Tests on monkeys raise hope of HIV cure

**An experimental vaccine tested on 16**

**monkeys protected only nine of them, but it**

**also did something curious — eliminating the**

**virus completely in those that were cured**

“Kafkaesque” is not a

word normally used to

describe immune responses,

but it’s how Dr Louis J.

Picker described what his

experimental vaccine did to

his rhesus monkeys: “It’s

like their T-cells were turned

into the East German secret

police, hunting down infected

cells until there were none

left.”Recent work by Picker,

a vaccine expert at Oregon

Health & Science University,

has shaken up the long,

frustrating search for an

AIDS vaccine. Picker tested

his vaccine in 16 monkeys

who were then infected with

simian immunodeficiency

virus, a close relative of HIV,

which normally would have

sent them spiraling rapidly

down to a miserable death.

The experimental vaccine

protected only nine of them,

but it also did something never

seen before: These monkeys

slowly “cleared” the virus

and now appear to be cured.

“Three years later, you can’t

tell them from other monkeys,”

Picker said.

Dr Anthony S. Fauci, the

head of the National Institute

for Allergy and Infectious

Diseases, said the effect was

“unique.”

And Dr Barton F. Haynes, the

director of the Human Vaccine

Institute at Duke University’s

medical school, said it

was “potentially extremely

important to understand how

this happened.”

Scientists often test ideas

for potential AIDS vaccines

by creating similar ones

against SIV. Never before has

one eliminated an existing

infection. In that sense, the

effect of Picker’s vaccine was

less like that of a measles or

flu shot and more like that

of the AIDS cures used in

two famous cases, known as

the Berlin patient and the

Mississippi baby.

The Berlin patient, Timothy

Ray Brown, was infected

with HIV and cured only

by obliterating his immune

system to defeat his leukemia,

and then injecting bone

marrow from a donor with a

rare HIV-blocking mutation.

The unidentified baby was

born to an infected mother in

Mississippi and apparently

infected with HIV, but then

cured with early and large

doses of antiretroviral drugs.

Both now appear to have no

HIV lurking deep in their

bodies, but it is impossible to

be sure because not every bit

of their tissue can be tested.

Because he works with

monkeys, Picker was able

to do something that would

be unthinkable with human

patients — necropsy them,

grind up every organ and take

240 samples from each to be

sure that they harbored no

hidden virus. Making vaccines

by simply weakening the virus

that causes AIDS has failed

because the virus mutates a

hundred times faster than even

the fast-mutating flu virus. In

Picker’s vaccine, SIV genes are

fused to those of another virus,

the cytomegalovirus. (The

name means “big cell,” and

it is in the herpes family but

different from its relatives that

cause lip and genital sores,

chickenpox and shingles.)

HIV fusion has been tried with

adenoviruses and others, but

cytomegalovirus seems to

work better. It’s not entirely

clear why, but one theory is

that cytomegalovirus has a

very long history of infecting

primates —so much so that

100 per cent of monkeys and

about 80 per cent of humans

get it in their lifetimes.

Therefore, we primates have

adapted to it. Although the

virus can be lethal to fetuses

and to those with immune

systems suppressed by

AIDS or transplant drugs,

in most victims it causes no

symptoms.The body responds

to cytomegalovirus more

slowly and calmly than it does,

for example, to a flu.

As in any infection, the

thymus gland generates new

white blood cells called T cells

— in this case, CD8 hunterkiller

cells — primed to target

the specific virus. But in

the case of Picker’s vaccine,

those cells stay in an unusual

“half-alert” state. A full-blown

immune response eventually

exhausts itself, and can even

be dangerous. For example,

the rare humans who catch

H5N1 bird flu often die of the

immune response itself; they

drown in the flood of CD8s

and other would-be saviors

pouring into the lung tissue,

spoiling for a fight.

That “half-alert” state is

the “Kafkaesque” element:

unactivated CD8s wander

around aimlessly, while fully

activated ones behave like

storm troopers. But the

half-activated CD8s persist

in tissues, eliminating their

targets quietly without

triggering inflammation

or even a mild fever. When

SIV genes are fused to the

cytomegalovirus spine, the

CD8s kill SIV-infected cells

too.Since it protected only

some monkeys, the new

technique might be best used

in combination approaches.

For example, Fauci said, it

could be given with a vaccine

that generates antibodies

against HIV “and maybe

eliminate the cells that sneak

past the antibody shield.”

Alternatively, the vaccine

might be given to infected

patients who are on

antiretroviral drugs to see

if it can “mop up” lingering

reservoirs of virus.It should

take up to three years to get a

human version ready for trials,

Picker estimated.

“Now the outstanding

question is, ‘Why only half?’”

said Dr Mike McCune,

an AIDS researcher at the

University of California, San

Francisco, referring to the

monkeys who were protected

in Picker’s trial.

Too often, AIDS advances that

work in lots of monkeys don’t

work in many humans.

“Not all monkeys are the

same,” McCune said. “They’re

not as inbred as mice, but

they’re sometimes from the

same families, they get the

same diets. ... Who knows

what will happen if this goes

into humans?” (NYT)