The Dynamic Topology of Sexually Transmitted Disease Epidemics: Implications for Prevention Strategies

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Each sexually transmitted disease (STD) epidemic evolves through predictable phases, shaped by a dynamic interplay among the pathogen, the behaviors of the subpopulations in which it emerges, and the prevention efforts that are developed to limit its impact. As STD epidemics move through these phases, the sexual and social networks that fuel them become located in subpopulations characterized by progressively higher rates of sex partner change and less contact with the health care system. As a result, phase-appropriate prevention strategies and research issues are essential to reducing STDs and their consequences.

The fundamental challenge to all prevention programs is to introduce into highly complex, dynamic, and inherently chaotic systems combinations of effective interventions that synergistically limit the spread and impact of disease, particularly among those groups most severely affected. Prevention programs addressing sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV) infection, face additionally a unique challenge. They must modulate factors that define the interface between human populations and communicable pathogens—pathogens that have been sufficiently diabolical to link their transmission to an act that is essential to survival of the human species, sex.

An understanding of transmission—the interplay between continuously evolving STD pathogens and equally dynamic human behaviors—must guide the development of effective STD prevention programs. The "core group" has, for almost 2 decades, been a central pillar of our conceptual framework for the epidemiology of STD transmission within populations and hence, at least theoretically, for the targeting of programmatic interventions. This concept postulates the existence of an epidemiologic "bull's-eye" for prevention programs in that it suggests that all endemic and epidemic transmission of curable STDs is, in fact, sustained by small subsets of the population. Introduced in 1978 by Yorke et al. [1] in considering the epidemiology of gonorrhea, the core group concept synthesized key biologic and behavioral characteristics of STD transmission, such as the fact that only sexually active persons are at risk, that infectiousness may persist for extended periods (both because of the natural history of these diseases and because of the high prevalence of asymptomatic infection), that bacterial STDs rarely generate a solidly protective immune response, and that sexual behavior is heterogeneous within populations.

The evolution of the core group concept is nicely summarized by Thomas and Tucker [2] in this issue. Its development has been facilitated by the convergence of research efforts in areas as disparate as mathematical modeling, geographic mapping, sexual and social network analysis, and sexual behavior research. The majority of this work has explored the core group as a static entity within a dynamic system, in essence taking single "snapshots" of the "engine" that fuels the persistence and spread of STDs in the context of profound temporal changes in human ecology and behavior at both individual and population levels [3].

A few investigators, however, have gone the next step to highlight the dynamic nature of the core group itself [4–7]. Some have described a tendency, over time, for the STD-infected population to contract around a stable or even an expanding core [4, 5]. Taking a more quantitative approach, Brunham and Plummer [6] have argued that effective STD control results in reduction of core group size. Using May and Anderson's elegantly simple formula [8], which defines the basic reproductive rate ($R_0$) of a sexually transmitted infection in a susceptible population in terms of the transmission efficiency of the organism ($\beta$), the rate of sex partner change ($c$), and the duration of infectiousness ($D$), they estimated the threshold values of $c$ required to sustain transmission of five major STDs (table 1). These estimates not only support observations that core groups differ for different STDs but also suggest that by shortening the duration of infectiousness, prevention programs drive up the rate of sex partner change that is needed to maintain the reproductive rate above 1. Brunham and Plummer [6] point out that the resultant high rates of sex partner change define a smaller core group, one that may well impose limits on the effectiveness of the program because of lack of accessibility or noncompliance.

In fact, it is likely that multiple, interrelated forces shape, often in predictable ways, the changing subpopulation structure or topology of STD epidemics over time. We believe that there are both a natural history and a controlled history to STD epidemics in terms of shifts in the size and character of core groups and other key subpopulations, as well as the distribution...
Hypotheses about the Dynamic Topology of STD Epidemics

Sexual network dynamics. Imagine that a new STD is introduced into a population that has previously never experienced this disease. What would we expect to see over the subsequent decades?

Clearly, what we would see would depend, in part, on the circumstances under which the STD was introduced. As discussed above, to establish itself and spread in the population, the STD must gain a foothold in a network of sexual partnerships with a rate of sex partner change above the threshold determined by the transmission efficiency and duration of infectiousness of the new organism (figure 1A, a) [6]. In other words, to kindle an epidemic, even a small one, the STD must start out among persons with sexual behavior and health care characteristics consistent with core group membership. Yet, particularly in this early phase of an STD epidemic, STD pathogens that require high rates of partner change are at a selective disadvantage because this severely limits opportunities for entry into most human populations. Furthermore, very early in an epidemic, both $\beta$ and $D$ are likely to approach their maximum pathogen-specific values. At this point, essentially all infection consists of incident cases, which may be transmitted more efficiently than the more chronic, prevalent cases that will occur as the epidemic grows [9, 10]. In addition, the prevalence of disease is so low that transmission is rarely preempted by contact between two infected persons. Finally, detection and treatment methods may not yet be available to shorten the natural duration of infectiousness. As a result, while networks with high values of $c$ may be more likely than those with lower values of $c$ to be exposed to new STD pathogens, we might expect that new STDs frequently establish themselves initially in networks with lower values of $c$.

