"tough sell, perhaps because there is an emphasis on treatment but not prevention," Chaisson told a press conference. "There seems to be a fear of developing resistance and of toxicity, but these are not warranted. Isoniazid has been studied perhaps more than any other treatment in medicine."

TB prevention, diagnostic and treatment services must become core functions of all HIV services in countries with a high prevalence of TB, De Cock said. People with HIV need to be screened for TB and get prophylaxis and people with TB need to be screened for HIV: "We need one-stop shopping." — Ann Silversides, Toronto

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Microbicide update

The US$62-billion Bill and Melinda Gates Foundation has poured money into microbicide research, because a woman "should never need her partner's permission to save her own life," Bill Gates told the opening session of the XVIth International AIDS Conference in August.

Microbicides are applied to the vaginal or rectal surface before sex in order to prevent HIV infection. Microbicide research began in the early 1990s, but it did not receive a great deal of funding or attention until a few years ago after the establishment of the non-profit International Partnership for Microbicides in 2002 brought new energy to the field.

There are now 5 gels, which must be applied immediately before sex, in phase 3 clinical trials. The products in earlier stages of development use direct antiretroviral effects. For example, a gel form of the drug tenofovir is in phase 2 trials.

A long-term goal is to develop a formulation or device that allows for the slow release of microbicide over a period of days or months. However, researchers are concerned that limited clinical trial capacity in countries with high rates of HIV infection is hampering advances. — Ann Silversides, Toronto

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Canada falters on promise of AIDS drugs for Africa

Canada will immediately review the federal legislation intended to facilitate the timely production and export of affordable, life-saving drugs to the developing world, pledged federal Health Minister Tony Clement at the XVIth International AIDS Conference in Toronto.

The legislation, introduced more than 2 years ago by the former Liberal government, has come under fire because no drugs have been shipped from Canada.

Apotex, the Canadian generic company that stepped forward and developed a triple-combination HIV/AIDS drug for export, has been frustrated by the lengthy process. But company officials say they are more optimistic now that the World Health Organization has given the drug its stamp of approval.

The WHO prequalification, which was granted just before the AIDS conference began in August, gives developing world countries "a sense of security [that] now they can make a free choice" to seek to import the Apotex drug, explained Bruce Clark, vice-president of regulatory affairs.

Canada received kudos as the first country to pass legislation allowing its generic drug manufacturers to produce copies of patented medicines to be shipped to those who need them.

The vast majority of HIV/AIDS drugs now used in the developing world are manufactured by generic drug companies in countries that, until recently, did not have to comply with international patent rules. India, for example, supplies a significant proportion of HIV/AIDS drugs under the Global Fund. It passed legislation last year to comply with the patent rules, but can still produce copies of AIDS drugs patented in the earlier years of the epidemic.

The Canadian legislation became possible as a result of a provision adopted 3 years ago by the World Trade Organization, whose members agreed that the health needs of people in the developing world should take precedence over international patent agreements.

With the non-governmental organization Médecins Sans Frontières agreeing to act as "broker," Apotex developed a 3-in-1 drug for which there is no brand name equivalent. The drug combines ziduvodine (AZT), lamivudine (3TC) and nevirapine.

Canapress

Thouands of people gathered for an AIDS vigil in Toronto on Aug. 17.

However, the Apotex drug has not yet been exported. The company says it is hung up in negotiations to obtain voluntary licences from the 3 patent-holding pharmaceutical companies involved. Such negotiations must take place, and be unsuccessful, before generic companies become eligible under the law to apply for compulsory licences.

As part of its application for a compulsory licence, Canadian law also requires generic companies to identify the developing country that is the intended recipient of a shipment. To date no country has publicly come forward to request the drug. Apotex's Clark attributes that reluctance to a country wondering "why should they be required to identify themselves in someone else's process." But the WHO pre-qualification should make countries more willing to come forward, he said, and Apotex is preparing its compulsory licence application.

