

RealHealthNews

Real action and research

The newsletter of real action and research • No.0 • November 2004

Contents

- 3 Biotechnology to "save millions of lives"
- 4 Tanzania study shows IMCI cost-effective
- 5 Polio vaccine: when science is not enough
- 6 AIDS transmission could be stopped before 2015
- 7 Child survival MDG to be reached in Brazil
- 8 Malaria vaccine breaks 50% barrier
- 9 "New dynamic" to support health research
- 10 Cold chain elimination proven by 2008?
- 11 Rotavirus: twice as common, twice as important
- 12 Only African science can beat HIV/AIDS

**Special issue:
Research for
the MDGs**

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> Health System Science

India plans to slash infant mortality

Home-based care could save a million lives a year

SUMMARY

Good research by SEARCH, an Indian NGO, supported by national scientists, has created an evidence-based community health intervention for mothers and children which the Indian government will now introduce to five states.

> by Rupa Chinai

INDIA: The Government of India is aiming to cut the high mortality amongst neonates and young infants fourfold in five Indian states through a well-researched programme of home-based care given by locally trained village workers.

Initiated by the Indian Council of Medical Research (ICMR), the project is based on the approach of an NGO, SEARCH (Society for Education, Action and Research in Community Health) in Gadchiroli district of Maharashtra.

Research on the SEARCH home-based neonatal care approach indicated that village care workers can cut the infant mortality rate (IMR) from 120 to 30 per thousand live births – a fourfold reduction.

India's IMR stands at 68 deaths per thousand live births for babies less than a year old, according to the National Family Health Survey. The 'National Population Policy 2000' aims to reduce this to 30 deaths before the year 2010.

But Vinod Paul, advisor to the Ministry of Health, told *Real Health* "Government interventions have failed to make any dent on newborn mortality. Nearly 2.5 million children die each year in India, and up to 62% (1.2 million) of all infant deaths occur in the first four weeks of life."

If this latter figure could be cut fourfold, nearly a million lives could be saved every year in India alone.

ICMR will attack and simultaneously research this problem in five project states

[continuing on page 2 >](#)



– Bihar, Maharashtra, Orissa, Rajasthan and Uttar Pradesh – covering a rural population of 6 million. A baseline survey of existing conditions of neonatal and infant mortality is already finished, and training nearly complete. Next year the project will be launching two years' intervention, to be followed by an evaluation phase.

The intervention phase of the project will compare two differing models. The first employs an Anganwadi worker (an existing worker in the present public health system, who provides services under the 'Integrated Child Development Scheme' to pregnant women and children).

The Anganwadi worker will deliver a package of 'home based care', focused on tackling the three main causes of newborn death – pneumonia, birth asphyxia, low birth weight and immature delivery – working in partnership with a trained birth attendant, traditional in rural India, and an auxiliary nurse midwife attached to a public health centre.

The second model replaces the Anganwadi worker with a village-based health worker, nominated by the community she comes from. This worker, called a 'shishu rakshak' (protector of children), will deliver the 'home based care'.

At ground level, the project will be monitored and managed by a team of selected NGOs and research organisations from the target states.

Says Vinod Paul, "By replicating the SEARCH model, the government aims to create a cadre of village based workers, who along with the traditional midwives, the Anganwadi worker and the auxiliary nurse midwife, will tackle the main causes of infant death."

"... Nearly 2.5 million children die each year in India, and up to 62% (1.2 million) of all infant deaths occur in the first four weeks of life"

The evidence that ordinary village women can work such miracles in areas with no doctors, comes from 39 villages in Gadchiroli, leading a dramatic decline in infant mortality there from 1993-98. The findings of a study of five years of SEARCH's research data were published in *The Lancet*.

SEARCH's strong research base, based on training received at John Hopkins University in the US, has attracted the attention of international donors. The NGO's work with women and children is being supported by the Indian Government's Ministry of Health, Ford Foundation, MacArthur Foundation, Save the Children (US), and CRY (Child Relief and You).

The current five-state project draws upon extensive subsequent data from

SEARCH's field and control areas (project and non-project areas) to gauge the communities' needs, and estimate the impact of the interventions. Trained data collectors worked with the reports of health workers and traditional birth attendants, and collected further detailed information on the population and incidents of birth and death, corroborated with the government's own registers.

The socio-economic profile of the population was also analysed, and repeated prospective studies of all vital events ensured that no information was missed. Validation and compilation of data was further cross-checked by a cadre of field supervisors, and fed to computer analysts at SEARCH's own research centre.

The validity of the SEARCH approach to home-based neonatal care was extensively studied by senior government officials and health policy experts.

The experts and officials carefully studied the research methodology and data, visited the Gadchiroli villages, and discussed the intervention with the community, health workers and others.

The well-researched model was then recommended as worthy of replication. The experts suggested suitable adaptations regarding certain operational issues, while stressing the various strengths of the approach that need to be rigorously maintained.

