

assembled governments will then decide the future of its proposals.

Tony Blair, the British Prime Minister, discussed the report at 10 Downing Street, London, last November, at a working breakfast with WHO's Director-General, Dr Gro Harlem Brundtland; the Ugandan High Commissioner, Professor George Kirya; Chris Viehbacher of GlaxoSmithKline; other pharmaceutical industry leaders; and representatives of the European Commission and charitable foundations.

Although Clare Short's spokeswoman described the breakfast as "private", it is clear that the main issue was how to implement the report's recommendations. According to the report itself, while Europe is more or less on board, the US position is less clear. "The European Commission has laid much of the groundwork for this agenda in Europe through their Plan for Action," the report states, "resulting in a European Parliament Resolution. Further work will need to be done to secure the commitment of European governments and industry to work in partnership on this agenda. Working with the US Government and gaining their support will be particularly critical given the importance and size of the US Industry. Continued dialogue directly with US Industry may be a promising way forward. There may be scope for tabling this agenda through regional and global industry associations".

According to Dr Brundtland, improving access to medicines will not be easy. "It is a complex struggle where governments, a range of actors in the private sector, and civil society all play important roles".

On the company side, John Patterson of AstraZeneca, commented: "this is a many-faceted challenge and needs the best efforts of all of us, in partnership, to make an impact. Companies are committed to making their contribution ... by providing more and better medicines so that they can be accessed more easily by patients in the developing world, without undermining the ability of industry to operate in the developed world."

Chris Viehbacher said "Glaxo-SmithKline welcomes this Report." He claimed that his company already offered "sustainable, not-for-profit preferential prices for our antiretrovirals and antimalarials to a wide range of customers in all the least developed

countries and all of sub-Saharan Africa — a total of 63 countries". But increasing the scope of preferential pricing "requires a sustainable framework, incorporating ... barriers against diversion of product. [This report] is a very useful step towards meeting these needs."

The full report is available from: URL: www.dfid.gov.uk/Pubs/files/access_to_medicines_report28.11.pdf ■ Robert Walgate, *Bulletin*

Vaccine against cervical cancer passes "proof of principle"

A recombinant vaccine against the human sexually-transmitted papillomavirus type HPV-16, which is thought to cause as many as half of all cervical cancers, has been shown to prevent long-term HPV-16 infections in a trial with 2400 young women.

This Merck vaccine is the first of what may be several candidates for a vaccine against HPV infections, some prophylactic and some therapeutic, but it has come through with flying colours. Although the trial was designed to measure HPV infection and not cancer, which occurs with only a small percentage of infections, it may prove significant that nine women in the placebo (unvaccinated) group developed clinical lesions — the beginning of cancer — but none did so in the vaccinated group (*New England Journal of Medicine* 2002;347:1645-51).

Sonia Pagliusi of the WHO Initiative for Vaccine Research told the *Bulletin* "This is a very interesting vaccine for developing countries as they have 80% of the world's cervical cancer. And they have few other options. They can do the Pap [smear test, requiring cytological observations] but it's not very effective — it's not working. People take the test, but follow-up is difficult".

According to Andreas Ullrich, who works on national cancer control planning issues at WHO, "Cervical cancer is a high priority: it's first or second in developing countries, among all cancers."

Pagliusi added: "This is the first proof of principle of an HPV vaccine in humans. But it is important to know if the result is relevant to the disease". So it will be necessary to do larger trials measuring the effect of the vaccine on

precancerous lesions. "HPV is not like HIV — it's only a small percentage of infections that go on to cause cancer."

Moreover, there are 15 high-risk HPV viruses. Type 16 causes 50% of cases of cervical cancer. Type 18 causes an additional 10–15%; then Types 31, 33, 45 and others account for another 5% or so. An ideal vaccine should cover several virus types. "But the object of this trial was a proof of principle, which would be more difficult to show with the other viruses because they are relatively rare. You'd need even bigger trials to get a statistical result" said Pagliusi.

Vaccines are the most cost-effective interventions to prevent life-threatening infections "And we hope we will need to vaccinate only once in a woman's lifetime, before they become sexually active — with a three-shot course like HepB" said Pagliusi.

The Merck HPV vaccine is based on the same principle as HepB: a recombinant capsid protein. The trial has so far only measured protection for 1.5 years. But it is a great beginning. ■

Robert Walgate, *Bulletin*

Peru tries vinegar against cervical cancer

Women in the isolated Amazon jungle region of San Martín in Peru are participating in a research programme to prevent cervical cancer, which kills an unusually large number of women in that country — some 40 per 100 000 women per year compared to just over 9 per 100 000 per year in North America, according to figures from WHO's International Agency for Research on Cancer.

Under the programme the women in San Martín, many of them small farmers who live far from the nearest health post, are being diagnosed and treated for precancerous lesions in one visit, rather than having to return at a later time to learn the results of the usual Pap smear test. Before the programme began, only 23% of the women with abnormal Pap smear tests had received follow-up treatment in San Martín, according to a survey done before the screening and treatment programme began.

The programme is sponsored by the Pan American Health Organization and the national and departmental health

ministries, with financing from the Bill and Melinda Gates Foundation through the Alliance for Cervical Cancer Prevention.