Impeded only by changes in sexual behavior that might result from symptoms that the population as yet has no basis for recognizing, the STD would probably spread within the sexual network into which, by chance, it had been introduced. With expansion of the pool of infected persons, eventually it would be seeded into other subpopulations by persons in relationships that bridge sexual networks in different subpopulations (figure 1A, b–e). Involvement of new networks with similar or higher rates of sex partner change would result in further spread, while involvement of networks with lower rates might result in the establishment of foci that maintain infection. Infections in the general population of individuals or networks with rates of sex partner change that allow $R_0$ to fall below 1 would, from the population perspective, reach a dead end and fail to propagate. The rate of spread and course of the epidemic, at this stage, would likely depend largely on the parameters in May and Anderson’s model [8], on sexual mixing patterns within the overall population, and on the proportion with and nature of symptomatic disease.

Another key facilitator of spread within these networks would be limited contact with the health care system, since even contacts with the health care system that were initiated for reasons unrelated to STD symptoms might contribute to early recognition of the emergence of the new disease or its inadvertent treatment. Ultimately, however, when sufficient
Figure 1. A, “Natural” and “controlled” history of STD epidemics from perspective of changes over time in subpopulations in which spread and maintenance sexual networks are located. Dense spheres depict subpopulations containing spread networks, while mottled “halos” represent subpopulations containing maintenance networks. Arrows that link spheres with halos or with new spheres represent bridge populations. This population-level, host-focused perspective emphasizes importance of program interventions and social networks as determinants of epidemiology of STDs. B, “Natural” and “controlled” history of STD epidemics from perspective of changes over time in disease patterns, highlighting key events that mark transitions into new phases of epidemic. This population-level, pathogen-focused perspective is complementary to that in A, and each disease phase corresponds to stage in evolution of sexual networks and subpopulations that are central to STD transmission.
Gonorrhea

1964: Thayer-Martin culture medium developed

1964-1968: 48% jump in reported rates (159 to 236 per 100,000)

1968: 6 demonstration projects established to screen asymptomatic women & treat partners of symptomatic men

1972: National gonorrhea control program initiated ($16 million)

1975: Reported rates began sustained decline

1980's: Declining interest in face of other STD epidemics

Chlamydia

1965: Development of tissue culture

1984: Introduction of non-culture diagnostics

1984-1988: 26-fold jump in reported rates (3 to 82 per 100,000)

1985: First national chlamydia prevention guidelines published

1985-1986: 8 demonstration projects established to screen asymptomatic women & treat partners of symptomatic men.

1988: Region X demonstration project established to screen asymptomatic women in family planning clinics in 4 states

1994: National chlamydia prevention program initiated ($8.3 million)

Figure 2. US STD prevention program development cycles.
subgroups will lead to extensive dissemination throughout the population rather than to the STD being confined within subgroups. Conversely, if a population is divided into isolated subpopulations with low rates of sexual interaction within each, an STD entering the population will tend to be confined primarily to one subpopulation and to spread slowly in that subpopulation.

Relationships between sexual and social networks. An important dilemma for STD prevention programs lies in the juxtaposition of sexual and social network structures. Unfortunately, the sexual networks that fuel the spread of STDs do not tend to overlap greatly with the social networks that fuel the spread of prevention information and preventive behaviors. Spread networks are most frequently located in subpopulations at the lowest levels (tails) of the education, income, power, and prestige distributions, whereas networks responsive to prevention efforts are generally located within subpopulations at the highest levels of these distributions. In addition, while for the great majority of the population, sex partners are chosen among those with whom social linkages already exist [14], particular types of sexual linkage (e.g., commercial or casual sex) take place between persons who are less likely to be socially linked to each other.

Permeability of social boundaries between groups is an important characteristic of societies that influences the linkages among social networks and among sexual networks. It ranges from examples of nearly complete impermeability (as in the traditional Indian caste system) to examples of considerable fluidity (as depicted in the American ideal of the “melting pot”) [15]. Permeability of some boundaries (e.g., religious boundaries) may be greater than others (e.g., socioeconomic status boundaries). Permeability of boundaries may change over time. Moreover, permeability of a particular type of boundary may be greater in different subgroups in a society (e.g., marrying within one’s religious group may be more important among lower than among higher socioeconomic groups). In addition, a particular social boundary may be more permeable for certain types of relationships (e.g., friendship, dating, or even casual sex) than for other types of relationships (e.g., marriage) and for certain categories of persons (e.g., for adolescents it may be easier to marry outside of their religious group than for older persons). In the United States, 72% of marriages compared with 53% of cohabitations are between persons of the same religious group [14].