SEARCH aims at developing evidence-based, simple, appropriate, low-cost solutions, which empower rural people to look after their own health. According to SEARCH the cost of delivering the home-based neonatal care package in villages in the year 1997-98 was Rs.200 per newborn (US\$4); Rs.9 000 per village (US\$200); Rs.4 000 per death averted (US\$90); and Rs.64 per life year saved (US\$1.60). ■

READ ON

Abhay Bang, Rani Bang et al.,
The Lancet, 1999, vol 354, issue 9194,
pages 1955-61

Indian Council of Medical Research
<http://www.icmr.nic.in/>

> Biology for Health

Biotechnology to "save millions of lives"

10 hot technologies need developing country collaboration

SUMMARY

Genomics and biotechnology could provide rapid diagnosis, prevent HIV/AIDS, and promote peace through international collaboration, says an international group of scientists.

> by Prakash Khanal

GLOBAL: Twenty-eight prominent scientists from the developed and developing nations say that new biotechnologies will help to meet the UN Millennium Development Goals (MDG) set in the year 2000.

Their report, *Genomics and Global Health*, was prepared by Genomics Working Group of the Science and Technology Task Force of the UN Millennium Project, and released at an international science journalists' conference in Montreal on 7 October.

Co-author of the report Peter Singer told journalists "genomics and biotechnology can save millions of lives". Managing Director of University of Toronto Joint Centre for Bioethics, Singer believes that the ten new biotechnologies identified by the task force (see box) could help meet five out of eight MDGs.

With biotechnology, simple molecular diagnostic tests are conceivable for diseases like TB, Hepatitis C, HIV/AIDS, malaria, kala-azar, Japanese encephalitis and several other

common diseases prevalent in the developing world.

"Imagine a world in which a doctor in the poorest country can instantly diagnose these diseases, or provide women a way they can prevent HIV/AIDS," said Singer. (See our story *AIDS transmission could be stopped by 2015*) "This report is about pathways to get there to save millions of lives and billions of dollars."

Even arsenic pollution could be tackled, argued Singer. "The largest mass poisoning in human history takes place each year in Bangladesh" said Singer. Arguing that this is caused by bacteria interacting with the substrata, bringing ground arsenic into the well water, he said "Bangladesh could profit from DNA sequencing to learn how to control the bugs."

Simpler storing and transport of vaccines (see our story *Cold chain elimination proven by 2008?*), refreshing polluted water, curing or preventing sexually transmitted diseases among young women, painless (needle-less) vaccines to avoid pain and cross contamination, enriched crops to counter micronutrient deficiencies, new

vaccines (see our story *Malaria vaccine breaks 50% barrier*), new cures for bacterial diseases, cheap production methods for insulin and other drugs, and faster drug discovery are possible, the report says.

Southern research organisations also need to share existing biotechnical knowledge, the report argues. Countries like China, Cuba and India are already using gene technology in the production of new medicines. Singer added that diseases cross national borders,

and technological collaboration between countries like India and Pakistan could even become a platform for building peace.

"This type of technology is approachable and is no longer expensive," said Abdallah Daar, co-director of the Canadian Programme on Genomics and Global Health, also a co-author of the report. "Developing countries themselves have to be in the driving seat and awareness has to be raised for this crucial factor," said Daar. ■

THE TEN KEY BIOTECHNOLOGIES

- Easy-to-use molecular diagnostic tests for the presence or absence of pathogen-associated molecules, such as DNA or protein, in a patient's blood or tissues.
- Recombinant vaccines against infectious diseases, which promise to be safer, cheaper and possibly easier to store and transport than traditional vaccines.
- Reducing pollution and making water safe to drink through bioremediation — the potential exploitation of microorganisms with remarkable biochemical properties.
- Creating microbicides for female-controlled protection against sexually transmitted disease like HIV, both with and without contraceptive effect.
- Better drug and vaccine delivery methods that avoid the use of needles and reduce cross contamination.
- Bioinformatics to identify drug targets and to examine pathogen-host interactions.
- Genetically engineering crops to counter nutritional deficiencies.
- DNA sequencing pathogen genomes to understand their biology and identify new antimicrobials.
- Recombinant technology to make therapeutic products (such as insulin for the growing epidemic of diabetes) more affordable.
- Combinatorial chemistry for drug discovery.

> Health System Science

Tanzania study shows IMCI cost-effective

Even partial IMCI is cost-effective, but family component needed, and inequity still endemic

SUMMARY

The Integrated Management of Childhood Illness package applied at health facilities, without direct improvement of family and community practices, is still worth supporting, although it decreases child mortality only slightly.

TANZANIA: A complex study of a real-life health intervention, just published in *The Lancet* – part of the Multi-County Evaluation of the Integrated Management of Childhood Illness (IMCI) – has shown it to be cost-effective, even though IMCI in the areas studied did not include what some consider to be its crucial third component: improving family and community health practices.

IMCI is a much-heralded UNICEF-WHO package of key, combined measures to improve child and maternal health. In 1996, Tanzania was one of the first countries in Africa to announce their intention to adopt it. Eight years later, researchers have studied and reported the impact of IMCI in two districts of Tanzania, compared to two without the intervention, over the period 1997-2002.

They observed that IMCI – at health facilities alone – improved the quality of care, didn't increase costs, and reduced child mortality 13%.

However the lack of the IMCI family component may have limited the potential impact of IMCI on child mortality and behaviour change.

For example, the study showed that appropriate home management of diarrhea remained under 10% in all

districts, though it increased by 4% between 1999 and 2002 in IMCI districts, and decreased in the comparison districts by 1%.

