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The development of effective, reversible, and safe contraceptives for men has lagged far behind the availability of methods for women, largely because scientists lack sufficient knowledge about male reproductive physiology. Improving this state of affairs has been a key aim of biomedical scientists in the Population Council’s Reproductive Health program. In one of the Council’s labs, biochemist and cell biologist C. Yan Cheng and his colleagues have found a way to target a new drug, known as Adjudin®, to the testis in rats. This method presents a way to develop a class of male contraceptives, potentially having few side effects.

“Chemical Postmaster Helps Deliver Contraceptive to Testis”

One hurdle Cheng and his colleagues needed to surmount was the blood–testis barrier created by the protective Sertoli cells. This barrier prevents immune system cells and foreign substances from entering the testis and damaging sperm. They overcame this blockade by means of a chemical “postmaster,” a synthesized variant of follicle-stimulating hormone (FSH).

Adjudin was attached to the variant FSH. Because FSH slips through the blood–testis barrier without difficulty, it is able to deliver Adjudin directly to the testis. Using this new approach, the researchers induced temporary infertility in rats using relatively low doses of Adjudin. There were no obvious side effects.

“These results show that it may be possible to develop a class of male contraceptives with few side effects by interfering with cell-to-cell attachment in the testis,” says Cheng.

Because the new low doses would have been broken down by the body if taken orally, the researchers instead injected Adjudin into the rats. Frequent injections may be unacceptable to men, so the researchers are considering other delivery systems, such as a nasal spray, gel, implant, or transdermal patch.

Adjudin interferes with the adhesion of germ cells to the supportive Sertoli cells that surround them. When this attachment is disrupted, germ cells are released when they are immature and incapable of fertilizing an egg. Cheng’s research has shown Adjudin to be a potent, effective, and reversible male contraceptive in laboratory animals. Normal fertility returns a few months after treatment with Adjudin stops. The compound does not influence hormones produced by the hypothalamus, pituitary gland, or testis.

When Adjudin was administered orally at a high dose, however, it caused liver inflammation and muscle atrophy in a small subset of animals. To remedy this, Cheng and his colleagues set out to develop a way of delivering the drug directly to the testis, so that it would not interfere with these other systems. This would also allow them to use a lower dose.

Sources


Outside Funding

National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health (NIH) and the CONRAD program
Complex Role for Marriage in HIV Risk, Studies Find

If present patterns continue, in the next decade more than 100 million girls will be child brides—that is, married before the age of 18—according to Population Council research. “In some cultures, girls are married off at very young ages due to poverty, custom, and in some cases the idea that it provides protection from HIV and other threats. But our research clearly shows that marriage per se, and child marriage especially, cannot be assumed to be a sexual safety zone,” explains Council researcher Judith Bruce. “Girls married at a young age are actually at a higher risk than unmarried girls for HIV infection in some settings.” Delaying marriage, however, does not necessarily improve safety. “Delaying marriage until the mid- to late-twenties may result in a period of risky unprotected sex involving multiple or serial partners,” says Council demographer John Bongaarts.

The Council is now looking at the nature of sexual relationships to discover what conditions make them more or less safe. Have women entered into their relationships voluntarily, for example? Are they able to negotiate condom use? “We’re designing programs to try to delay marriage until at least age 18 among girls who have not yet married and to reach married girls and give them more negotiating power within their relationships,” says Bruce.

There are a number of factors that increase HIV risk among girls married at a young age in areas with high HIV prevalence. At marriage these girls make a transition from virginity or infrequent sex to a very high frequency of sex. The most common HIV-prevention strategies—abstinence and condom use—are not options for married adolescents, who are under tremendous pressure from family and society to bear children.

Girls married young tend to have husbands who are much older than they are. This age gap may further intensify the power imbalance between husbands and wives, discouraging the open communication required to ensure voluntary counseling and testing for HIV, the sharing of test results, and planning for safe sexual relations throughout marriage.

Married adolescents are often missed by programs designed to reach married women with information about HIV infection. Married girls also typically have little education and no schooling options, limited control over resources, restricted mobility, and little or no power in their new households. Thus, they face significant challenges in negotiating safe sexual relations.

