Volume 16, Issue 4, August 2009

TAG
Treatment Action Group

tagline

NEWS ON THE FIGHT FOR BETTER TREATMENT, A VACCINE, AND A CURE FOR AIDS

The 2009 Pipeline Report
TAG's Annual Review of What's New

The *Pipeline Report* is a concise compendium of new drugs and technologies with the potential to benefit people living with HIV within the next few years.

BY BOB HUFF

TAG's annual pipeline report for 2009 was distributed in July at the Fifth International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention in Cape Town, South Africa, where eager attendees snatched up 2,000 copies during the three-day meeting. The 90-page booklet is popular because it provides an easy-to-read overview of drugs, vaccines, and diagnostics that are being developed for HIV, viral hepatitis, and tuberculosis. Here are some highlights.

HIV Drugs in Development

The antiretroviral (ARV) drug pipeline for 2009 shows—as TAG's executive director Mark Harrington explains in the report's introduction—a lull in new drugs to treat HIV after an unusually active period of drug approvals during 2007 and 2008. Aside from a few specialty drugs (bevirimat, ibalizumab) moving into late-stage clinical trials that might be important for people with few remaining treatment options, the most significant progress may come in the form of new, more tolerable, and more convenient combinations of drugs in single-pill formulations. Four new drugs that boost blood levels of certain ARVs are moving through the pipeline, and these could facilitate a breakthrough in how several protease inhibitors (PIs) are offered in the future. Currently many of these drugs—such as Prezista, Reyataz, and Lexiva—depend on Abbott Laboratories' Norvir for boosting. Alternative boosters could break the Norvir monopoly and allow all-in-one boosted PI tablets as well as a boosted integrase inhibitor from Gilead.

The drug in the pipeline likely to first achieve approval is a new non-nucleoside reverse transcriptase inhibitor (NNRTI) from Tibotec called rilpivirine. The drug is being groomed to compete with efavirenz as a first-line treatment choice and offers the potentially important advantage of having fewer side effects. In late-breaking news from the Cape Town conference, it was announced that Tibotec and Gilead are teaming up to create a single-tablet regimen containing rilpivirine plus Gilead's Truvada combination of the nucleoside reverse transcriptase inhibitors (NRTIs) tenofovir and emtricitabine. This once-a-day pill will compete with Atripla, the highly popular single-tablet regimen containing efavirenz plus Truvada, a collaboration between BMS and Gilead. Gilead's integrase inhibitor elvitegravir, now in advanced phase III trials, will also be offered in a single-pill regimen containing a booster plus Truvada.

Vicriviroc, a CCR5 antagonist HIV entry inhibitor from Schering-Plough, is also working its way through advanced trials and will likely be the second approved drug in this class. Maraviroc, the first CCR5 blocker, approved in 2007, experienced only limited uptake by physicians due partially to a requirement for an expensive diagnostic test to identify patients who are likely to respond to the drug. However, simpler and cheaper tests are starting to come to market, and this barrier may soon be removed.

Some of the biggest ARV buzz coming out of the Cape Town conference was over the new GlaxoSmithKline (GSK) integrase inhibitor, now entering phase II trials. At the end of a ten-day trial of the drug alone, the majority of patients receiving the highest dose had an undetectable viral load. No resistance was seen in this short study and the only side-effect complaint was headache. GSK, in a joint venture with

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Pfizer, has formed a new, independent company to do its HIV drug development and marketing work. This consolidation of forces, alongside the collaborations among other HIV drug companies, gives hope that the current lull in the pipeline may be followed by some creative new developments in ARV therapy.

Hepatitis B Drug Development

The hepatitis B virus (HBV) infects more that 400 million people in the world and is a leading cause of liver disease; yet, as TAG's Lei Chou reports in the *2009 Pipeline Report,* drug development for HBV has come to a "virtual standstill" in the past year.