And for malaria, although children's use of untreated bednets increased dramatically in all four districts by 2002 to as much as 85% in one district, the use of the recommended insecticide-treated treated nets remained uncommon, rising only to a maximum of 20%, with no difference between the IMCI and other areas.

"Very few large-scale effectiveness evaluations of health system interventions have been done"

The study also showed a marked difference in the availability of medicines to the poorest and richest of the mostly rural population, where the average family income is just US\$100 a month, making all effectively poor. But among the poorest fifth of these, none received antibiotics for probable pneumonia, and just 31% got antimalarials for fever. Among the "least poor" fifth, 39% got antibiotics and 62% got antimalarials

The brief conclusion: IMCI should continue to be supported in Tanzania, but with special attention to reaching a high coverage with the family component, and to ensuring the least poor are cared for even in poor rural villages.

Joanna Schellenberg, co-investigator in the Multi-County Evaluation of the Integrated Management of Childhood Illness (IMCI) in Tanzania, told *Real Health* that such health system studies were "not easy to do."



"Very few large-scale effectiveness evaluations of health system interventions have been done" she said. "And it obviously needs to have a lot more attention paid to it, because without the health system, nothing can happen!"

"The Ministry of Health in Tanzania have taken a very big interest in our work", she said. The team wrote a policy brief on the basis of their results, and presented it to 300 health officials and donors at the country's annual health sector review in March. **RW** ■

READ ON

Joanna Armstrong Schellenberg et al., *The Lancet*, 2004, vol 364, issue 9445, pages 1583-94

> Polio Eradication Campaign

Polio vaccine: when science is not enough

Even a classic scientific health product like polio vaccine can face popular fear. Religious leaders in India are helping out

SUMMARY

Religious leaders have played a key role in India in helping quash fears about polio vaccine, and with female foeticide and HIV/AIDS. They are trusted, and belong to wide, influential networks.

> Bishakha De Sarkar

INDIA: It seemed like any other Polio Sunday, with small children and health volunteers lining up camps in a small town in northern India. But what was out of the ordinary was the presence of Muslim religious leaders, some moving from house to house, urging the people of Aligarh to bring their children out for polio drops.

The anti-polio drive has met with success in Aligarh in the state of Uttar Pradesh, where the virus continues to strike in the western region. In 2004 the state had the highest number of polio cases in India - 47 out of a total of 67. But in Aligarh there were no cases of polio at all this year. In 2003, 18 cases had been reported in the town.

Local volunteers believe that the involvement of religious leaders in the anti-polio drive is one of the main reasons for its success.

Religious leaders are gradually being drawn into several health campaigns across India. In Punjab, where the number of women to men is on the decline, Sikh religious leaders have spoken out against the practice of female foeticide, believed to be one of the reasons behind the adverse sex ratio. Christian and Hindu leaders are spearheading campaigns

on HIV/AIDS. And Muslim clerics are urging members of the community to immunise their children against polio.

The involvement of the Muslim clergy came in the aftermath of a rise in polio in India. Health experts were worried after India recorded 1600 cases of polio in 2002, up from the 272 of 2000.

A senior Indian government official told *Real Health* that polio began to spread again in India because of complacency that set in after 2000. But rumours that hit mainly Muslim neighbourhoods also had an impact. Word spread that the polio vaccine caused impotency, which stopped thousands of Muslim families from immunising their children.

But in the last several months, health workers have been in touch with religious leaders to allay the fears of the Muslim community. "We met the leaders and discussed at length the disinformation that was spreading about the polio vaccine," says Mohammed Furquan, an Aligarh-based health worker with UNICEF. "And when religious leaders told the members of their community that there was nothing to fear, they came out of their houses for the vaccine," he says.

Religious leaders are also taking part in the HIV/AIDS campaigns. In the southern Indian city of Chennai this December, leaders of religious communities from India and abroad are expected to take part in an inter-face on ways of strengthening the global fight against AIDS. The Buddhist leader, the Dalai Lama, is also expected to take part in the conference organised by the Chennai University and the World Bank.

A Hindu religious leader, Swami Agnivesh, is campaigning against HIV/AIDS.

Agnivesh, who runs an organisation against bonded or forced labour, has been discussing problems posed by the virus with migrant labourers, one of the high risk AIDS groups.

"We tell them about the virus, and urge them to speak out because having AIDS is nothing to be ashamed of," says Agnivesh.

The Indian government, too, is encouraging the participation of religious leaders. Discussions have already been held with members of leading Islamic institutions in India on polio, and the imams of local mosques have been urged to support the vaccine in prayer meetings.

"We have seen that people listen to religious leaders," a government official told *Real Health*, "and religious communities have a network that can be effectively used."

A leading Indian poet, Javed Akhtar, believes that ordinary people tend to view government volunteers canvassing against polio with suspicion. "The credibility of the administration is such that people often think it has an ulterior motive," says Akhtar, who joined a UNICEF campaign in Aligarh last year to allay fears about the polio vaccine. "Religious leaders, on the other hand, have a certain credibility." John Dayal, the president of the All India Catholics' Union, agrees. "They are in a position to be able to speak out when a government goes wrong," he says.