Within the above context of mixing patterns and network relationships, spread networks tend to be located in subpopulations marked by higher rates of concurrent relationships, by large numbers of sexual linkages throughout the subpopulation, and by some sexual contact with other subpopulations (sexual bridges). On the other hand, maintenance networks tend to be located in subpopulations with relatively lower rates of sexual interaction, lower rates of concurrent relationships, smaller numbers of sexual linkages, and relatively more limited contact with other subpopulations.

Recent evidence from the United States [14], France [16], and the United Kingdom [17] indicates that the sexual mixing patterns and sexual network structures in these societies actually constitute limits to the spread of STDs [18]. In the United States, a great majority of the general population (>80%) report having one (or no) sex partner over a typical 1-year period. The majority of people who report multiple partnerships have serial rather than concurrent partnerships. Only 15% of men and 7.6% of women report concurrent partnerships within a 5-year period [14]. Furthermore, the frequency of concurrent partnerships increases with increasing age, beyond ages of high STD incidence. Finally, in these societies, 12% of adults do not report any sexual partnerships and 72% are members of partnerships that are not connected to anyone else. In addition, many sociodemographic groups are apparently self-contained with respect to sexual partnership, connected within themselves but not connected to other sociodemographic groups. For example, in the United States, 90% of African-Americans and whites report same-race partnerships [14]. The tendency to form partnerships within one’s religious and educational groups is similarly great. Thus, sexual network structures and mixing patterns in these societies tend to confine STD spread to the tails of the population distribution. A small proportion of the members of these societies would have to account for the great majority of spread networks.

Just as the routes of transmission of STDs are determined by the structure of sexual networks and sexual mixing patterns, the routes of the diffusion of attitudes, beliefs, life styles, and behavior patterns in a society are determined by the structure of social networks and social mixing patterns [18, 19]. Social networks tend to be more open than sexual networks and are marked by higher rates of interchange within population subgroups, greater numbers of social contacts, and greater numbers of linkages across population subgroups. Thus, attitudes, beliefs, and behavior patterns, including preventive patterns, would spread more rapidly and more extensively throughout the population. Moreover, the responsiveness of persons to prevention information and interventions varies across population subgroups. For example, population subgroups marked by higher levels of education would be more accessible to prevention programs and more responsive to prevention messages. Similarly, population subgroups with lower prevalences of risk behaviors may respond more effectively to prevention efforts because of their higher levels of education and their health-seeking orientation [20]. In summary, prevention efforts first reach and affect subpopulations that are least likely to contain spread sexual networks. Furthermore, the nature of social networks within these subpopulations may be such as to hinder prevention information and interventions from diffusing into the spread networks.

Even in the absence of prevention programs, the spread of STDs would be self-limiting in certain segments of the society. Two main factors account for this: health orientation and sexual and social networks. Subpopulations marked by higher levels...
of education, income, power, prestige, and access to good health care tend to seek health on their own. They have resources available to them (including competence) to access the relevant information they need to maximize their health. They also have the motivation (perhaps because they have so much to lose or relatively less to worry about) needed to implement preventive measures [21]. These subpopulations are characterized by dense social networks through which health information diffuses effectively. On the other hand, members of these subpopulations mostly tend to interact sexually with other members of the same subpopulation and, therefore, do not expose themselves to sexually transmitted pathogens circulating primarily within other subpopulations. Thus, both the patterns of sexual and social mixing and the health orientation of higher-socioeconomic-status persons tend to function as forces that limit STD spread. A key role of public health (prevention and control) programs is to compensate for the absence of these spread-limiting social patterns among those subpopulations that lack the health orientation, the motivation, the resources, and the homophilous mixing patterns, while reinforcing and facilitating existing health strategies in higher-socioeconomic-status groups.

Disease dynamics. Traditionally, STD patterns have not been viewed through the population-level, host-focused lens of sexual and social networks that we have just described. Instead, although it has rarely been made explicit, a population-level, pathogen-focused communicable disease model has been used to conceptualize changes in STD epidemiology in terms of a series of phases (figure 1B).