Part of this has to do with scientific difficulties in discovering and testing safe and effective new HBV drugs, but the main reason must be due to the paltry amount of money spent on research. Though six drugs have been approved to treat HBV, several of them from the NRTI class—which are also used to treat HIV—have been rendered ineffective due to widespread resistance. People who have taken earlier, less potent versions of these drugs may have compromised responses to the newer ones.

One of the more promising drug approaches being tested employs the HIV combination Truvada. Otherwise, the HBV drug development pathway is littered with failures. The development of the NRTI clevudine, a front-running HBV drug candidate in 2008, has been canceled due to potentially dangerous side effects. Hopes for using an approved drug, telbivudine, in combination with pegylated interferon to achieve better treatment responses were dashed due to increased rates of nerve damage that occurred in the study.

Other, more novel approaches to treating HBV using immune modulators and therapeutic vaccines are under active investigation, but studies are going slow. News on using gamma interferon to clear the virus may be forthcoming in late 2009.

With the central questions of when to start HBV therapy and how long to continue it still unanswered, the field is all but mired in stagnation. One bright spot, though, is the establishment of a new clinical trials network for HBV funded by the National Institutes of Health that expects to begin clinical research later in 2009.

While TAG's pipeline report usually covers the burgeoning drug development scene for hepatitis C virus (HCV), this year that report will appear in a separate booklet.

There is hope that the current lull in ARV development will be followed by some creative new products.

Tuberculosis Drug Development

After 40 years with no new class of drugs approved for treating tuberculosis, there are finally signs that new agents may soon contribute to improving cure rates for this age-old disease. Current treatments are effective, but they fall short when used in the real world due to resistance, toxicity, inconvenience, and interactions with other medications—and these problems are exacerbated in people with HIV and in children. Yet, notes TAG's Claire Wingfield, "while there are currently more new compounds being investigated to treat TB than there have been for decades, there are still too few sponsors and too few resources dedicated to moving these products through the drug development pipeline."

If 400 million people infected with HBV sounds like a vast number, consider that perhaps 2 billion people may have a latent tuberculosis infection. Most of them will never have TB symptoms, but the risk of developing active TB is far greater for people with HIV. Six to twelve months of single-drug treatment with isoniazid is effective at reducing this risk, yet this regimen is not widely prescribed. Studies are under way to shorten the treatment duration by using combinations of drugs.

If active TB is diagnosed or suspected, current treatments are effective—as long as the TB organism is susceptible to the drugs. The main focus of clinical trials for drug-susceptible TB is on shortening the time individuals must take their drugs; the goal is to reduce the number of patients who stop therapy before they are cured.

The big news in TB drug development, however, comes from a handful of drugs from new classes with novel mechanisms of action against TB—drugs that are also effective against TB that is resistant to the conventional drugs. Multidrug-resistant TB is a dangerous and deadly problem that has begun to appear in the past five years wherever TB outbreaks occur, often overlapping in places with high HIV prevalence. Because untreated and untreatable TB can be rapidly fatal in a person with HIV, the urgency to develop new classes of drugs has pushed industry to take up the challenge. TAG lists two new drugs from Tibotec and Otsuka that are specifically being developed to treat drug resistant TB.

Yet, as Wingfield warns, because there have been so few large clinical trials for new TB drugs in the past 40 years there are few people with experience in developing new TB drugs that meet modern regulatory standards. Greater investment in research going forward—not only for discovering and developing new drugs but on finding the best ways to test these drugs and then put them into clinical practice—will be increasingly critical if TB is to be controlled within the next few decades.

Tuberculosis Diagnostics in Development

If the lack of new drugs to treat TB seems like a daunting problem, consider that the main technique for diagnosing active TB infection was developed over 125 years ago and is only reliable about half the time. Furthermore, while there are new DNA-based technologies that can be used to diagnose TB with greater confidence, these are mostly useless outside of well-equipped laboratories and are of no use in most developing-world settings—the very places that TB is rampant. In fact, as TAG's TB project director Javid Syed reports, there is only one product under development that appears to be appropriate for use in rural heath care settings—places without reliable

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electricity or running water that are often far from urban centers. This product, a skin patch from Sequella, is applied to the arm. If a localized inflammation appears within three or four days an immune reaction to TB has occurred, which is diagnostic of a prior TB infection. As simple as that sounds, there are still many unanswered questions about the patch that ongoing research must address.