Clearly, the Muslim leaders' role has made a visible difference to the polio campaign. "There were neighbourhoods where volunteers had earlier been turned away four times in a row," Akhtar says. "But they came out at the end of our campaign to immunise their children." ■

> Biology for Health

AIDS transmission could be stopped before 2015

Molecule stops vaginal transmission of HIV in macaques

SUMMARY

A very strong candidate for a microbicide that will stop HIV being transmitted to women during intercourse has been proven in monkeys. Next steps: safety tests in people in a northern country then fields trials in Africa, which should be completed by 2014.

GLOBAL: An artificial molecule known in the HIV/AIDS research world as 'PSC-RANTES' stops a hybrid HIV/SHIV virus – a cross between human and monkey HIV with all the relevant, external pieces of human HIV intact – infecting female macaques through their vaginas.

That's the key and potentially dramatic result of a study published in the journal *Science* by Robin Offord and Oliver Hartley at the University of Geneva, Michael Lederman of Case Western Reserve University in Cleveland, Ohio, and nine other colleagues at four other US research institutions.

The molecule stops the HIV latching on to a human cell-surface receptor called CCR5, one of its principal routes of infection. HIV first grabs the molecule CD4, and then swings over for a second handhold on CCR5. But CCR5 is a natural receptor for certain messenger molecules in the body called chemokynes, and Offord and Hartley modified one of these to make the molecule PSC-RANTES,

which grabs CCR5 and stops HIV getting a grip.

These researchers "are applying true antiretroviral science to microbicides", Mark Mitchnick, who heads R&D for the nonprofit International Partnership for Microbicides, told *Science*.

If the molecule, or even a modified version, eventually works as well in people, the dream of a vaginal microbicide to stop the transmission of HIV during intercourse takes a giant leap forward.

"There is a real need for an HIV prevention strategy that women can control. This is particularly important in settings where men won't necessarily use condoms," said Lederman.

Offord and Hartley designed PSC-RANTES. They spoke to *Real Health* soon after their paper was published in the journal *Science*.

"A number of microbicides [against HIV] are being developed. We very much hope that one of them will succeed. Of course we hope it's

ours, but the essential thing is that one of them gets out there" Offord told *Real Health*.

Fifteen minutes after coating the vagina with PSC-RANTES, the group challenged 15 female macaques with doses of free virus. Twelve remained uninfected.

"CCR5 does have a function in the natural immune system, but it's a function we can probably do without!"

"We now think we've now done as much as we should in animals, and the next thing to do is to prove the safety and then the efficacy of the molecule in a genuine field trial" said Offord. "The very same molecule could be used in humans."

It's not expected that blocking CCR5 will cause the body problems. "CCR5 does have a function in the natural immune system, "but it's a function we can probably do without!" said Offord.

Oliver Hartley explained to *Real Health* that a significant number of people genetically don't have the gene to produce CCR5. "These people are apparently in perfect health – and the only thing that makes them stand out is

that they are extremely well protected from being infected with HIV."

There are around a million such people in the world, and HIV infection among them is so rare that "each time one is infected it's an event, and results in a publication. There have been only a handful of cases" said Hartley. "So it looks like CCR5 is pretty much essential for HIV infection, but dispensable for health."

"We have to get the cost down" said Offord. "It would currently be well out of reach of a poor country... But we have clear leads as to how to reduce the amount [of PSC-RANTES] that would be required," These could "very significantly reduce the cost of making the material."

Already a sub-Saharan African country has invited the team to test the cream there, but Offord would not reveal the name. And when could the trials be finished? "There's more urgency for these trials than for others, so it could end up a little bit quicker than a decade", said Hartley. So potentially the dream cream could be out there and in use before 2015. **RW ■**

READ ON

Michael Lederman et al., *Science*, 2004, vol 306, issue 5695, pages 485-7

> Health System Science

Child survival MDG to be reached in Brazil

'Action research' in poor communities showed the way

SUMMARY

Brazil will reach its child survival millennium development goal (2/3 reduction, 1990-2015) by 2008, and politicians were re-elected four times, because research created the evidence for expanding a doctors' experiment

> by Claudia Jurberg

BRAZIL: Young Guilherme, son of the Brazilian housemaid Keila Rejane Souza Santos, 27 years old, was saved with the help of community health workers from the Family Health Program (PSF).

But they weren't even there when he was suffering life-threatening severe diarrhea and dehydration.

Keila lives in Jardim Catarina, São Gonçalo Municipality, in Rio de Janeiro, and had learned the 'recipe' for oral rehydration therapy (ORT) from the PSF workers. That saved her son.

Such stories can be repeated all over Brazil, and they can be traced back to an action programme in one of the poorest Brazilian states, Ceará, North East of Rio. Now even the World Bank is using Ceará as classic example of an effective intervention to meet Millennium Development Goals.

Behind the programme were Jocileide Sales Campos, a maternal and child health doctor in Ceará, and a large team of committed paediatricians and other specialists.

The Ceará group had devised the initial intervention – 'Viva Crianca' ('Let people live') – in 1986, as soon as a new government in Ceará had announced that reduction of child mortality must be a top priority.

Cesar Victor and Fernando Barros of the University of Pelotas in South Brazil were then invited to join as epidemiologists to measure the baseline health data, show what was needed, and then measure what was working and what wasn't – crucial to developing an effective health system intervention, and to its political recognition and usefulness.