Midwives are being trained to perform a gynaecological examination and screen women with an experimental method known as Visual Inspection with Acetic Acid (VIA), that is, vinegar. Application of the vinegar causes suspicious lesions to appear white with clear borders.

If such a lesion shows up, a physician performs a second VIA test under magnification. If the existence of abnormal cells is confirmed, the women are offered a biopsy and immediate treatment with cryotherapy, the freezing of the lesions.

A research study conducted on women aged between 25 and 55 years in Zimbabwe and published in *The Lancet* (1999;353:869-73) showed that the VIA screening method detected "about 77% of all abnormal tissue, about the same rate achieved with Pap smears according to Silvia Robles, programme coordinator for noncommunicable diseases at the Pan American Health Organization (PAHO) in Washington. Robles told the *Bulletin* the number of false positives is somewhat higher than with a Pap smear, which has a relatively low sensitivity. She added that a false positive is better than a false negative in these cases.

Robles said the programme in Peru is designed to determine if this screening and treatment method will work under "real life conditions" in developing countries, where transportation is difficult, money for expensive equipment is scarce, and there are frequent changes of government.

More than 160 community leaders and government workers have been trained to teach women about cervical cancer and encourage them to participate in the programme. The equipment used is portable and the health workers can take it by river to women who live far from the nearest health post.

Since the women can be treated the same day they are screened, it is expected that more women will get treatment than would have if they had to return to the health post to learn the results of a Pap smear. Marie Andrée Diouf, Director of PAHO in Peru, said the programme, which began in 2000, is already a

success. "It is saving many women's lives," she said.

In Geneva Sonia Pagliusi of the WHO Initiative for Vaccine Research told the *Bulletin* she considered VIA to be "a new method still under evaluation — it's in the research stage in India, comparing different methodologies. It's promising but not yet proven. WHO has no formal recommendation to use it." ■

Terri Shaw, *Lima*

Is breast cancer linked to smoking?

Women who begin smoking during the five years after their first menstruation were 70% more likely to develop breast cancer than non-smokers, according to a study by Canadian researchers (*Lancet* 2002;360:1044-9) which hit headlines around the world.

Derek Yach, WHO's Executive Director of Noncommunicable Diseases and Mental Health, called the Canadian study "important", but stressed that additional work is needed to confirm a definitive link between smoking and breast cancer. "If [the link] proves to be real," says Yach, "the breast cancer issue would be additional motivation to quit smoking."

While the link between smoking and maladies such as heart disease, stroke and lung cancer is well proven, relating breast cancer to tobacco has been more elusive. Some studies have suggested a positive link, others found no relationship, and a few have suggested that smoking has a protective effect, Yach said.

In the current study, a team of researchers led by epidemiologist Pierre Band, now at Health Canada, evaluated the risk on the basis of the biology and physiology of human breast development. Breast tissue only fully develops after a full-term pregnancy. Until then, the immature cells are more susceptible to environmental carcinogens, such as those in cigarette smoke, he argued.

The team analysed the responses to a health questionnaire answered by more than 2000 women living in British Columbia, about half of whom had been diagnosed with breast cancer. The researchers found that women who began smoking in the five years after their first period were 1.7 times more likely to develop premenopausal breast cancer than non-smokers.

For women who smoked heavily but had never been pregnant, and thus whose breasts never fully matured, the risk of pre-menopausal breast cancer jumped more than sevenfold, this study suggested, no matter when the women took up the habit.

Breast tissue before the first menstruation may be even more vulnerable, according to studies of breast cancer among Japanese women who survived atomic bomb blasts. Too few women in the Canadian study began smoking at very young ages for the researchers to evaluate the risk, "but it is possible that smoking before the first occurrence of menstruation would even be more detrimental," Band says.

The study also found evidence of the controversial protective effect that tobacco appears to have *against* breast cancer in women past their reproductive years. Women who began smoking after a first full-term pregnancy (so their breast tissue had matured) and had gained weight since their teen years halved their risk of developing *post*-menopausal breast cancer compared to women who never smoked but had gained weight. *Post*-menopausal breast cancer is associated with obesity, and scientists think the biochemical reaction that converts the hormone androgen to estrogen, the female hormone associated with breast cancer, occurs in fat tissue. Smoking inhibits the reaction, Band explains.

The findings are worrying in light of recent statistics that indicate smoking among young people and women is on the rise. With information from 43 countries to date, the Global Youth Tobacco Survey estimates that 20% of children between 13 and 15 years of age smoke worldwide, while in some countries the figure jumps to more than 60%. Nearly a quarter of the young smokers lit up their first cigarette before age 10. And in some countries, including Denmark, Germany and the United States, young (14-19 year-old) women who smoke outnumber the young men who do.

The Tobacco Free Initiative programme at WHO reports that rates of breast cancer have been "eerily tracking" the increase in female smoking during the past several decades. According to the International Agency for Research on Cancer, more than 1 million women worldwide were diagnosed with breast cancer in 2000. About half of those cases occurred in less developed countries. ■

Charlene Crabb, *Paris*