For settings with an intermediate level of resources, such as regional hospitals and larger clinics, many more techniques and products are under investigation to help improve current methods of microscopically examining stained sputum samples to identify TB organisms coughed up from the lungs. Many of these advances aim to make the diagnostic process more efficient. But even if diagnostic methods can be improved, simply obtaining a sputum sample that contains a sufficient amount of TB will likely remain a hit-or-miss process.

There is also a long list of techniques and products being developed for use in high-tech laboratories, though most will have little relevance to a person who has had to walk a day and a half to visit a part-time village clinic. Even a patch test that takes four days falls short. What's needed are point-of-care dipstick tests that can identify active TB and tell a doctor or nurse if the organism will respond to conventional drugs or if special drugs are required to

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Treating Earlier Saves Lives—But Treating Everyone Could End the Epidemic

By Bob Huff

At the International AIDS Conference in Durban, South Africa, in 2000, when the movement to provide universal access to antiretroviral treatment for people with HIV around the world began in earnest, guidelines for the standard-of-care treatment of people with HIV were similar everywhere: begin therapy when CD4 counts fall near or below 200 and use a non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor with two nucleoside RT inhibitors (NRTIs) such as stavudine and lamivudine. Subsequently, treatment guidelines have diverged. While stavudine is no longer recommended in the United States and other northern countries due to toxicity concerns, as the lowest priced antiretroviral (ARV) drug available in a generic form it remains a staple of regimens in the developing world. And though initiating therapy is now generally recommended once CD4 cell counts reach 350, this standard has been implemented in few African countries.

At the Fifth International AIDS Society (IAS) conference in Cape Town in July 2009, Daniel Fitzgerald of the Weill Cornell Medical College presented an important study demonstrating that initiating ARV treatment when CD4 counts are below 350 (but not waiting until they reach 200) reduces the incidence of tuberculosis and death. The CIPRA HT 001 study randomized 816 patients in Haiti to either begin ARV treatment at a CD4 cell count of 350 cells/mm^3 or to defer treatment until the CD4 count approached 200 cells/mm^3 or when symptoms of AIDS appeared. There were 23 deaths and 38 cases of TB in the group that put off starting treatment compared with only 6 deaths and 18 cases of TB in the group that started earlier. The results were statistically significant.[1] This study is especially important for understanding how to prevent death from TB, the biggest killer of people with HIV in the developing world and a disease that can be deadly at CD4 counts above the treatment threshold of 200 set for the prevention opportunistic infections associated with AIDS.

These results illuminate the gaps in current practices and the commitment of resources required to make universal treatment a reality. Reuben Granich, of the World Health Organization, presented a sobering look at the challenges but made a strong case for why investing in ARV access will be essential for ultimately controlling HIV.[2] In 2007, only 31% of people eligible for ARV treatment (those with a CD4 count under 200) were on therapy, with resource commitments falling short by about half of the need. As treatment guidelines change to recommend therapy earlier in the course of the disease, the access gap will be magnified. And it is likely that existing and emerging evidence will convince many that to prevent TB and other non-AIDS events, starting even sooner is better. But Granich is mainly concerned with the population benefits of suppressing HIV replication with drugs, and at the Cape Town conference he presented a theoretical model that suggests that the HIV epidemic could be tamed by universal testing and treatment for all with the virus, regardless of CD4 count. Control of the epidemic would come from reducing the spread of new infections by reducing the number of people who are infectious. This theory is based on observations that people with very low viral load levels have a much smaller chance of infecting others. If nearly everyone with HIV is on treatment, according to the model, the virus should virtually cease to circulate in the population.

