the clinician's roles in implementation, be addressed in a demonstration project supported or conducted by CDC **(high consensus, high priority)**.

- CDC should undertake or support operational and behavioral research on the acceptability of using antiviral chemotherapy in infected persons to prevent transmission, including assessment of therapeutic compliance and effects on sexual behavior and practices **(consensus high, priority high)**.

5. Interactions Between Genital Herpes and HIV Infection

The evidence for a substantial contribution of genital herpes to HIV transmission in the United States was reviewed, as were data suggesting that HSV infection may adversely affect the progression of immunodeficiency in HIV-infected persons. Studies also show that among persons with HSV-2 infection, the frequency of subclinical shedding of HSV-2 is higher in HIV-infected than in HIV-uninfected persons. It is unknown whether antiherpetic chemotherapy might reduce the potential for HIV transmission in dually infected persons. Similarly, it is unknown whether highly active anti-retroviral therapy (HAART) might influence HSV shedding. These observations suggest a possible future role for antiviral chemotherapy in preventing HIV transmission, HSV transmission, or clinical management of persons infected with both HSV and HIV.

- ♦ CDC should recommend that all HIV-infected persons be evaluated for genital herpes, including type-specific serological testing. There were **strongly asserted opinions both for and against this recommendation, without consensus**; it was viewed as **high priority by those in favor**. The experts recommending against this advice prefer to await the results of the following research agenda.

- Research should address the efficacy of antiherpetic chemotherapy in reducing HIV transmission and the effect of such treatment on HIV viral load and progression of immunodeficiency **(consensus high, priority high)**.
- CDC should conduct or support operational and behavioral research on appropriate counseling and testing messages and strategies for HSV/HIV coinfection (e.g., reinforcement of the need for compliance with the antiherpetic regimen, avoidance of sex during symptomatic recurrences, use of condoms) **(consensus high, priority high)**.
- The effect of highly active antiretroviral therapy (HAART) on clinical manifestations of genital herpes and subclinical shedding of HSV in dually infected persons should be studied **(consensus high, priority high)**.
- The legal and ethical implications of serial HSV-2 testing in HIV infected persons deserve special attention in designing demonstration projects and/or formulating recommendations for clinical management **(consensus and priority not stated)**.

6. Public and Provider Awareness and Knowledge

Although the state of public and provider knowledge about genital herpes was not identified as a specific topic for discussion prior to the meeting, it emerged as a dominant theme in all three work groups. There was broad consensus that knowledge levels about incidence, prevalence, subclinical shedding, transmission risks, neonatal herpes and other complications, and the availability and efficacy of antiviral therapy are low among health care providers, public health agencies, persons at risk for STDs, the general public, and even persons with herpes themselves; and that many infected persons, their sex partners, and others at risk therefore receive suboptimal (often frankly inadequate) health care and prevention advice. Nevertheless, the actual knowledge levels, specific practice patterns, and health department policies and procedures relative to genital herpes are poorly understood. There was further consensus that improved provider and public awareness would bring benefits not only in regard to genital herpes per se, but for other STDs. For example, awareness and acknowledgment that at least 22% of the general population (higher in many settings) acquires genital HSV infection might serve to destigmatize and enhance prevention of all STDs.

Thus, improved understanding of provider awareness and practices was viewed as a critical first step in enhancing prevention and the quality of clinical services for persons with genital herpes. There was consensus that CDC has a duty to raise awareness among the American public about the prevalence and significance of genital herpes, although modifying risk behavior would not necessarily be a specific goal of such broadly based education efforts. New communications strategies and technologies (e.g., internet, interactive video-conferencing) should be evaluated as potentially effective tools to convey herpes-related messages. The continuing role of traditional telephone hot-lines and the use of television also should be assessed.

A. <u>Public awareness</u>

- ♦ Without awaiting definitive results from the foregoing research, CDC should now undertake or support campaigns to enhance public and provider awareness of the frequency, clinical manifestations, and transmission of genital herpes **(consensus high, priority high)**.
- CDC should promptly conduct or support demonstration projects to assess varied strategies and messages to inform the public in order to raise awareness and enhance knowledge about clinical manifestations, and prevention strategies; novel methodologies to get the messages out (internet, television, others) should be

assessed **(consensus high, priority high)**.

