of the French group. Montagnier and Cher-  
mann did not realize that virus from a pa-  
tient called LAI had contaminated their  
LAV/BRU isolate. Although Montagnier be-  
thieved he was sending LAV/BRU to us—  
and so did we—one culture persisted pre-  
dominantly of LAI. The properties of LAI  
are very different from those of LAV/BRU,  
which does not grow in cell lines. Com-  
pounding the complexity, although IIIB was  
clearly derived from LAI, it is not identi-  
cal with LAI, but rather is a variant that grows  
vigorously because of mutations in some of its  
regulatory genes. All of this was ac-  
wnowledged by our group and the French  
group in 1991 (18) (see the Viewpoint by  
Montagnier, on page 1727).

The period after the May 1984 publica-  
tion of our papers was marked by rapid ad-  
vances (15, 19). The HIV-1 genome was se-  
quenced, HIV antigenic variation was dis-  
covered, the virus was found in the brain of  
AIDS patients, genomic sequence variation  
was found in viral populations from the  
same patient, macrophages were found to be  
targets for HIV, various modes of HIV trans-  
mittance were elucidated, all of HIV’s genes  
and most of its proteins were defined, and  
the blood supply in most developed nations  
was rendered safe as a result of screening  
for HIV. Next, came identification of the  
HIV receptor (CD4), the discovery of SIV  
in chimps, and the development of the first  
anti-HIV drug, AZT.

The late Jonathan Mann heralded the  
years 1982 to 1985 as a period of intense  
discovery, noting that the pace of research  
was the fastest in medical history. For some  
scientists, these were also years of disquiet  
and frustration; in which we would  
encounter in an unprecedented manner the  
negative face of politics, the media, patient  
activists, and legal issues. For myself and  
others trained in science and disciplined by  
the rigor and analysis that are the essence  
of scientific endeavor, the rough and t uncle  
of the outside world provided harsh and  
bitter lessons. In retrospect, it is clear that  
these lessons needed to be learnt, and I can  
say we are better for the experience. But  
our job is far from over, and it is up to the  
scientists to ensure eradication of the AIDS  
epidemic that continues to rage in many re-  
regions of the world.

Prospects for the Future
Robert C. Gallo and Luc Montagnier

With close to 70 million people al-  eady infected with HIV and more than 20 million dead, AIDS  
is one of the greatest pandemics in medical  
history. Not only is this a human tragedy of  
umimaginable di-  
dimensions, it is also  
a threat to world se-  
curity because of the  
potential for po-  
itical destabilization. The AIDS epidemic  
must be halted soon. We need a policy of  
prevention that can be adapted to the socio-  
ological and cultural conditions of the most  
devastated countries in Africa and Asia,  
and that encompasses sustained interna-  
tional political will. New developments in  
AIDS research will contribute decisively to  
the decline of the epidemic and eventually  
it eradication. From the beginning of the  
epidemic, science has produced the most  
important practical advances: from discov-  
ering the cause of AIDS to developing a  
blood test and anti-HIV drugs. Now, sci-  
ence must develop new therapies that are  
practical alternatives for the developing  
world, as well as new microbicides that  
block sexual transmission, until an effica-  
cious vaccine arrives.

In developed nations, the judicious use  
of combination anti-HIV drug therapy has  
substantially benefited HIV-infected peo-  
ple and has ended the pediatric epidemic.  
The Global Fund to Fight AIDS, Malaria  
and Tuberculosis—launched by Koffi An-  
nan, the secretary-general of the United  
Nations—is spearheading efforts to trans-  
late these advances worldwide. However,  
the challenge is huge and has been com-  
plicated by many factors, including the  
emergence of multidrug-resistant HIV mu-  
nants. New antivirals that target not only  
dividing cells but also “resting” cells, and  
strategies that augment intracellular levels  
of active drug through modulation of  
metabolic pathways, may improve the suit-  
ability of existing drugs (1, 2). New class-  
es of drugs, particularly HIV entry in-  
hibitors, show promise. They have the ad-  
vantage of stopping HIV before it estab-  
lishes new infections in host cells. Prelim-  
inary studies show impressive results with  
inhibitors that block each stage of HIV en-  
try: attachment and binding to CD4+ T  
cells, coreceptor binding, and fusion of the  
viral and cellular membranes (3, 4).

What can be done to bring anti-HIV therapy to developing countries with limited  
infrastructure? Administering these  
thepathies is complex, and patient compli-  
ance is a major challenge. If compliance  
and careful follow-up of patients is not  
achieved, we will see a dramatic increase  
in multidrug-resistant HIV mutants whose  
further spread will only exacerbate the  
epidemic. With our 20 years of experience,  
we propose the following priorities for  
eliminating AIDS worldwide.