Meanwhile, Anil Soni of the Clinton Foundation said he would be "thrilled" to see Canada issue a compulsory licence to export copies of life-saving drugs. Soni noted that the Apotex price for the new combination drug — the company is charging only its cost — is one-third less than what is now being

charged in the developing world. (Two Indian generic companies, which did not have to seek voluntary or compulsory licences, recently received formal regulatory approval for the same combination pill that Apotex has produced.)

The Clinton Foundation contracts with companies to supply needed drugs in over 60 developing-world countries. — Ann Silversides, Toronto

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"Damage control" surgery techniques used on soldiers

Surgical "damage control" techniques developed at US urban trauma centres to keep victims of multiple gunshot wounds alive are now being used to save the lives of soldiers injured in Iraq and Afghanistan.

The military use of techniques pioneered in American inner cities is a reversal of the usual historical pattern, in which war has stimulated medical advances that subsequently found application in the civilian world.

"It's a real paradigm shift," said Dr. C. William Schwab, chief of traumatology and surgical critical care at the Hospital of the University of Pennsylvania and professor of surgery at the University of Pennsylvania School of Medicine. "The history of trauma surgery has been a history of war. [Now] so much of what is going on in Iraq is being modelled after American urban trauma centers."

Schwab recently completed a stint as a senior visiting-surgeon at the US Regional Medical Center in Landstuhl, Germany, where he operated on wounded US and Canadian soldiers. He is the first to serve in the volunteer program developed by the American Association for the Surgery of Trauma and the American College of Surgeons' committee on trauma.

Many of the techniques of damage control surgery were developed in the late 1980s and early 1990s at urban trauma centres after the introduction of 9-mm semi-automatic pistols in the US led to an increase in the number of young men with multiple penetrating wounds.

Taking the time to perform definitive surgery immediately often resulted in "a fully repaired but dead patient." Schwab and his colleagues instead began to use abbreviated resuscitative surgery to halt the downward spiral associated with the lethal triad of acidosis, hypothermia and coagulopathy, which often develops in the catastrophically injured.

To control bleeding from damaged vessels or restore flow where needed, they inserted plastic tubes or vascular shunts, "like a quick fix in a broken plumbing system," said Schwab. They clamped, stapled or sutured bowel ends to control intestinal spillage and contamination. After packing all raw or dissected surfaces, they then temporarily closed the abdominal or chest wall.

Patients were then moved to intensive care. After restoration of normal physiology and re-examination of all injuries, the surgeons then did definitive repair surgery a day or so later.

In a retrospective review of medical records of 22 patients with penetrating abdominal wounds with combined major vascular injury and 2 or more visceral injuries (*J Trauma* 1993;35:375–83), the damage control techniques could have resulted in a survival rate of 77% compared with 11% using the usual (definitive laparotomy) techniques. A 2000 review article (*J Trauma* 2000;49:969–78) found a survival rate of up to 60% across several studies.

During his Navy days, Schwab had observed a "damage control" call on an aircraft carrier, and watched the ship's crew rush into a flooding compartment to seal the damage.

The steps that surgeons take to save life while restoring physiology were also best described as "damage control," Schwab decided. The strategy, which defied the traditional approach, has been hailed as a major advance in surgical practice, and its use has spread beyond abdominal injuries to cross all surgical disciplines.

Most recently, wounded soldiers in Iraq or Afghanistan have undergone damage control in-country by forward surgical teams. The wounded are then quickly transferred to a US military hospital in Balad, north of Baghdad, usually just for a day. They are then airlifted to Landstuhl — some arrive within 24 hours of being wounded — for stabilization and to begin definitive care.

Schwab wonders if, in another 20 years, damage control will pass into surgical history like ultra-radical mastectomy or truncal vagotomy, as physicians learn how to prevent the downward physiological spiral that makes it necessary. "One can only hope," Schwab concluded. — Janet Brooks, Salt Lake City

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Hospital of the University of Pennsylvania

Dr. Schwab (right) recently used his "damage control" technique on Canadian soldiers.