News focus

Tragedy of the uncommon

Mediawatch: **Bernard Dixon** looks at the response of the British media to the disastrous reactions of volunteers in the recent first clinical trial of a new drug in London.

On 13 March six men were admitted to intensive care at Northwick Park Hospital, London, after suffering severe reactions while taking part in a phase 1 clinical trial of an experimental drug in a research unit run at the hospital by US-owned Parexel International, a contract research company. Two days later, the story hit the front pages, as successive editions of the London *Evening Standard* announced "Guinea Pig Drug Students In Fight For Life" and "Drugs Victim Left Like The Elephant Man". The *Daily Mail* trumpeted "Hell Of Human Guinea Pigs".

In the days following, *The Sun* in particular highlighted the human story. "Ryan was a healthy young man and he saw the trial advertised on the internet. He is at college and was doing it to make a bit of extra money," a family friend had said. "He told us he would be paid £2000 and did not think there would be any problems. His mother got a call last night to say his head and neck were swelled up and his legs had turned purple."

"Give us answers, demand families," added the *Daily Mail.* Alongside a photograph of "the one who got away" (a volunteer given placebo) a caption read "They were writhing, screaming, burning up and begging for help." Virtually ignoring the story itself, the *Daily Mirror* allocated a whole page to "The Vulture – Exposed… hospital porter who tried to sell pictures of the drug trial victims".

For the most part, journalists from right across the media spectrum worked hard and quickly to determine the underlying facts about the trial, and to explain the various ways in which it might have gone awry. The "drug" was in fact an immunomodulatory humanised agonistic CD28 monoclonal antibody, TGN 1412, developed by the company TeGenero at the University of Wurzburg in Germany. Its purpose was to bind to and activate killer T cells, as a possible means of treating leukaemia, rheumatoid arthritis and multiple sclerosis, and it had been administered to six healthy volunteers. Another two, who received a placebo, had not become ill. Previous animal tests had reportedly given no indication of possible toxicity.

The Independent weighed in with a curious item headed "German drug company had never tested its products on humans before." It emphasised that Parexel, commissioned by TeGenero to conduct the trial, had been refused permission to do so in Germany. But the article later explained that permission *had* been given after protocol changes, though by then arrangements had been agreed with Northwick Park.

Most newspapers provided competent summaries of the sequence of tests and trials used to evaluate new medicines. They also explained the role of the UK's Medicines and Healthcare Products Regulatory Agency (MHRA), which had

Hyper: The plight of the drug-trial volunteers made headline news across the media. The Sun newspaper acquired exclusive rights to some of the stories of volunteers involved and gave an early account of the experiences of one of the subjects who received a placebo dose and witnessed the rapid onset of illness in those that had received the drug. A later report in the newspaper at the end of last month gave a first-hand account of one of the subjects who had received the drug, and recounted his alarm at the rapid onset of symptoms. A press release from the Northwick Park Hospital on March 31, flagged to be the last on the condition of the volunteers, announced that four had improved sufficiently to be allowed home. The fifth patient is out of critical care and making steady recovery under close observation and the sixth remains in critical care but is conscious and doctors are encouraged by his progress.


THE Sun

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Agony . . . victim Ryan

Horror of men fighting for life as drug trial ends in disaster

WE SAW HUMAN GUINEA PIGS EXPLODE

EXCLUSIVE by NICK PARKER and VIRGINIA WHEELER

HUMAN guinea pigs collapsed writhing in agony after getting trial injections of a new drug, witnesses said last night.

Raste Khan, 23, who escaped the test unharmed, said: "Some of them screamed that their heads were about to explode."

One victim, Ryan Wilson, 21, turned purple. The girlfriend of another tester said his head was so swollen he looked "like the Elephant Man".

Six men were in intensive care last night in a North London hospital. Two were critically ill.

Full story — Pages Four and Five

Critical: The six affected volunteers were swiftly transferred from the Parexel drug-trials unit to the intensive care department of Northwick Park Hospital in north London. (Picture: EMPICS/AP Photo: Kirsty Wigglesworth.)

immediately suspended the clinical trial authorisation and also reviewed the data submitted with the original application for authorisation.

The most comprehensive coverage came in *The Times*. Just one day after the initial disclosure, it allocated four pages to the latest news from the hospital plus a detailed review of monoclonal antibody technology and therapy, an account of how clinical trials are organised and material about measures normally taken to combat the type of total organ failure suffered by some of the victims.

Heralding these pieces, however, was an article by Health Editor Nigel Hawkes, headed "Drug Trial Ignored Guideline On Safety", which argued that the study did not conform to best medical practice. "Senior doctors expressed concern that all six were given the same dose…at the same time," Hawkes wrote. "According to the standard medical text, trials of this sort should avoid giving all the doses simultaneously. *The Textbook of Pharmaceutical Medicine* specifically gives warning that such practices can be 'very difficult to manage' and 'put subjects at unnecessary risk.'"

At this stage, there was confusion regarding the results of animal tests with TGN 1412. But then *The Mail on Sunday* claimed that "the drug at the centre of the 'elephant man' testing scandal caused monkeys' necks to swell up before it was used on humans…At least one of the mammals tested with the drug… suffered swelling of the lymph nodes." The newspaper cited as the source of its information the Paul Ehrlich Institute, "the health ministry body that controls all research on biological drugs in Germany". *The Lancet* (25 March) later announced that preclinical trials had been conducted in rabbits and 20 monkeys, two of which showed a transient increase in lymph node size.

The Times, however, argued that animal tests "create a false sense of security". One reason in this case was that an animal's immune system would perceive a humanised antibody such as TGN 1412 as foreign and try to reject it before it could exert its full effect. In addition, experimental animals would not carry the specific proteins to which the antibody was directed in the human body.

An unexpected twist to the story at this stage came in *The Guardian* under the headline "Interest surges in trials despite patients' plight". The article explained that the Medical Research Council and other bodies were being "inundated with people wanting to sign up for drug trials despite the disastrous tests at Northwick Park…There has been a surge of interest from people keen to take part in trials and enquiring about the payments they can receive."

Nearly three weeks after the original revelations, press reports indicated that two of the volunteers had recovered sufficiently to return home. At that stage, however, there was no clarification of whether the incident had been attributable to contamination of the material administered, to its poor quality, to a departure from the agreed protocol regarding dosage and timing or to an entirely unpredictable adverse reaction. Investigation by the MHRA (and by the police) may provide the answer.

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