While the costs and logistics of implementing universal testing and treatment are massive, Granich's model suggests that the effort would become cost-effective by 2030 as the epidemic comes under control. But what's most convincing about the model are the projections of the human and monetary cost of continuing on the current course of treating only those whose CD4 counts have declined. Anything less than universal testing and immediate treatment will allow the number of people with HIV to continue to grow, with no end to the epidemic in sight. ●

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control a drug-resistant strain. No product in the current TB diagnostics pipeline comes close to meeting these requirements.

Tuberculosis Vaccines in Development

As with any disease that affects millions of people, the most cost-effective intervention will be one that prevents infection or allows the body's immune system to resist or control an infection. This is why vaccines are the holy grail of infectious disease—one shot (and maybe a booster or two) and you are protected for life. There is an effective vaccine for tuberculosis called Bacille Calmette-Guérin (BCG), and while it is a lifesaver, it falls far short of the ideal. BCG given to children does not protect against pulmonary TB and the protection it provides against disease in the rest of the body only lasts until adolescence. Still, it is estimated that BCG immunization saves the lives of 40,000 children per year. Because scientists are building on the modest success of BCG, there is a relatively robust effort to discover and develop better TB vaccines—though initial steps aim for incremental progress. Each of the four new vaccine candidates listed in TAG's report is a booster designed to enhance the effectiveness of BCG. Farther down the line come candidates intended as improved versions of BCG. Overall there may be 50 vaccine candidates in the pipeline, notes TAG's Wingfield. As with TB treatments and diagnostics, this work could go faster if it received adequate research investment. Wingfield notes that an estimated $1 billion gap exists in just the funding required to test the most advanced TB vaccine candidates in large-scale clinical trials to prove that they work and can save lives.

Immune-Based Therapies and Preventive Technologies in Development

Lack of investment is not necessarily the problem for preventive vaccines and other technologies in restricting the transmission of HIV. As TAG's Richard Jefferys notes, after the failure of Merck's vaccine candidate in a large trial in 2007 (which seemed to make some vaccinated volunteers more susceptible to HIV infection), scientists have been scrambling to reorient the field away from its premature focus on product development and back toward basic scientific investigations about HIV, the immune system, and how the two interact over time. After years of commitment to developing vaccines that activate the T-cell wing of the immune system, the pendulum may be swinging toward stepping up research on understanding and enhancing B-cell immunity, which involves provoking antibody responses to infectious agents, and to exploring advanced concepts of vaccination that involve genetic manipulation of immunity.

Vaccines are the holy grail of infectious disease—one shot (and maybe a booster or two) and you are protected for life.

Vaccines and other treatments that affect the immune system are also being explored for their potential to help people who are already infected with HIV control their virus without drugs. But the news on this front has also been bleak. A nearly decade-long study of the immune system messenger IL-2 to boost the T-cell counts of people with HIV and AIDS finally ended in failure in 2009. Efforts to substitute immune control of HIV for antiviral drugs are up against a formidable barrier, since ARVs are so thoroughly effective and since even incomplete viral suppression has now been associated with health risks. Still, researchers continue to investigate the reasons why some people naturally manage to control HIV and live long lives without significant immune deterioration or disease.

The extraordinary efficacy of antiretroviral drugs is shaping the development of other approaches to HIV prevention. The development of microbicides—vaginally or rectally applied gels to prevent transmission of HIV via mucosal surfaces—has regained momentum after a few setbacks with early products. Older microbicide candidates create physical barriers or alter the chemistry of the vaginal environment to limit HIV transmission. The newer and more promising generation of microbicides will likely contain antiretroviral drugs to halt an HIV infection from taking root. Clinical trials of some of the newer candidates are in progress.

As Jefferys notes in his introduction, "The biomedical approach to HIV prevention generating the most optimism is pre-exposure prophylaxis (PrEP)." PrEP involves taking antiretroviral medications—either episodically or on an ongoing basis—by people who do not have HIV but who are at risk for becoming infected. Currently, Viread (tenofovir) and Truvada (the combination pill that contains tenofovir plus emtricitabine) are in clinical trials, but several other newer antiretrovirals with minimal toxicity are under consideration. Obviously, tolerability of the drug is a major requirement for PrEP since it will be taken by people without disease. Approaches like PrEP and microbicides fall far short of the ideal "one-shot protection for life" that a vaccine might promise, but for targeted communities with high rates of HIV transmission these products might help stem the tide of what remains an epidemic out of control.