- CDC should conduct or support opinion polls to assess the willingness of the public, especially those at risk for genital herpes, to learn whether or not they are infected through serological screening **(consensus high, priority high)**.
- Because NHANES-IV subjects will be given the opportunity to learn their test results, the proportion of those who seek their HSV serology results should be monitored, and studies should be conducted to determine the impact of positive test results in NHANES subjects without known genital herpes **(consensus high, priority high)**.

B. Provider awareness and knowledge

- ♦ CDC should immediately take action to get basic information to clinicians; an important role for the STD/HIV P/T Centers was envisioned **(consensus high, priority high)**.
- Surveys should be undertaken or supported by CDC to determine health care providers' knowledge, attitudes, beliefs and practices concerning genital herpes prevalence, clinical manifestations, treatment, and prevention; parallel surveys should determine what is currently taught concerning genital herpes in medical and other health professions schools **(consensus high, priority high)**.

7. Preparation for Immunization Strategies

Immunization strategies were not intended as a primary focus of the consultants meeting, in the belief that practical and effective vaccines against HSV were to be expected only in the relatively distant future. (The possibility was recognized that the gG2-based recombinant vaccine currently in trials sponsored by SmithKline Beecham might prove effective, but skepticism has been engendered by the failure of the Chiron Corporation's similar vaccine.) However, there was consensus that an effective vaccine represents the best hope for a maximally effective prevention program, and promising developments in research into other vaccine candidates were raised by several consultants. Thus, there was strong consensus that it is not premature to begin to undertake studies of behavioral, patient acceptance, and other aspects of future immunization strategies to prevent genital herpes.

- CDC should promote HSV vaccine development **(consensus high, priority high)**.
- CDC should develop a plan for vaccine use, distribution, and administration **(consensus high, priority high)**.
- CDC should conduct or support research to assess the acceptability of vaccination strategies by populations at current or future risk **(consensus high, priority high)**.

APPENDIX

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Appendix 3

Selected HSV Type-Specific Antibody Assays Based on Glycoprotein G

Test	Type	Antigen Source	Sens./Speci. for HSV-2	Comment
Western blot [13, 15]	Research/Reference	Infected cell lysates (HSV-1 and HSV-2)	>99 >99	Tested against culture Available in Seattle & Australia
HSV-1 and HSV-2 IgG Differentiation Immunoblot	Commercial (MRL)	Recombinant gG-1 and gG-2	95 95	Tested in-house; In trials for FDA Includes type-common protein
Immunodot enzyme assay (IEA) [13, 17]	Research	Monoclonal antibody-selected gG-1, gG-2	98 100	Tested against culture
HSV-1 and HSV-2 gG ELISA [21]	Commercial (Gull)	Monoclonal antibody-selected Native gG-1 and gG-2	98 97	In trials for FDA
gG-1 and gG-2 capture ELISA [6]	Research	Infected cell lysates (HSV-1 and HSV-2)	89 100	Tested against culture and IEA
Indirect gG-2 ELISA [25]	Research/Reference	Lectin-selected Native gG-2	98 >99	Tested against culture Available in Australia
POCkit™-HSV-2 [26]	Commercial (Diagnology)	Lectin-selected Native gG-2	94 98	In trials for FDA Detects light chain
Cobas® Core HSV-2 IgG EIA [27]	Commercial (Roche)	Lectin-selected Native gG-2	98 98	Macrobead format Tested in-house
Baculovirus gG immunoblot [28]	Research	Baculovirus-recombinant gG-1 and gG-2	92 100	Tested against IEA
Centacor Captia Select HSV-2 gG EIA [22]	Commercial	Baculovirus-recombinant gG-2	90 99	Tested against Gull and Chiron tests Europe only
Monoclonal antibody blocking RIA [7]	Research/reference	Infected cell lysates (HSV-1 and HSV-2)	91 ND	Tested against culture Available in UK

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