“Our research clearly shows that child marriage is not a sexual safety zone. However, delaying marriage until the mid- to late-twenties may result in a period of risky unprotected sex involving multiple partners.”

Based on these findings, the Population Council—in collaboration with partners around the world—continues to advocate for the elimination of child marriage and to develop and test programs to delay age at marriage, support married girls, and increase the ability of all girls and women to protect themselves from HIV infection.

Clearly, however, having sex with multiple or serial partners also increases HIV risk. In several southern African countries the average interval between age at first sex and age at marriage is about a decade, and HIV infection levels are far higher than anywhere else in the world. High average age at marriage in a population, because it is associated with a longer period of premarital exposure to the risk of infection, apparently contributes to the spread of HIV. This appears to be a key factor in countries with the largest epidemics. “The implications of these results are that sexually active unmarried women and men should make every effort to protect themselves by using condoms and by avoiding multiple partners,” says Bongaarts.

Bongaarts analyzed the causes of the large variation in epidemic size among sub-Saharan countries. The countries with the largest HIV epidemics all have late marriage. Bongaarts found that being married is less risky per year of exposure than being sexually active and never married. The elevated risk of infection among never-married sexually active women is likely caused by a higher rate of partner change and higher levels of infectivity among partners of never-married than of married women.

These complex findings are actually consistent with one another. Child marriage raises the risk of infection for young girls, because they would otherwise not be at risk, but marriage after the age at first intercourse raises exposure to higher-risk sex, thus contributing to the rapid spread of the virus. The policy implications of the findings are also consistent with one another. In countries with significant AIDS epidemics, the safety of sexual activity cannot be assumed either outside of or within marriage. Outside of marriage, sexually active people should practice abstinence or use male or female condoms to protect themselves. Within marriage, those seeking to avoid pregnancy and HIV infection should use condoms.

SOURCES

OUTSIDE FUNDING
Examining the Rollout of Pediatric Antiretroviral Treatment in South Africa

“We are grossly undersupplying antiretroviral drugs to children, and our prevention of mother-to-child transmission program is not working at this site. As a result children are dying in hoards,” explained one doctor who was interviewed as part of a study of pediatric HIV treatment in South Africa. While not all the findings were as grim as the one just quoted, the studies revealed significant deficiencies in pediatric HIV treatment in South Africa. Researchers communicated their findings and their informed recommendations to healthcare workers, program managers, health ministers, and other policymakers.

The USAID-funded study, which looked at pediatric antiretroviral (ARV) programs at 16 institutions in five of South Africa’s nine provinces (Eastern Cape, Free State, Gauteng, KwaZulu-Natal, and Western Cape), was the result of a collaboration between the Population Council and the University of Cape Town. A similar study, which looked at 15 institutions in the province of Limpopo and was funded by Irish Aid, resulted from a collaboration with the University of Venda. In addition to doctors, nurses, and pharmacists, the second study also looked at the role of traditional healers in pediatric HIV care. The study sites were selected to reflect variation in clinic characteristics and location within the health system (for example, the researchers investigated pediatric clinics at highly specialized institutions in urban settings as well as combined adult and pediatric general care clinics in rural areas).

HIV infection in children

In 2005, more than half a million children died of AIDS, the vast majority of whom lived in the developing world. In sub-Saharan Africa, AIDS is one of the leading causes of death among children younger than five. In South Africa, 40 percent of deaths of children younger than five are attributable to HIV. Children are known to have a higher vulnerability to opportunistic infections and a faster rate of disease progression than adults. Prompt initiation of ARVs is known to increase child survival and reduce deaths.

In 2003, the South African cabinet approved a plan for a national HIV program, whose goal was to have at least one general HIV service delivery point in each district providing treatment by the end of March 2004. The aim of these two Population Council studies was to gauge the success of the pediatric element of the HIV programs and to determine knowledge gaps that can be addressed by operations research. (Operations research focuses on the day-to-day activities, or operations, of programs. The findings of operations research can be used to formulate specific recommendations for changes that program administrators can make to improve their operations, and thus the health of their patients.)