Overall, the product pipelines covered in TAG's 2009 report show slow progress being made in bringing new technologies to bear on the HIV epidemic. When and if these developments will make a significant impact is uncertain. Economic recession and a flagging sense of urgency among the funders of research and health care could prove to be a larger impediment to achieving widescale lifesaving changes than either the daunting scientific or regulatory barriers. ●

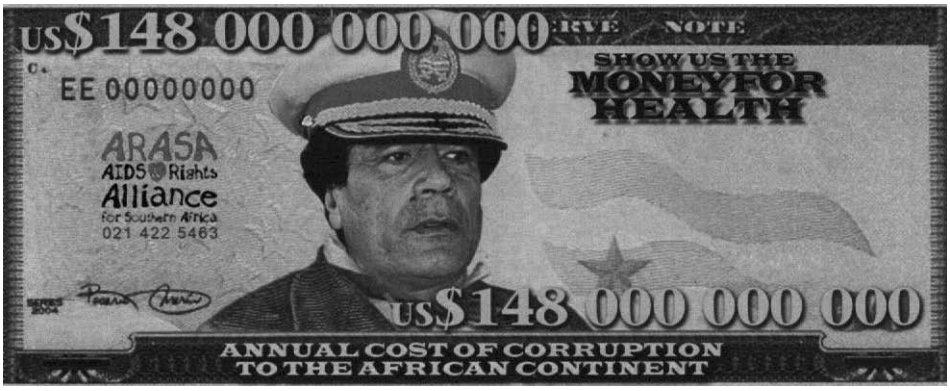
TAG's 2009 Pipeline Report is available online at www.treatmentactiongroup.org.

AIDS Is Not in Recession
Treatment Shortages Increasing

HIV is not in recession: This was the recurring theme of the IAS conference repeated in speeches and displayed on PowerPoint presentations.

BY SCOTT W. MORGAN

At the Fifth International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention in Cape Town, South Africa, this year, the AIDS Rights Alliance for South Africa (ARASA) won hands down for the most clever and effective advocacy campaign by handing out fake currency with international heads of state in denominations that reflect gross misuse of funds. A $250,000 currency note pictured Zimbabwe president Robert Mugabe enjoying his quarter-million-dollar 85th birthday party—a dollar amount that happens to be the rough equivalent of the cost of 10,500 courses of tuberculosis treatment. ARASA's video on YouTube, *Lords of the Bling, Volume 1*, is a barbed portrayal of the abysmal failure of African heads of state to meet their commitments in the Abuja Declaration to increase health spending to 15% of the national budget of each leader's country.



Among the fake currency notes bearing the slogan "Show Us the Money for Health" that ARASA handed out, a $700 trillion note sported the face of President Barack Obama, indicating the cost of the U.S. economic bailout. I can't exactly compare Mugabe's quarter-million-dollar birthday bash to the bailout, and I'm not downplaying the importance of the global crisis; the future of the AIDS epidemic would be considerably bleaker if other world economies followed the way of Iceland. However, as activists, public health professionals, researchers, and policy makers wrangle over each sliver of "the pie" allocated for global health, it's hard to grasp that a multi-trillion-dollar "pie" bigger than any global health budget in history was appropriated and put to work in a matter of months. A mere two fiscal quarters later, U.S. executives are lining their pockets with huge bonuses that buy Hummers and other conspicuous consumer "bling." In stark contrast, it has taken eight years to scale up antiretroviral (ARV) treatment to the point where only 4 million of the 33 million people who need it now or will need it in the future are actually on such treatment.

