Monitoring global health: time for new solutions

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leukaemia\(^1\)) were not predicted by animal studies using similar doses of vector.

One set of questions on toxicology related to gene transfer arises because most studies in humans—as with many other trials of hazardous agents—enrol participants with advanced illness. Such participants are likely to misinterpret the purpose of the trial as providing therapy rather than producing generalisable knowledge.\(^2\) Enrolment in studies on the safety of gene transfer is therefore susceptible to being based on “misinformed” consent. Also, participants who perceive a trial as providing therapy may be less willing to comply with intrusive procedures (for example, long term follow up and autopsy) that are aimed at testing safety. By policing consent procedures for language that promotes misconceptions about therapy, investigators may encourage participants to cooperate with a trial’s toxicological aspects.\(^3\)

Premarketing studies of drugs often have insufficient power to expose rare adverse events\(^4\); the collection of toxicity data is further hampered because gene transfer trials generally enrol participants with severe illness. For instance, attributing causes for adverse events is confounded by underlying medical conditions. Moreover, such populations are unlikely to survive and experience theoretically predicted latent adverse events. Therefore, many risks will only be characterised once gene transfer extends to populations with less severe medical conditions; patients and the public (rather than trial participants) will likely bear many of the risks involved in characterising latent toxicity.

Owing to the uncertainties and inexperience surrounding risks from gene transfer, systems may need to be established for postmarketing surveillance (for example, registries) and the long term follow up of trial participants. In the United States, such long term follow up is not mandatory, and anecdotal evidence indicates that it is not widely practised.\(^5\) In contrast, the United Kingdom\(^6\) and Australia (www7.health.gov.au/nhmrc/research/gra/p.htm) track the medical records of recipients of gene transfer. Follow up and postmarketing surveillance are potentially costly; can medicalise people’s lives, and infringe on their privacy. Nevertheless, spontaneous reporting of adverse events is unreliable for detecting latent adverse events,\(^6\) and more active measures may be necessary to protect the public, and patients and their descendants, should gene transfer extend to milder medical conditions.

Although recent trials confirm the feasibility of gene therapy, they also highlight that its risks are poorly understood. The task for researchers in gene transfer will be to characterise these risks while attending to the complex ethical challenges of conducting gene transfer studies in humans.

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References


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