These studies included three activities: a consultative workshop with doctors, nurses, program administrators, and health ministers; a review of published HIV policies; and an evaluation of pediatric ARV programs. The study results have direct policy relevance for South Africa and other countries in the region that are seeking to expand HIV treatment programs for children. The findings will be useful for the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR) in meeting its goal of providing antiretroviral treatment to 2 million people living with HIV. Additionally, they address two Millennium Development Goals, those of reducing child mortality and combating HIV and AIDS.

Policy review

The main South African government document providing guidance to doctors and program managers on the rollout of HIV treatment for adults and children is the “Operational plan for comprehensive HIV and AIDS care, management and treatment for South Africa.” The researchers reviewed this as well as other key documents. The review showed that while current policy documents cover a wide range of services and interventions for HIV-infected children, the information is scattered over several documents. Documents are not uniform in their presentation of information and often give only limited information on certain issues. For example, there are no specific recommendations for managing the care of infants living with HIV, treating HIV-positive adolescents and youth, or caring for children who lack reliable caregivers. Thus, “these guidelines do not facilitate efficiently the development of comprehensive services for HIV-infected children,” said Naomi Rutenberg, a study investigator from the Population Council, and director of the Council’s program on HIV and AIDS.

Key results of situation analysis

Through interviews with healthcare workers, the researchers found that there was no standardized or coordinated training program for South African medical personnel on the
management of pediatric HIV and AIDS. Most practitioners said they either were self-taught or studied under a more experienced mentor. Many of the nurses reported they were uncomfortable dealing with younger children, in part because they are harder to draw blood from and because determining the dosage of their liquid medication can be more difficult. One primary care nurse said, “I can do the children if they are above eight years…below that age, they are on syrups…syrups can be more complicated and they need a more professional person to do it.”

Pharmacists dispense ARVs, maintain stock levels of drugs, and monitor adherence to the regimen by counting remaining pills and measuring syrup. Monitoring adherence can be time consuming, and the researchers said that the burden of this duty could be reduced through the use of unannounced in-home pill counting and by a method known as modified directly observed therapy. Under this strategy, originally developed and used successfully for tuberculosis patients, health workers or community volunteers watch clients take their medication, thus making adherence to the regimen more likely.

The research teams found that pharmacists also play a key role in counseling patients and other unusual duties. One pharmacist, from a specialized care facility in an urban area, stated that in addition to his regular responsibilities, he is “part of trying to get the support group running and trying to start income generation for patients.”

**How do patients access services?**

The researchers found that one of the biggest stumbling blocks to fully implemented ARV care is a lack of strong links between services for the treatment of pediatric HIV and other services that would seem to be natural complements. Very few pediatric patients were referred from programs for the prevention of mother-to-child transmission of HIV (PMTCT) or from programs for HIV voluntary counseling and testing (VCT).

Most children were referred from community clinics and had been either chronically ill or hospitalized, suggesting that HIV infection had progressed to a point at which it severely compromised the child’s immune system. Only 5 percent had been tested through a PMTCT program. Caregivers—usually mothers, grandmothers, and aunts—indicated that fear of stigmatization and prejudice made them delay seeking HIV- and AIDS-related healthcare for their children. Stronger relationships between PMTCT programs and pediatric HIV programs, as well as improved blood-taking skills at primary-level facilities, are essential for early identification of children who need treatment, according to the researchers.

Doctors and nurses mentioned a number of other tough obstacles to full rollout of the pediatric ARV program, including clinic space constraints, problems maintaining adequate stocks of ARVs, and fewer drug options for children. Also of concern were the lack of services for adolescents; widespread poverty and unemployment, which impedes access to services; and a lack of community awareness about the availability of ARVs and the benefits of ARV treatment.

In Limpopo, researchers interviewed traditional healers, from whom many South Africans seek their healthcare at one time or another. The traditional healers said that they had heard of HIV and AIDS on the radio but that they do not use ARVs, relying instead on traditional medicines. As one healer put it, “my ancestors do not know it and they do not use it in their communication with me. So I treat what they tell me to treat.” Ultimately, however, the researchers were left with the impression that traditional healers see few pediatric HIV patients and that children are usually taken to regular healthcare facilities.

**Conclusions and recommendations**

The research teams found that ARV programs that are treating children successfully vary according to local circumstances. However, there were a few clear components of success: child-oriented human resources, such as nurses with technical proficiency in drawing blood from young children, and the availability of adequate stocks of ARVs.