Victor and Barros showed that diarrhea was causing 48% of infant deaths in 1987.

To treat it, 260 'ORT corners' were created in health facilities. Large numbers of doctors, nurses and 6000 community health agents were trained. Mass media campaigns on radio and TV and theatre groups promoted diarrhea management. A million measuring spoons for ORT sugar-salt solution were manufactured and distributed. And packets of the ORT mixture were distributed at facilities and through community health workers.

But continuous monitoring by Victor and Barros showed the need for improvements, and where and in what measure improvements were needed.

Similar attention was paid to vaccination. Initial coverage was low. Major improvements were made, and by 1994 vaccination had nearly doubled, reaching around 90% across all social groups. "In the 1980s Ceará was ranked last among the 27 Brazilian States in terms of vaccine coverage, and it is currently in third place" says Victora.

Mothers were also not forgotten. In 1987, only 65% of women had any antenatal care, says Sales Campos. Now, the coverage is almost 100%.

Today, 1 300 teams in Ceará, each composed of a doctor, a nurse, four nurse's assistants, and six community health workers, each visiting 120 families a month,



have reached health indicators unimaginable even ten years ago. Infant mortality is down to 22 per 1 000 live births in 2003, a fifth of the 1980s figure, according Brazil's Ministry of Health, with every child under five years old vaccinated against polio, DTP, measles, tuberculosis and hepatitis.

"At this rate, the child survival millennium development goal (2/3 reduction, 1990-2015) will be reached in 2008" says Victora.

Integration of prevention, cure, family and child "was a key element" says Sales Campos. Governors and policy makers also advertised their success broadly. "One may even say that improvements in child health contributed to the reelection of the same political party in four consecutive polls!" says Sales Campos.

Today Brazil's community health agents number more than 195 thousand, working in over 20 thousand teams, reaching nearly 100 million people.

The Datasus (Ministry of Health Data System) records that nationwide infant mortality nearly halved from 48 per thousand to 26 from 1990-2002. And the cost, says Datasus, is around US\$380 million a year. This represents only 10% of the annual budget of the Brazilian Health Ministry, Pistelli told *Real Health*. ■

> Field Trial

Malaria vaccine breaks 50% barrier

58% of 1-5s, and 77% of youngest children protected

SUMMARY

A field trial of a malaria vaccine that has been 20 years in development has had the best results ever — protecting over half of young children from severe disease.

MOZAMBIQUE: WHO has expressed caution about overemphasising the real impact of an extraordinary malaria field trial in Mozambique, in which the Belgian GlaxoSmithKline Biologicals 'RTS,S/ASO2A' vaccine reduced life-threatening disease in 1-5-year-olds by 58%.

Pedro Alonso of the University of Barcelona, who led the clinical trial, told *The Scientist* cautiously "The importance of this result is that it's the first conclusive evidence that we can produce a malaria vaccine."

"Up to now it's just been controversy in the international research community, a vaccine is possible, yes, no, perhaps; after this paper that discussion is over" said Alonso.

But co-researcher Ripley Ballou, who is now with GSK, and started work on a related concept over 20 years ago at the US Walter Reed Army Institute of Research, emphasised the importance of the special protection this vaccine gave to the youngest children.

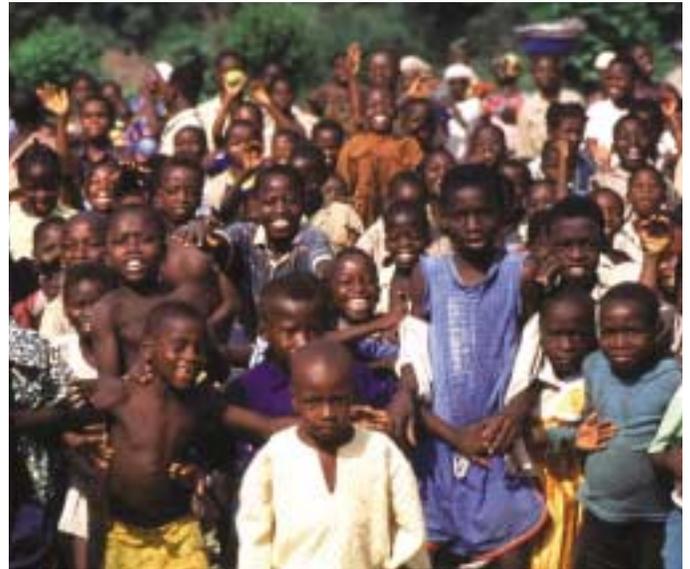
The study, published in *The Lancet*, was done with 2 000

children in a fairly typical malaria zone, with perennial transmission with some seasonal variation. The children were immunized before the peak, and were then followed during the period of greatest transmission. Mild disease was reduced 30%, and severe disease 58%, suggesting an impact on parasite load.

"But if you look at the very youngest children, those under two years old, the efficacy was 77% against severe malaria" Ballou told *Real Health*. "And the children who are at greatest risk of severe disease and death are in that age group."

No earlier malaria vaccine trial has reached anything like these figures.