Phase I is an early growth phase, with $R_0 > 1$, during which STD rates increase until a population-pathogen equilibrium is achieved or interventions are implemented; next is a hyperendemic phase often consisting of two parts (II and II'), with $R_0 = 1$ and with relatively stable but high disease rates compared with rates in other populations. Phase II is marked by the absence of formal prevention efforts, while phase II' begins with the initiation of interventions. A decline phase (phase III), with $R_0 < 1$, of falling rates is entered when the relationship between prevalence and incidence begins to change. (In the case of bacterial STDs it is likely that this will frequently consist of a more rapid decline in prevalent than in incident infections due to both their greater number and their greater ease of access. Incurable viral STDs, on the other hand, are likely to exhibit an increase in the prevalence-to-incidence ratio during this phase, as new cases decline in the absence of an impact on preexisting infections.) Phase IV is an endemic phase, with $R_0 = 1$, characterized by lower, stable STD rates and defined by a new population-pathogen-program equilibrium, or ultimately, elimination, if $R_0$ persists below 1.

This description is clearly overly simplistic in a number of ways. Smooth lines depicting broad trends are, in fact, made up of numerous fluctuations in disease rates and in their reporting. Although prevention programs in the United States have often been started during the hyperendemic phase, ideally they are launched much earlier, in the growth phase, as was the case for national HIV prevention efforts. In addition, these phases rarely occur in the orderly sequence depicted in figure 1B. The population-pathogen or population-pathogen-program equilibrium may be disrupted by myriad factors, triggering growth or decrease in disease rates at multiple points in time. Nevertheless, this general conceptual framework allows us to examine the status of specific STDs in a broad, dynamic context that may provide new insights and stimulate new questions. Furthermore, just as effective interventions at the individual level require understanding of the host, the pathogen, and their interactions in the context of changing individual sexual, substance-use, and health care behaviors, effective interventions at the population level require insights into sexual network dynamics (figure 1A), disease dynamics (figure 1B), and their interactions in the context of interventions and the social networks that mediate the diffusion of those interventions. As is indicated by the alignment of figure 1B with respect to figure 1A, each of the disease phases described above corresponds to a stage of evolution of the networks that are key to STD transmission (figures 1A and 1B viewed together). In other words, the dynamic topology of STD epidemics must be defined in terms of a synthesis of these two perspectives in light of the third critical element, prevention programs.

Reality Testing: STD Patterns in the United States

STD morbidity trends. Let us consider four common STDs in the United States: syphilis, gonorrhea, chlamydial infection, and genital herpes. Where would they lie in the scheme depicted in figure 1B? What do we know about the subpopulations in which each STD is currently concentrated? And how does that knowledge fit with the relationships postulated between figures 1A and 1B?

From the long-term, national perspective, syphilis lies in phase IV. It presents an excellent example of an STD for which a 50-year perspective reveals an endemic disease with low-amplitude fluctuation, while a more short-term view suggests repeated mini-epidemics. On the heels of recent declines, it is now endemic at the lowest levels in 35 years, with overall primary and secondary (P&S) syphilis rates in 1994 of 8 cases/100,000 persons and projected rates in 1995 of 6/100,000 (figure 3) [22]. After World War II, with the advent of penicillin and vigorous public health efforts led by then Surgeon General Thomas Parran, syphilis rates fell almost 95%, from 66 cases/100,000 in 1946 to 4 cases/100,000 in 1956. Syphilis elimination appeared to be within reach. But this exhilarating decline phase was interrupted in the late 1950s by the first of a series of increases in P&S syphilis that spanned 3 decades and culminated in the epidemic of the late 1980s, with a peak rate of 20 cases/100,000 in 1990.

The fragile population-pathogen-program equilibrium that appeared to be establishing itself in the mid-1950s was disrupted by several factors. William Brown's [23] aphorism held
that "... as a disease control program approaches the end point of eradication, it is the program, not the disease, which is more likely to be eradicated ... due to the increase of the cost in skill, effort, and resources to trace the last remaining cases and treat them; and to the increase in the disinterest of society in bearing that cost."

This was borne out with a vengeance as federal resources for syphilis control were slashed by 83% from $17.4 million in 1949 to $3 million in 1955. It was not until 17 years later, in 1972, that federal resources to control STDs rebounded to exceed 1949 levels, and these dollars were appropriated to address not only syphilis but also gonorrhea. Equally important, profound changes in sexual and substance-use behaviors began in the 1960s and were well documented by the 1970s [4]. The resulting syphilis epidemic hit the country in two waves. The first, from ~1960 to 1980, was concentrated among homosexual men, and the second, during the latter half of the 1980s, affected minority heterosexuals, particularly marginalized African-Americans [24]. In both cases, with 20/20 hindsight, it is likely that these syphilis trends contributed to emerging HIV epidemics and may, simultaneously, have been exacerbated by unrecognized HIV infection [25, 26]. Syphilis is now highly concentrated across the southern states, where its epidemiology is strongly linked to exchange of sex for drugs and, increasingly, to a rural distribution that presents new challenges in terms of access to preventive and curative services [27, 28].