“We found that the human factor is one of the most critical components of a successful pediatric site. Dedicated doctors demonstrate how individuals are capable of making a difference, for example by partnering effectively with other healthcare workers and organizations,” said Lewis Ndhlovu, a Population Council public health researcher.

The research teams generated several specific recommendations for improving pediatric HIV care in South Africa, including:

- ensure that children are placed on the ARV rollout agenda by making sure that community-based programs have the expertise and capacity to monitor children’s T-cell counts, and offer appropriate drugs, nutritional support, anti-TB treatment, routine immunizations, and appropriate referrals;
- standardize treatment protocols and referral guidelines;
- encourage early identification and referral of HIV-infected children from PMTCT programs;
- provide additional, standardized training for health professionals, including upgrading nurses’ skills;
- improve drug procurement and supply channels;
- address the special needs of infants and adolescents with HIV; and
- improve community awareness and reduce stigma.

“The need for greater family and community involvement in pediatric ARV provision cannot be overemphasized,” stated Ndhlovu. “The widespread fear of stigmatization tends to delay treatment and can have far-reaching negative effects on the health of mothers and children.”

**SOURCES**


**OUTSIDE FUNDING**

Irish Aid and the President’s Emergency Plan for AIDS Relief through the United States Agency for International Development
Appropriate antenatal care is a key element of programs to improve the health of mothers and newborns. Recently the Population Council and partners studied antenatal care in Ghana, Kenya, and South Africa. These investigations showed that a focused approach, emphasizing quality of care over quantity, is acceptable, but can be difficult to implement because of scarce resources and staff turnover.

Approaches to antenatal care

On the whole, antenatal care programs in developing countries have been modeled on those in developed countries. These programs, however, have been poorly implemented and largely ineffective. In response, the World Health Organization (WHO) designed and tested a focused antenatal care package that includes only counseling, examinations, and tests that serve an immediate purpose and have a proven health benefit. For example, many antenatal care programs screen for suspected risk factors for pregnancy complications. However, this approach has been challenged and WHO's focused approach does not use it. The WHO recommends reducing the number of antenatal care visits to four, and this has not been found to pose a risk to the health of mother or baby.

South Africa

The Maternal, Child and Women’s Health Unit of the KwaZulu-Natal Department of Health wanted to improve the quality of antenatal care provided in its clinics. To this end, it collaborated with the Population Council’s USAID-funded Frontiers in Reproductive Health program, the Reproductive Health Research Unit of the University of Witwatersrand, and the Department of Medical Microbiology and Infectious Diseases of the Nelson Mandela School of Medicine at the University of Natal. These groups developed and pilot-tested a version of the WHO-recommended package of care, involving five (rather than four) antenatal care visits and two postnatal care visits. The focused package also included counseling on the prevention of sexually transmitted infections, onsite syphilis screening with same-day results, and HIV prevention information and referral.

The teams used a pre- and post-test comparison group design, comparing the current standard of care in six clinics with focused care in another six clinics. They found that the introduction of the programs was feasible. However, patient care did not improve as much as hoped. Not as many women as planned received counseling on nutrition in pregnancy, breastfeeding, and postpartum family planning. Nor were women adequately educated about pregnancy danger signs. Such disappointing results might be attributable to high staff turnover. By the time of the endline survey, only two of the six intervention clinics had at least one staff member who had covered all the training modules. Thus, interventions such as this, which rely heavily on teaching staff new ways of organizing and providing services, must develop strategies that allow for relatively rapid rates of staff turnover.

Frontiers has been working with the Department of Health in KwaZulu-Natal province to develop a comprehensive package of policies, tools, and job aids to strengthen antenatal care services; the national Department of Health is also interested in adapting these products.

Ghana and Kenya

In Ghana, Frontiers collaborated with the Noguchi Memorial Institute for Medical Research and the Ghana Health Service to examine the extent to which adaptation of the package influenced the quality of care received by pregnant women and its acceptability to both providers and clients. The study took place at ten intervention clinics and four comparison clinics.