Access to Antiretroviral Treatments
One of the main objectives of the Global  
Fund to Fight AIDS is to make anti-HIV  
drugs accessible to all of the developing  
world. The problem of cost can be partly  
solved by reducing drug prices (through  
lower pricing acceptable to pharmaceutical  
companies, use of generic drugs, and finan-  
cial help from the Global Fund). But the in-  
frastructure necessary for performing fol-  
low-up of patients during treatment will be  
costly and difficult, and the duration of such  
treatments will make them ultimately unaf-  
fordable for patients in poor countries. This  
is an unprecedented situation. The decrease  
in plasma viral load achieved with triple  
drug therapy does not stabilize after treat-  
ment interruption, which results in a rapid  
increase in circulating virus. Moreover,  
there are severe limitations to antiretroviral  
therapy, including toxic side effects (lipid  

References and Notes
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2. M. G. Samagdhanaran, P. S. Sarin, M. S. Reitz, R. C. Gal-  
3. Z. S. Salahuddin, P. D. Markham, F. W. Ruscetti, R. C.  
13. R. C. Gallo, Virus Hunting AIDS, Cancer and the Hu-  
meman Retrovirus: A Story of Scientific Discovery (Basic  
17. Repetitions of IIIB/LA1 contamination occurred in  
Robin Weiss’s laboratory in London, at the Frederick  
National Cancer Institute laboratories, at Duke Uni-  
iversity, and very likely in several other laboratories,  
as well as the original contamination in France.
deposition, increased risk of diabetes and cardiac infarcts, muscular and neurological toxicity). Therefore, it is imperative to launch clinical trials to test additional treatments that are less toxic and less expensive.

**Therapies for the Developing World**

After 6 months of continuous antiretroviral therapy, a patient’s immune system is usually partly restored, and it is then possible to mount a relatively potent immune response against HIV. We suggest that patients on drug therapy for 6 months might benefit from being vaccinated at this stage. The efficacy of vaccination could be rapidly assessed by comparing the intensity of viral rebound in unvaccinated versus vaccinated patients after cessation of drug therapy.

**Vaccines and Microbicidal Agents**

Developing a vaccine is, of course, the ideal way to contain and even eradicate the scourge of AIDS. To quickly evaluate the efficacy of immunization, we propose that candidate subunit vaccines be tested in HIV-infected persons as therapeutic supplements after initial antiretroviral therapy. The end-point—a lack of viral rebound after interruption of drug therapy—should be easy to measure. From such therapeutic trials the best subunit combination could then be selected for testing in a full-scale clinical trial. There have been encouraging data with candidate microbicidal agents such as the cyclodextrins, which block infection when delivered at portals of entry (8).

**Blocking Mother-to-Infant Transmission**

In developed countries, mother-to-infant transmission has been blocked by several approaches: blood testing of mothers and, if they are positive, advising them to avoid breastfeeding; caesarean delivery when intrapartum risks are great; reducing HIV levels in mothers by treating them with triple drug therapy throughout pregnancy; and postpartum prophylactic treatment of the exposed newborn for its first week of life. In Africa, a single dose of a reverse transcriptase inhibitor given to mothers and their newborns decreased transmission from approximately 30% to 10% (9). However, postpartum infection continues to be a major problem in developing nations because of HIV transmission through breast-feeding. We are collaborating with colleagues in Rome on a program called “Families First Africa.” In sites in West Africa, we plan to administer prophylactic antiretroviral therapy to pregnant mothers and to vaccinate their newborns with HIV peptides matching their HLA genotype; we will take advantage of the BCG vaccination routinely given to newborns in these countries by adding the HIV peptides to the BCG vaccine, which acts as a strong adjuvant. This approach will primarily induce cellular immunity without excluding an antibody response.

**Prevention, Treatment, and Research**

Scientists and clinicians in developed countries must contribute to the creation of infrastructure in the countries worst hit by AIDS. They need to train health care specialists in these countries, help to conduct clinical trials, and set up laboratories to analyze viral strains. There needs to be a transfer of technology from the North to the South and a two-way exchange of information. A center was created in 1996 in Abidjan by the World Foundation for AIDS Research and Prevention under the aegis of the government of Côte d’Ivoire and UNESCO for this purpose. The center integrates three activities under one roof: prevention by education (training of industry and administrative managers), treatment of ambulatory patients (within the UNAIDS initiative program), and laboratory and clinical research (in preparation for clinical trials). The Institute of Human Virology has also established programs in Africa and the Caribbean with similar goals. We suggest that each country create and develop a reference center integrating these three activities, with the possibility of radiating to rural regions through satellite mobile units. This will require close interactions between local governments, United Nations international agencies, and nongovernmental organizations. There needs to be a strong political will on the part of the governments of developing nations and generous financial contributions from the developed world, conveyed through a United Nations organization, such as WHO or UNESCO, in coordination with UNAIDS. It is also important that developing countries themselves participate financially. We suggest that the amount of funding from developing countries for AIDS projects should be deducted from their national debts to developed countries. More than ever, a global coordinated response is required to fight the scourge of AIDS.

**References**