In the mid-1990s, gonorrhea lies in phase III, continuing a sustained decline pattern that began ~3 years after the establishment of the national gonorrhea control program in 1972. At 165 cases/100,000, gonorrhea rates in 1994 were the lowest that they have been since 1964. This rate and the projected 1995 rate of 150 cases/100,000 represent annual declines of 4%–9%, one of several transient slowings in the pace of reduction of gonorrhea rates in the United States, which averaged, for example, >14% between 1990 and 1993.

National gonorrhea rates have long overshadowed national P&S syphilis rates in magnitude and have diverged in trend (figure 4). Yet the divergence may be less mysterious than it appears at first glance, if it is examined in light of prevention and control interventions and their impact on sexual network dynamics [29, 30]. Undoubtedly, biologic properties of the gonococcus and Treponema pallidum (such as differences in infectivity, immunity, duration of infectiousness in the absence of treatment, and the incidence and nature of symptoms) are responsible for a substantial portion of the observed differences in disease trends. It is also possible that much of the divergence may be due to differential effects of the same behavioral trends cited above occurring not only in the context of different biologic properties but also in the context of radically different stages of program development, in terms of both disease reporting and the sexual and social networks through which the two STDs and the prevention efforts were disseminated.

For example, the tripling of national gonorrhea rates between 1964 and 1975 undoubtedly reflected, in part, increases in screening and reporting with the advent of Thayer-Martin culture medium in 1964, the launching of six demonstration screening projects in 1968, and the initiation of nationwide gonorrhea control efforts in 1972 (figure 2). In contrast, we must recognize that what appears to be a relatively modest increase of only 32% in P&S syphilis rates over this same period occurred despite the cushioning of 3 decades of prevention and control efforts. Furthermore, the major changes in sexual behavior during this period were concentrated among white women in middle- and upper-socioeconomic-status groups, the subpopulations in which gonorrhea, but not syphilis, was spreading.

Over the next decade, with increasingly widespread screening and partner notification not only through publicly funded STD clinics but also through family planning clinics and other women's health care providers, gonorrhea rates fell 17.5%, from 464 cases/100,000 in 1976 to 373 cases/100,000 in 1986. The fact that P&S syphilis rates remained stable, in the range of 11 to 12 cases/100,000, during this time may be due in part to shifts in resources and emphasis of STD control programs away from syphilis towards gonorrhea prevention and in part to the greater ease with which prevalent infection can be eliminated compared with incident cases. From 1987 to 1993, as syphilis rates crescendoed to their 1990 peak of 20 cases/100,000 and declined, the velocity of the fall in gonorrhea rates slowed dramatically and then built back up to earlier levels. During this period, limited available data suggest that at least in some parts of the country, these two diseases had become entrenched in networks located in different subpopulations [31, 32].

Similar to the case with syphilis, the populations in which gonorrhea was concentrated between 1960 and 1990 shifted from homosexual men to minority heterosexuals. Between 1985 and 1991, racial differentials in reported gonorrhea rates widened, from 15-fold to 40-fold higher rates for African-
Americans than for white Americans, while those for reported P&S syphilis rates went from 14-fold to 60-fold differentials. However, the sex ratio for reported gonorrhea rates peaked at 3.4 males to 1 female in 1966 and then fell steadily to 1.2:1 by 1994, while that for P&S syphilis peaked at 3.6:1 more than a decade later in 1979 and declined to 1.1:1 by 1994. It is unclear how much of the earlier drop for gonorrhea was precipitated by the introduction of screening of asymptomatic women through the pilot projects established in 1968.

One of the most striking differences between the epidemiologic patterns of gonorrhea and syphilis lies in the age distributions of the two diseases. While the highest P&S syphilis rates persist among 20- to 24-year-olds, gonorrhea has become increasingly concentrated among adolescents. By 1986, the highest gonorrhea rates among women and the second highest rates among men were in 15- to 19-year-olds. After adjustment for the proportion of the population that is sexually active, the gap between adolescents and young adults grows even larger [33]. Furthermore, the slowing in the overall rate of decline in gonorrhea that was observed in 1994 was due, in large measure, to increases in gonorrhea rates among 10- to 14-year-old and 15- to 19-year-old females. These shifts, resulting in a greater concentration of gonorrhea among adolescents, are consistent with the hypotheses elaborated above because of the ineffective health care contact that characterizes adolescence.