HIV is not in recession: This was the recurring theme of the IAS conference. It was repeated in speeches and displayed in PowerPoint presentations, and a pall hung in the rafters of the convention center as activists discussed the gravity of the financial shortfalls for treatment programs across the globe and the growing financial chasm that threatens to reverse the progress of ARV treatment rollout and scale-up that has been made in the past eight years.

Reports of "stockouts" (which occur when government and nongovernmental organization treatment programs do not deliver committed ARV treatment for enrolled patients) are increasing at an alarming rate. As of this writing, Uganda is investigating the deaths of 17 HIV-positive patients linked to stockouts. These people died during the past month after being unable to access their ARV drugs. Stockouts are occurring for a multitude of reasons, almost always leading back to lack—or poor management—of funding. Choke-points include ministries of health, ministries of finance, supply chains, and "registered" drug suppliers. Activists in Kenya, Malawi, Uganda, and Zambia recently carried out an "SMS pill check week" that uses SMS text messages on cell phones to gather information from public-sector health facilities about stockouts and low availability and are working to put a standard four-digit SMS code system in place that will allow patients and providers to report when drugs are not available. (See the interactive map at http://www.stopstockouts.org.) There is also mounting evidence that ARV treatment programs across sub-Saharan African countries are limiting or altogether stopping enrollment for fear they will not be able to handle the volume of current patients, let alone newly diagnosed people with HIV seeking treatment.

Widening ARV stockouts and growing lists of people with HIV infection waiting to gain access to treatment programs have consequences at the levels of both individual and general population health, to say nothing of the subsequent effects to community stability, overstretched family-based safety nets, and the ever-increasing population of orphans. As people on ARVs face the prospect of being temporarily turned away from treatment (after having been counseled regularly about the importance of strict

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adherence), family members and/or friends start sharing tablets, cutting them to make them last longer—or they stop taking them altogether. Consequences are certain and often swift: viral loads will increase, CD4 counts will drop over time, and opportunistic infections will result in clinical manifestations of AIDS. Resistance from unchecked mutating virus replication will make it more difficult to treat these people when or if they can resume treatment before they die. Higher viral loads may result in increased levels of transmission at the population level, and mutations in the virus make first-line treatment fail more quickly. First-line treatment in resource-constrained settings is already a colossal challenge to extending efficacy as long as possible. Access to second-line treatment is even more difficult—in large part due to huge price disparities: $80–$243 per person per year on first-line treatment to $620–993 per person per year for second-line treatment.

The global economy shows some signs of stabilizing. That's good news for everybody, but for some more so than for others. Recipients of the U.S. Troubled Asset Recovery Program ($303 billion disbursed as of March 2009) posted billion-dollar profits in the second quarter and plan to hand out hundreds of millions of dollars in executive compensation. In Africa, people with HIV are being turned away from treatment that costs less than $1 per day.

In comparing the funding gaps being faced by proven treatment-access programs like the President's Emergency Plan for AIDS Relief (PEPFAR) and The Global Fund to Fight AIDS, Tuberculosis and Malaria to the trillions of dollars that were pledged and disbursed in 2008 and 2009 to bail out Wall Street, one can only say "Show Me the Money for Health"!

Eight years ago, bureaucrats thought it was impossible to put people in resource-poor settings on ARV treatment; today there are 4 million people receiving life-saving treatment. The G20 and the global community must not shirk commitments and responsibilities to the 4 million people on ARV treatment or the estimated 29 million people who are HIV positive and will soon need access to such treatment.

As Nobel laureate Françoise Barré-Sinoussi concluded her plenary speech at the Fifth IAS Conference, "We can predict that reducing the international efforts on universal access to [antiretroviral therapy] because of the global recession will be a disaster . . . HIV is not in recession!" ●

Visit ARASA at http://www.arasa.info/healthmoney and sign the petition: An Open Appeal to African Heads of State.

Watch the Lords of the Bling, Volume 1 *video at http://www.youtube.com/watch?v=MkWoKgLhDVs.*

Blister Packs for ARVs Could They Improve Adherence?