Alan Schapira, Coordinator of the Strategy and Policy Team of the Roll Back Malaria Department at WHO, however, was determined to be unimpressed, stressing the statistical uncertainties in the trial. They gave a two-standard-deviation range of 20% to 80% effectiveness, he told *Real Health*, rather than the central value of 58%. At 58% the vaccine would be



worth employing, but only as part of a whole suite of measures like insecticide treated bednets, he said.

Decades of research on malaria vaccines has been a catalogue of enormous effort, great science and dashed hopes. The parasite that causes the worst, mostly African form of the disease, *Plasmodium falciparum*, has proved immensely difficult to attack.

The current vaccine, which began with pioneering work by Ruth and Victor Nussenzweig at the New York University Medical School in the 1980s, primes the immune system against the 'sporozoite stage' — the very first form in which the parasite enters the blood from a mosquito bite, before it plunges into the liver to begin its deadly transformations, multiplication and infection.

The Nussenzweigs worked on ways to get the immune system to attack a surface protein on the sporozoite, the CS or 'circumsporozoite' protein. RTS,S contains a large chunk of this molecule, mimicking the sporozoite for the immune system to get prepared.

This was essentially the Nussenzweig's idea, but it's taken 20 years of research to get to the current half-effective vaccine structure. And it needed the ASO2A component — a modern GSK adjuvant, one of the rather more mysterious recipes that vaccines need, to awaken the immune system to even take an interest in their active part. **RW** ■

READ ON

Pedro Alonso et al.,
The Lancet, 2004, vol 364,
issue 9443, pages 1411-20

> Research Funding

"New dynamic" to support health research

10/90 problem still exists, but it's a brave new world

SUMMARY

TB, HIV/AIDS and malaria get eight times less research than they should, but disease patterns are changing, and pharmaceutical companies in low- and middle-income countries offer hope of progress

GLOBAL: Amidst a tripling of global health research spending to US\$106 billion over the last decade that still mostly neglects low and middle income countries, there's hope yet.

Out of the gloom comes a "new dynamic" towards supporting research on the health problems of the poorest countries, says Andrés de Francisco, Deputy Executive Director of the Global Forum for Health Research, co-author of an extensive new report by the Forum on financial flows in health research worldwide.

Studies in the mid-1990s, following the Commission on Health Research for Development, identified what it called the '10/90 gap', a rough estimate that only 10% of the world's health research spending goes on what are 90% of the world's health problems.

This time the new report looks particularly closely at HIV/AIDS, TB and malaria – accounting for about 12% of the world's disease burden. It calculates that US\$1.4 billion, 1.4% of the world's current annual

spend on health research, is spent on research on those diseases. That's arguably eight times less than what might be needed.

Moreover, 98% of the 10.5 million child deaths around the world each year occur in developing countries, the report notes, and a high fraction of these is due to still under-researched diseases like malaria, diarrhea and acute respiratory infection.

But to get an exact '10/90' figure for all diseases proved much more complicated than in the mid-1990s, de Francisco told *Real Health*.

In 1990 the low and middle-income country (LMIC) burden was taken to be an obvious collection of infectious diseases. But now there are significant shifts in the health burden in these countries towards non-communicable disease, so "what fraction of all the research done on cardiovascular disease or psychotropic disease in the rich countries should be attributed to developing countries?" asks de Francisco. "Look at China. Over 60%

of its health burden is non-communicable disease."

Much of the first world research on non-communicable diseases may be producing interventions that are too expensive to be relevant to a LMIC – but how to put a proportion on that? Such issues would need to be done disease by disease, country by country.

Basic research too, for example on the immune system, or on the human genome – it's relevant to any vaccine or drug, but how to measure its relevance? And the private-for-profit sector, which the report says accounts for 48% of the world's health research spending, publishes no relevant breakdowns of what it spends on what. The Global Forum is now working on ways to gather this information, said de Francisco.

"There's still a large imbalance, that's certain, but the exact value is not important" said de Francisco. Moreover, there are positive signs. "There's a new dynamic in health research for neglected diseases, that's capturing some of the increased investments in health research of the past few years," he said.

For example, The Bill and Melinda Gates Foundation in the US has become by far the top foundation in health, giving some US\$520 million in

BRIEFS

GLOBALIZATION AND HEALTH

A new open-access online journal will encourage debate on globalization on health. The editors invite contributions at www.globalizationandhealth.com

BRITAIN'S KNUCKLES RAPPED

DfID was criticised by politicians for ignoring research — and has advertised for its first Chief Scientist.

2002, focusing on diseases of highest burden worldwide. And national research institutes like the National Institutes of Health in the US "are more and more aware of these [global] issues".

Public-private research partnerships have made a mark, but need to be expanded and funded, argues de Francisco. And LMIC pharmaceutical and vaccine companies can also be encouraged to consider research, as there are new markets for them in their backyard, he says.

According to the report, the markets in LMIC economies such as Brazil, China, India, and South Africa are becoming attractive to such companies – at levels of US\$10-100 million (rather than the US\$1 billion sought by Big Pharma in the rich world). "This could improve the chances of new drugs being developed for neglected diseases in both local and global settings" the report says. **RW** ■

> Biology for Health

Cold chain elimination proven by 2008?

UK company sends bioencapsulated vaccines for rapid trial in India

SUMMARY

Natural desert plant sugars could eliminate the costly refrigeration of vaccines. A three-year trial in India will tell if the technology works.