Chlamydial infection provides an example of an STD that lies in phase II'. It remains hyperendemic following the 1994 initiation of a national prevention and control program. With the advent of antigen detection methods in 1984, establishment of eight demonstration projects over the next 2 years, implementation of a chlamydia screening demonstration project in the Pacific Northwest (Public Health Service Region X) in 1988, and the subsequent expansion of the Region X model to other parts of the country (figure 2), reported cases have increased steadily from 3.2/100,000 in 1984 to 188/100,000 in 1994 and are projected to reach 197/100,000 in 1995 (figure 5). However, these changes reflect improvements in detection and reporting capacity, rather than true disease trends. This point is highlighted by the almost 6-fold higher rates among women than among men in 1994, an artifact of legislative and programmatic targeting of resources to detect infection among women. On the other hand, where chlamydia screening has been widely implemented, positivity rates have repeatedly fallen rapidly, usually by ~50% during the first 5 years [34].

Finally, genital herpes is also hyperendemic in the United States, but in the absence of national prevention efforts to address this STD, it lies in phase II. Routine surveillance is not conducted for herpes simplex virus, limiting our information on national trends to surrogate measures such as numbers of initial visits to physicians for genital herpes from the National Disease
and Therapeutic Index. These data suggest that patient awareness of genital herpes has increased dramatically during the last 30 years and that infection is widespread, but they provide few insights into actual disease trends (figure 6). The best national estimates of trends in herpes simplex virus infection come from serologic data collected as part of the second and third National Health and Nutrition Examination Surveys (NHANES II and III). These data indicate that between 1978 and 1990, antibody prevalence to herpes simplex virus type 2 increased from 16% to 22% and that prevalences are markedly higher among African-Americans than among white Americans [35, 36].

In summary, routine passive surveillance of gonorrhea and syphilis have documented dramatic epidemics of both diseases. Both epidemics are subsiding and have moved into somewhat different subpopulations. Currently reported chlamydial infection trends, like those of gonorrhea in the late 1960s and early 1970s, are partly an artifact of the introduction of increased case detection in women and partly a result of increased requirements for reporting by states. Although the increase in office visits for genital herpes may have been influenced by increased patient awareness, the NHANES surveys leave little doubt that a true epidemic occurred.

**Characteristics of US populations affected by different STDs.** Our definition of the dynamic topology of STD epidemics and our hypotheses about the relationships between disease phases (figure 1B) and the characteristics of populations that contain the sexual and social networks involved in STD spread (figure 1A) imply that as we move from genital herpes (phase II) through chlamydial infection (phase II') and gonorrhea (phase III) to syphilis (phase IV), we would expect to find affected populations characterized by progressively higher rates of sex partner change (c) and/or increasing duration of infectiousness (D) due to relatively less effective contact with the health care system. Simultaneously, as we move along this spectrum, we would expect these affected populations to exhibit progressively lower exposure and responsiveness to preventive interventions because of factors such as decreasing educational and socioeconomic status and decreasing similarity between the population and providers of health services. Finally, we would expect that the density of sexual networks might increase along this continuum, at least to the extent that exchange of sex for drugs or money is part of the epidemiology of these diseases.

However, as we shift from the perspective of disease dynamics to that of sexual network dynamics, we encounter several problems. First, in contrast to STD morbidity trends, which are meaningful and complementary when both national and local data are examined, sexual and social networks are generally local structures that must be described using local data [18]. Second, because the importance of the latter perspective is just beginning to be appreciated, we lack longitudinal data on the characteristics of sexual and social networks (e.g., density, concurrency, permeability, mixing patterns) and on variables that would elucidate β, c, D, and program exposure and responsiveness for the populations in which these networks reside. For example, measures of condom use, rate of sex partner change, duration of symptoms, and frequency of STD screening have not been well-defined or systematically collected and analyzed either in STD-infected populations or in uninfected populations. As a result, data related to sexual and social networks and specific STDs are limited and are largely cross-sectional findings from research studies that in most cases use sociodemographic or sociogeographic surrogates in lieu of more direct measures.
One of the few US attempts at a direct comparison of observed values of the parameters affecting $R_0$ across multiple STDs recently took place in Seattle [37]. The investigators examined the reported number of sex partners in the past 90 days (as an approximation of $c$) for the people participating in sexual networks consisting of named sexual contacts to heterosexual patients diagnosed with genital herpes, chlamydial infection, gonorrhea, and syphilis. Consistent with the hypotheses outlined above, mean numbers of sex partners in the past 90 days increased from 1.0 for herpes to 1.9 for chlamydial infection, 3.1 for gonorrhea, and 4.0 for syphilis. These findings echo those of a Baltimore study that compared the epidemiology of only two STDs, gonorrhea and chlamydial infection [38]. Examining number and types of sex partners among STD clinic patients themselves (rather than among patients and their sexual contacts), these investigators found that gonorrhea, but not chlamydial infection, was associated with increasing numbers of recent sex partners and, among males, with a recent new partner.