Are we doing all we can to boost adherence to antiretroviral treatment? Can packaging help people take their drugs more consistently?

BY BOB HUFF

My doctor recently gave me a starter pack for a new medication. The pills were packaged individually in pop-out blisters and numbered 1 through 30. Every day I popped out a new pill and looked at the pack to see how many I had taken so far and how many remained to be taken. It was simple, easy, and kind of fun to interact with the pack and track my progress. I remembered my experience of a year ago when I had to take daily eye drops following surgery. I had the bottles lined up on a shelf so I could remember to use them, but I still would forget to take my doses sometimes—or I would forget if I had taken them earlier, or would lose track of which one I had taken and which I hadn't. I remember thinking at the time, "Even though I could go blind if I don't get this right, I can't get this right." I don't think they can put eye drops in a blister pack, but I didn't have any problem at all taking my preprogrammed course of pills a year later. Meanwhile my daily vitamin D supplement dispensed from a bottle is hit-or-miss at best.

Putting pills into blister packs is called unit-dose packaging. Packaging designed to help the consumer remember to take the pills is called adherence-prompting packaging. A blister pack that prompts for the day or time a dose is to be taken is called a calendar blister pack. Studies have shown that this kind of packaging can improve adherence and improve outcomes from medications; yet in the United States, they are rarely used.

Adherence means understanding why, how, and when to take a medication and sticking to it once you have begun. Studies of medication adherence have shown that, in general, people have a hard time taking their pills. Depending on the drug and the purpose, adherence rates range from 20% to 100%, with good adherence for chronic disease treatment estimated at 80% or better. But that's not good enough for HIV.

The virus replicates so fast, and the mutation rate is so high, that if drug levels drop there is a chance that a drug-resistant mutant will spin off and take over the viral population despite the drugs. With some antiretroviral (ARV) regimens for HIV, this could happen after missing just two or three days' doses. The best chance of keeping HIV fully suppressed comes from maintaining adherence that is 95% or better.

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The problem is that adherence is difficult, and some drug regimens make it even more difficult. There are many reasons for nonadherence to HIV drugs. Some people may want to avoid a wave of nausea or diarrhea that follows a dose. Others get tired after years of pill taking and opt for a break. Some forget, and go to bed without taking their pills. Weekend schedules, partying, or travel may upset a routine and cause missed doses. Complicated regimens with food restrictions are harder to take consistently than all-in-one pills. Once resistance to a first regimen has developed, subsequent regimens are usually more complicated and have more restrictions. Some doctors would prefer a patient not begin taking HIV drugs until they are certain that the individual can develop the adherence habits that will make the treatment a success. But in general, studies have shown, doctors assume that patients do what they are told once they leave the office. Unfortunately, they do not.

In the United States, pharmaceuticals are typically distributed in bulk packaging, such as in plastic bottles that contain 500 or 1,000 tablets. The U.S. Food and Drug Administration requires stability testing for drugs in the packaging they are distributed in. This means the drugs have been shown to be stable in their unopened bulk pack bottles for six months or more. But once the bulk pack gets to the pharmacy, it is opened and the pills for an individual's prescription are counted out and repacked in an amber, child-resistant pill container. ARVs, however, are typically shipped in smaller bottles containing a 30-day supply that can be labeled and given to the patient unopened, though some pharmacists may repackage the pills in an amber container. The containers must be child-proof, but in effect that often means that they are difficult to open, especially for seniors. Labeling on pill bottles can also be difficult to read, which can lead to dangerous dosing errors.

To help keep track of their complex regimens (and people with HIV often take many other pills a day on top of their ARVs) some people put a week's worth of pills into a special seven-day container with individual compartments for each day of the week. This is a do-it-yourself form of unit-dose packaging, and it is a great way to boost adherence and avoid skipping or inadvertently doubling up on doses. But it still requires time and organizational skills on the part of the patient. Having the pills come in a bottle makes more sense for people who use pill organizers and take multiple medications. But for people on simple, once-daily medications, a calendared blister pack might be an adherence booster. One packaging maker is researching custom multiple medication packs that would be created at the pharmacy for people with more complicated daily regimens.