The researchers found that the new model is well accepted by clients and providers because of its comprehensiveness and individualized care. But some components of the package were lacking in several clinics, in particular procedures for disease detection, including syphilis and HIV/AIDS. Existing opportunities for referral were not fully used. Client privacy was sometimes compromised, as many clinics partition their consulting rooms. And essential drugs and supplies were not always available. Nevertheless, the focused antenatal care model did result in improved quality and continuity of care in Ghana. Clients visiting the intervention clinics obtained more comprehensive care than those visiting comparison clinics.

In Kenya, the Frontiers program collaborated with the Ministry of Health to determine whether focused antenatal care has increased the coverage and quality of services. The study compared clinics in two intervention districts with clinics in a control district. The researchers found support for the focused services among policymakers. But, as in the other countries studied, inadequate staff training and shortages of equipment and supplies inhibit the full provision of services. Despite these challenges, the new model did increase the quality of specific components of care, such as detection of diseases and counseling on family planning use postpartum. Further, clients report satisfaction with most aspects of the new model of antenatal care provision.

“Focused antenatal care is acceptable to both clients and providers and can improve care,” said Council researcher Harriet Birungi. “However, to optimize the introduction of the new model, program managers and other key stakeholders need to develop strategies to deal with high staff turnover and a scarcity of needed supplies.”

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OTHER PUBLICATIONS


The demographic transformation of the world in the 100 years between 1950 and 2050 will be marked both by a vast expansion in human numbers and by the emergence of a low-fertility, highly urbanized, and increasingly elderly world population. These changes are posing challenges for national governments and international institutions. The responses those bodies have arrived at, or must now formulate, are the subject of a new volume, *The Political Economy of Global Population Change*, a supplement to the Population Council’s journal *Population and Development Review*. The volume’s contributing authors, representing the disciplines of history, economics, political science, and demography, take up major components of this subject—looking both to the experience of the second half of the twentieth century and forward to 2050.

**Challenges of population change**

Several essays cover the political demography of major world regions. Oxford demographer David Coleman examines the demographic future of Europe, where the extent and pace of population aging—a consequence of very low birth rates—present policy difficulties for many governments. Coleman looks at the array of possible responses, both demographic and non-demographic. None is likely to prevent considerable population decline over future decades and one, higher immigration, could lead to European societies that are “unrecognizably different from those of 2000.”

Cambridge political scientist Christopher Clapham explores African population change. Africa’s situation combines a heavy burden of disease, still-rapid population growth, and deep problems of governance. Clapham paints a nuanced picture of the region’s prospects for development and demographic transition, but with the AIDS epidemic an overshadowing reality.

Two other regionally focused essays cover India and China, the world’s demographic giants and emerging economic heavyweights. Eduard B. Vermeer, an expert on China, investigates the country’s dramatic demographic change in its political context, and economist Deepak Lal of the University of California offers a sweeping appraisal of population in India’s development, past and future.

A pair of essays take up environmental issues. The Georgetown University environmental historian J.R. McNeill surveys the effects of population change on the natural environment as they have played out in the industrial era. Less alarmist than many, he sees new technologies—more resource efficient and less polluting—as key to a greener future. A companion essay by David G. Victor, of Stanford University and the Council on Foreign Relations, treats the problematic concept of sustainable development, studying what it means for the urban built environment (where humans are increasingly concentrated), for the lightly populated countryside, and for unpopulated “wilderness.”

Political scientist Aristide R. Zolberg, of the New School for Social Research, examines the management of international migration in the United States and other rich democracies in the post–World War II period. While recognizing the heightened security concerns following 9/11 and the demands for stricter border controls against illegal entry, Zolberg favors a broadly liberal stance on immigration, both temporary (such as guestworker programs) and permanent.

Finally, two essays by the editors introduce and conclude the volume. The first recounts the history of political responses to high fertility and rapid population growth since the 1950s; the second surveys the emerging political demography of the world system—looking in particular at the social and political problems that Western societies are likely to face as economic globalization extends to encompass the demographic giants.

*Population and Development Review* seeks to advance knowledge of the interrelationships between population and socioeconomic development and provides a forum for discussion of related issues of public policy. The editors of this special issue are Paul Demeny, Distinguished Scholar and editor, *Population and Development Review*, and Geoffrey McNicoll, Senior Associate, both at the Population Council.