Two other recent studies examine the role of substance abuse in the epidemiology of STDs and may provide indirect evidence that even within the same community, different STDs are currently concentrated in different subpopulations. In Baltimore, injecting drug use, cocaine use, and frequent alcohol use were each associated with syphilis, while they were not linked to gonorrhea and were associated with a decreased risk of chlamydial infection, although the latter association was not statistically significant [31]. Investigators in New York City documented similar results in examining the association between crack or other cocaine use and syphilis and chlamydial infection [32]. As suggested previously, to the extent that drug use is associated with the exchange of sex for drugs or money, the observed differences may also imply differences in the density of sexual networks related to these STDs.

Sociogeographic mapping has also provided important insights into the subpopulations most affected by STDs [39], but most of the US studies that have used this approach have done so only for a single disease rather than in a design that permits comparison of subpopulation characteristics across STDs. Both in Seattle [40] and in Colorado Springs [41, 42], this type of analysis of gonorrhea cases has highlighted the unequal distribution of the disease within local subpopulations defined by characteristics such as residence, gang affiliation, socioeconomic status, race/ethnicity, age, and sex. In these two settings, gonorrhea is clearly found in subpopulations with characteristics that are linked to poor exposure and responsiveness to program interventions. In Winnipeg, Canada, sociogeographic analyses of gonorrhea and chlamydial infection cases from 1988 through 1994 have demonstrated that the proportion of cases found in subpopulations living in areas in which disease is most highly concentrated was substantially greater for gonorrhea than for chlamydial infection. Although overall numbers of reported cases declined 68% for gonorrhea and 56% for chlamydial infection during this 6-year period, the proportion of gonorrhea cases residing in these core areas remained stable at 48%, while the proportion of chlamydial infection cases residing in core areas increased from 28% to 33% (Blanchard J, personal communication). These findings are consistent with the hypothesis that in Winnipeg, too, chlamydial infection lies at an earlier point than gonorrhea with respect to the sexual and social network dynamics described above.

**Implications for STD Prevention Programs and Research**

If validated, the concept that the subpopulation structure of each STD epidemic evolves through phases, driven by a reciprocal interaction with preventive interventions, has important implications for STD prevention strategies and research. In postulating a recurring pattern of movement of STDs through networks and subpopulations that mirrors the phases of STD morbidity trends, we acknowledge that basic parameters such as high-risk groups, risk factors and markers, program approaches, and research issues may vary across the different phases. To the extent that these patterns are predictable, this framework may also help public health authorities preempt the late-phase concentration of disease in subpopulation pockets that are difficult to reach and, if accessed, poorly responsive. In addition, validation (or refinement) of the hypotheses discussed in this article will require new research directions.

If, as STDs move from phase I to phase IV, the networks that fuel them become located in subpopulations characterized by progressively higher rates of sex partner change, less effective contact with the health care system, or lower educational and socioeconomic status, STD prevention programs must intervene with approaches that are phase-appropriate (figure 7). The initiation of national STD prevention program activities in the United States has usually been clinic-based and has often focused on members of maintenance networks or members of the general population. Another implication of our hypotheses is that initiation of STD prevention efforts (e.g., for STDs currently in phase II) simultaneously in subpopulations in which spread networks are located and in those in which maintenance networks reside might well result in earlier, more rapid, and more sustained declines in STD morbidity. Such efforts would have to be tailored to these different subpopulations and would, therefore, require greater initial resource investments. However, the comprehensive costs of such a two-pronged approach might well be lower and should be evaluated. Furthermore, this approach might well reduce the stigma associated with an STD by focusing on marginalized subpopulations at the same time that the needs of higher-socioeconomic-status persons are addressed. Once prevention programs have been established, repeatedly retargeting resources to subpopulations in which spread networks are located becomes increasingly essential as we move from phase II through phase IV.

In phase II, for example, prevention efforts should include mass media campaigns to promote public awareness of the "new" STD and what can be done about it. Detection and
treatment services and risk-reduction counseling should be offered by public and private providers. Client-initiated partner notification should be emphasized. If effective tools are available, this combination of interventions will reduce infection in subpopulations containing maintenance networks. However, these interventions should not be expected to be successful in subpopulations containing spread networks. To reach these subpopulations, a complementary strategy must be implemented simultaneously. This strategy should include targeted health promotion, often through one-on-one encounters at the community level, screening and treatment services delivered in outreach formats (e.g., mobile vans or urine screening in storefronts and parking lots), peer risk-reduction counseling, health department-assisted partner notification, and sustainable community-level behavioral interventions to change sexual and health care behaviors within relevant social networks.