GLOBAL: Current childhood vaccines, and the polio vaccine now in use for global polio eradication, have had massive success, but they have one major drawback – they need a "chain" of refrigeration technology from manufacturer to patient to keep the vaccines cool. This is complex, costs an estimated US\$100-200 million a year, and frequently fails, causing the loss of up to half of all vaccine supplies.

But soon the chain could be eliminated, if a revolutionary new technology gets through clinical trials. The approach is based on the extraordinary natural sugars in desert plants. These solidify slowly to a solid glass on drying, without damaging plant tissues, to allow the plants to survive the desert.

Combined with a vaccine, the sugars can be dried to create stable sugar-glass vaccine spherules that survive at ordinary temperatures. The spherules retain the vaccine's potency, as they dissolve on contact with water, releasing the vaccine.

"Our technology is stolen from nature" said the inventor, **Bruce Roser**, a British scientist who created a company to develop it – 'Cambridge Biostability'.



Howard Smith, Research and Development Manager of Cambridge Biostability told *Real Health*: "We've been going about five years, working on developing formulations for current vaccines – hepatitis B, diphtheria, measles, tetanus and so on – and we've now found a

formulation that gives a very strong response in animal models."

The precise animal results can't be reported publicly, however, as they remain a commercial secret with Cambridge Biostability's industrial partner – who also does not want to be revealed.

The first scientific publications on which the technology can be finally judged will concern the bottom line: human clinical efficacy trials of a pentavalent vaccine, due to be completed in India by 2008 by the company Panacea Biotec.

This period is extremely short for most efficacy trials. But, says Smith, the vaccines used in the spherules are already known to be effective, and "...all our materials are approved for use by the US FDA... So we are looking at a very short timescale."

Rajesh Jainn, Joint Managing Director of Panacea Biotec, commented: "The vaccine world is undergoing a radical rethink about how vaccines might be stored and administered... We are delighted that Panacea Biotec is taking a world leading role by manufacturing this revolutionary vaccine." **RW** ■

BRIEFS

KENYA: INFANT MORTALITY RISES BY A QUARTER

From 1993-2003 infant mortality rate rose from 62 per thousand to 78, and full child immunization coverage fell from 79% to 59%, Richard Muga, the director of National Council for Population and Development of Kenya, tells *Real Health*. "We are unlikely to meet all the MDGs."

NIGERIA: RUMOUR REINFECTED FOUR COUNTRIES WITH POLIO

David Heymann, Representative of the Director-General of WHO for Polio Eradication, tells *Real Health* in an interview on our website (see www.globalforumhealth.org) exactly how false, worldwide rumours about polio vaccine were contained.

CHINA: HEALTHY MOTHER BUSES REACH MILLIONS

The Healthy Mother Express, a welfare project to promote health education and to send medical services — by specially adapted bus — to women in impoverished regions of western China, has reached 1.6 million women.

> Vaccine Development

Rotavirus: twice as common, twice as important

Data from Asia suggest Mexico's new rotavirus vaccine could have double the expected impact

SUMMARY

Rotavirus may cause twice as much severe diarrhea, an important child-killer, as previously thought. If so, a vaccine just approved in Mexico could have double the impact. A further vaccine is undergoing trials, but a 'cocktail vaccine' against all causes of diarrhea is the great goal.

> Prakash Khanal

GLOBAL: Reports from eight Asian countries have found that 45% of children hospitalized for severe diarrhea were infected with rotavirus, nearly double previous estimates of 25%.

According to an ongoing study by the Asian Rotavirus Surveillance Network (ARSN), 45% of stool samples collected from 16 000 children of 0-5 years of age admitted with diarrhea in 33 hospitals in China, Hong Kong, Indonesia, Korea, Malaysia, Taiwan, Thailand and Vietnam showed rotavirus infection.

Tony Nelson, a professor of paediatrics who coordinated the surveillance in four Hong Kong hospitals, said that the findings indicate that the toll from rotavirus "could be significantly higher than the current worldwide estimate of half-a-million childhood deaths a year."

The classic answer to a virus is a vaccine – and in the case of rotavirus vaccine the pub-

lic need not wait long. The US Federal Drugs Administration (FDA) approved a vaccine – Wyeth-Ayerst's Rotashield – in 1998, but that was withdrawn in little more than a year for causing intussusception (an acutely painful penetration of the small into the large intestine) in a few vaccinees.

But Tore Godal, Executive Secretary of the Global Alliance for Vaccines and Immunization (GAVI) told *Real Health*: "GlaxoSmithKline (GSK) in Mexico has already been licensed to produce a [new] rotavirus vaccine – Rotarix."

GAVI was established in 2000 as a public-private partnership between governments, UNICEF, WHO, The World Bank, the Bill & Melinda Gates Foundation, the vaccine industry, public health institutions and NGOs to increase access of children to vaccines in poor countries.

According to Godal, Rotarix – a live attenuated vaccine – "is now privately available in

Mexico. The Board of Health gave the vaccine the go-ahead [in July] after successful trial in 60 000 children in which the vaccine showed high level of efficacy in preventing rotavirus diarrhea".