How Packaging Can Help Improve Outcomes of ARV Therapy

With unit-dose packaging, each dose stays in its own protected container until it is used. In the United States, only a few medications, like short courses of antibiotics, are blister packed. Birth control pills have long been supplied in unit-dose packs with a dial calendar feature that prompts adherence. One study found that compliance with birth control pills reached 92% while compliance with organ rejection drugs following transplant surgery was only 82%.[1] Calendar blister packs were also reported to improve adherence at a sexually transmitted disease clinic in South Africa.[2] A systematic review of eight randomized trials concluded that reminder packaging "may represent a simple method for improving adherence."[3]

The most advanced type of packaging is a leaflet pack that opens up and displays all of the pills on one card. There is educational information printed on the card, and there is a sleeve to hold the package insert; labeling is clear and easy to read. The pills push through the blister backing without effort or spilling. These packs get high marks for child resistance, yet are easy for seniors to use. It is simple to tell at a glance where you are in the month and how long before you need to refill the prescription. A downside for HIV is that the packs are not discreet and some patients may not wish to carry a product that prominently displays the name of the drug.

As a report from the Institute of Medicine concluded in its review of studies of unit-dose packaging, "The strategy of using calendar blister packs could help large numbers of patients (including seniors, children, and those challenged by cognitive, physical, and functional impairment) take their medication more reliably and safely, and enhance their treatment outcomes."[4]

The current generation of HIV treatment options is fairly good, and forthcoming drugs promise to be even more tolerable and convenient as more complete regimens are formulated into single, daily pills. Yet a small percentage of patients develop drug resistance due to inadequate adherence within a year after starting HIV therapy. Since it is difficult to predict who will and won't be adherent, it makes sense to give all patients a better shot at treatment success by offering packaging that helps make adherence more likely. ●

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TAG NEW WAYS TO CONTRIBUTE

Supporting TAG is a wise investment in AIDS treatment advocacy. With a small but well-organized and highly respected staff of professionals, every donation to TAG brings us one step closer toward better treatments, a vaccine, and a cure for AIDS.

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Support TAG's Research in Action Awards
Each December, TAG's Research in Action Awards event honors some of the most important scientists, artists, celebrities, and activists working for better treatments, a vaccine, and a cure for AIDS. Past honorees and presenters have included New York State Senator Tom Duane, director and artist John Waters, award-winning playwright Terrence McNally, actor Nathan Lane, and stage and screen actress Kathleen Turner, among many other scientists and dedicated AIDS activists. Join us this December!

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If so, you can double or even triple the donation you make to TAG. If your company offers a matching gifts program, please complete its matching gift form and send it in with your donation to TAG.

Make a gift of stock to TAG
Gifts of stock benefit TAG and the donor. The donor who purchased the stock at a lower price receives the tax-deductible benefit of the stock's price on the day it is transferred to TAG.

For more ways to support TAG, please visit our website at www.treatmentactiongroup.org or contact Joe McConnell at 212.253.7922.

TAG BE INVOLVED

About TAG

Treatment Action Group is an independent AIDS research and policy think tank fighting for better treatment, a vaccine, and a cure for AIDS. TAG works to ensure that all people with HIV receive lifesaving treatment, care, and information. We are science-based treatment activists working to expand and accelerate vital research and effective community engagement with research and policy institutions. TAG catalyzes open collective action by all affected communities, scientists, and policy makers to end AIDS.

Program areas include antiretroviral treatments, basic science, vaccines, prevention, hepatitis, and tuberculosis.

Join TAG's Board

TAG is always seeking new board members. If you are looking for a great place to invest your time and talents, please call Barbara Hughes, TAG board president, to learn more about board opportunities with TAG.

Call 212.253.7922 or email:
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TAG is a nonprofit, tax-exempt 501(c)(3) organization. E.I.N. 13-3624785

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