By phase III, both the constellation of interventions within each strategy and the balance between the two strategies should begin to shift. In this phase, there is an ongoing need and ethical imperative to provide services to the subpopulations in which maintenance networks are located. However, mass media campaigns, for example, begin to be of limited value because basic knowledge about the STD and availability of services has risen to high levels within these subpopulations. Furthermore, by mid- to late phase III, private providers (including managed care organizations) can and should assume increased responsibility for clinical services, risk-reduction counseling, and client-initiated partner notification to address the shrinking burden of disease in these subpopulations. Aided by the reduced need for mass media efforts, increasing participation of private providers, and falling disease rates in subpopulations containing maintenance networks, public health authorities should begin to place greater emphasis on the spread network strategy. It is these targeted, community-level interventions that have not, to date, been delivered effectively by the private sector and that continue to be the primary responsibility of public health programs.

Finally, in phase IV, the vast majority of public sector resources should focus on strategies to reach subpopulations containing spread networks. During this phase, it is particularly important that programs emphasize outreach strategies, including health department-assisted partner notification, that mes-
sages are delivered using media and language that are educationally and culturally appropriate, that efforts are made to bridge the increasingly apparent differences between service providers and the people who are at highest risk, and that the need for more intensive, direct behavioral interventions is recognized. In moving from phase I to phase IV, community-level behavior change interventions also grow in importance, and by phase IV, it is likely that disease patterns are determined more by the effectiveness of behavioral interventions than by the effectiveness of detection and treatment approaches. If, in late phase IV, community-level behavioral interventions are not feasible or effective, reduction of disease rates may be impossible in the absence of communitywide preventive interventions, such as vaccines or selective mass treatment. It is noteworthy that selective mass treatment may be most effective if initiated as early in the development of an STD epidemic as possible. However, ethical and political concerns often preclude instituting such a policy in that phase.

Key research issues also vary across disease phases. During phases I and II, basic biomedical, clinical, and epidemiologic research are central and attempt to define the etiology and, subsequently, the microbiology, immunology, pathogenesis, and natural history of the STD, with an eye toward development of diagnostic and therapeutic tools. Further epidemiologic research must then identify behavioral and other risk factors and characterize affected populations. As the infection diffuses through phases II' and III, biomedical and behavioral intervention research, operations research, and research focusing on changes in risk factors become more important.

In phases III and IV it becomes increasingly important to focus intervention research on identification of hard-to-reach populations, increasing effectiveness of outreach, and health systems and provider behaviors to improve their ability to have an impact on the hard-to-reach. In these phases, program-relevant and policy-relevant research also become necessities; of course, it is desirable to start such research earlier in the course of the epidemic (e.g., in phases II and II'). By late phase III and phase IV, a pivotal program issue is to maintain society's interest and resources for prevention activity, and attention to factors that influence societal priorities and resource allocation decisions becomes relevant.

Throughout all phases and even in the absence of a new STD, it is very important to conduct network research focusing on patterns of social and sexual networks. In addition, behavioral research is essential to address the sexual and health behaviors of different subpopulations, factors affecting such behaviors, factors affecting the differential permeability of different subpopulation boundaries, parameters that influence changes in such permeabilities, and normative and cultural factors that shape different types of mixing across subpopulations.

In the context of sexual networks and the subpopulations that contain them, the concept of bridge populations is important. Persons who have sex with members of high- and low-prevalence subpopulations concurrently may be the most important agents of STD spread in the society. Bisexual men, sexually active drug users, and their partners have played important roles in spreading several STDs from homosexual to heterosexual and from drug-using to non–drug-using populations during the past few decades. Research focusing on the identifying properties of bridge populations, their behavior patterns, factors that affect these behaviors, and the potential for members of bridge populations to serve as change agents in catalyzing behavior change would provide crucial answers in an area in which we currently have no information.

Finally, measures of variables relevant to these prevention and research issues must be developed, tested, and used. For example, an operational set of measures of prevention program responsiveness has yet to be designed and evaluated. In addition, while approximations of $\beta$, $c$, and $D$ are available, they have not been incorporated into routine surveillance activities in most parts of the United States.

STD prevention program goals are 2-fold. At the public health or population level, the goal is to reduce the spread of STDs within the society. At the personal health or individual level, goals are to prevent infection, eliminate symptoms, and prevent development of severe, costly sequelae. We must understand the topology of STD epidemics both in terms of disease dynamics and in terms of network dynamics if we are to achieve these critical and synergistic public health goals.

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