"In fact the total number of children dying from diarrhea caused by shigella, dysentery, typhoid and other microbes has gone down, which means fewer children compared to before are dying of diarrhea now" Godal told *Real Health*.

But millions are at still risk, and "the development of a cocktail vaccine against all these microbes is on the horizon – that will protect children from most forms of diarrhea," said Godal.

Another pharmaceutical giant, Merck, is in the process of testing yet a third rotavirus vaccine, RotaTeq, which is based on a bovine strain of rotavirus, in the United States. Roger Glass, chief of the viral gastroenteritis section of the US Centers for Disease Control and Prevention (CDC), told *Real Health*: "Merck is aiming first for the US market; then it will gradually go to the European market. But GSK is aiming for the Latin American countries and then some countries in Asia."

Both Rotarix and RotaTeq are intended to be administered along with other routine childhood immunizations.

The development of a rotavirus vaccine will have several benefits to a nation. First and foremost, according to Glass, would be reduction in diarrhea-related hospitalization by 33-50% within two years of administration of the rotavirus vaccine in children.

According to current figures, "one child in 250 dies of severe diarrhea caused by rotavirus, 5% of all death among children under five years of age," said Glass.

But this estimate could double if the new Asian prevalence figures are confirmed.

Widespread use of a successful rotavirus vaccine would have several benefits to a nation, said Godal. Counter-intuitively, fewer children dying means parents will produce fewer children, leading to a slowing of population growth, greater attention to individual children and better performance at school.

"This is what we call the demographic gift," said Tore Godal. ■

> Opinion

Only African science can beat HIV/AIDS

Fake ARVs, and drug-resistant HIV, need local science

SUMMARY

Without local science, Africa could end up being called the source of the next global plague — drug resistant HIV.

> by Otula Owuor*

KENYA: The present chaotic and dangerous market for antiretrovirals (ARVs) in Africa was inevitable after Africa's failure to invest effectively in the science of HIV/AIDS epidemic. Despite the disease threatening Africa's survival, governments have not trained enough hands-on virologists, molecular biologists, immunologists, vaccine experts, biochemists and others.

There are few efficient centres that routinely monitor the composition of ARVs and their impact on both the patients, or the virus itself – including detection and analysis of any emerging resistance. And the few experts and institutions that we have, work at unsustainable levels of dependency on external donors or collaborators.

Already resistance against ARVs exists in America and Europe. Thus fears of worse to come in Africa may not be far fetched. The region may be soon find itself correctly or

incorrectly branded the epicentre of new HIV-strains.

Africa is already a favourite destination of counterfeit drugs, especially in nations where health or the biomedical infrastructure is minimal due to wars or poor funding.

Without national or regional ARV quality assurance centres, then even expired painkillers added to pellets of ugali or mealie mealie can easily be packaged to be sold as antiretrovirals.

ARVs offer hope, and opportunities for more effective counselling leading to behaviour change, apart from minimization of stigma and fear linked to HIV because there was no treatment that could directly help prolong lives.

However, for Africa the truth is that alarming scientific, technological and administrative problems are emerging in the provision of appropriate AIDS drugs to those who need them. The complex problems may easily minimize the

positive impact of the good intention of many groups to provide effective treatment.

There are lessons to be learnt from some of the initial mistakes that have already occurred in the provision of ARVs. Towards the end of last year in Nigeria the official stock of AIDS drugs declined rapidly causing widespread shortages. Expired drugs were allegedly found at Federal Medical Centre, Markudi.

This forced some desperate medics to say the expired drugs still had potency, and were better than nothing, despite also being unacceptable in Europe where they were allegedly sourced.

Senegal's President once fired one of his HIV/AIDS experts after a scandal that allegedly involved re-exportation of ARVs to Europe. Early this year Kenyan health officials did not deny media reports that some ARV outlets were operating under highly unethical and unscientific conditions. However, prompt actions seem to have been taken to curb street sales of fake ARVs.

But in the war-torn Democratic Republic Congo with its

minimal health infrastructure middlemen are selling fake ARVs, according to reports by *Médicins sans Frontières*, and the situation may well be widespread in much of central Africa.

Honey-tongued middlemen and manufacturers with up-beat advertising designed to exploit regulations that are not easy to implement are criss-crossing the region seeking quick profits and local collaborators in the importation or production of generics. So what were expected to be simple life saving operations have complications that had not been expected.

Networks of locally sustained and highly publicized national or regional centres analysing ARVs and monitoring resistance trends plus other positive or negative clinical factors are essential – but they are still missing. And Africa, with its own harsh realities, also needs frank discussions with Europe and Asia to help curb the peddling of dangerous and ineffective drugs. ■

* Otula Owuor is a past Science Editor of the *Daily Nation Kenya*, and has written widely and trains African journalists on HIV/AIDS.

Further information:

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Intervention: Health challenges in Nagaland

Real Health is supported by the Global Forum for Health Research. Views expressed are not necessarily those of the Global Forum.

Editor: Robert Walgate, London, UK
Designer: Lisa Schwarb, Lausanne, Switzerland

Pictures: TDR Image Library (WHO/TDR/Crump), APOC, Cambridge Biostability.

The Editor offers his heartfelt thanks to those special people at the Global Forum and all over the world who have given time, help, and invaluable advice to create this first edition of *Real Health*.