The Moral Imperative: Protecting Children's Welfare in Research and Experimental Therapies

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Introduction

Charlie Gard, an 11-month-old baby who passed away in 2017, sparked international debate surrounding his battle with mitochondrial depletion syndrome, a rare terminal illness that lacks a cure (BBC, 2017; Nogueira et al., 2014). Burdened with progressive brain damage and muscle weakness, Charlie required a ventilator to breathe. After his story was publicized, Dr. Michio Hirano suggested that an experimental treatment involving nucleoside bypass therapy - aiming to restore Charlie's ability to synthesize mitochondrial DNA by supplementing his body with naturally occurring compounds it couldn't produce - may, in theory, benefit Charlie (Amtamm et al., 2023). However, ethical questions surfaced as the treatment had never been tried in a human or animal subject with mitochondrial depletion syndrome, prompting a deeper exploration into the ethical implications involving the pediatric population in research studies and experimental treatments. This controversial narrative underscores the ethical considerations surrounding health research regulations concerning human, specifically pediatric, subjects.

Should Children Receive Experimental Treatments Despite Risks?

Some contend that it is reasonable for children like Charlie, who have exhausted conventional treatments, to undergo experimental treatments despite risks. They posit that the potential for children's lives to be in their interests and worthy of living justifies their use (Savulescu, 2017). They assert that a patient's best interests can be achieved through approaches that provide the potential to prolong their lives or avert damage to their health, as the experimental treatment may prove beneficial (Ross, 2020; U.S. Food and Drug Administration, 2022). Moreover, proponents argue on the basis of justice, which calls for considering conflicting interests when determining how to distribute benefits and burdens, especially in resource scarcity and competition. Administering therapies with a low likelihood of benefit for one patient denies others with better prognoses; however, denying treatments based on minimal benefit could be considered unjust, especially if patients can afford them, as in Charlie's case, where his parents raised £1.3m to cover the nucleoside bypass therapy (Savulescu, 2017; BBC, 2017). Therefore, the ethical principle of justice may not hold grounds in a decision to withhold experimental treatments in such circumstances. A child's life may not be considered in their interests when it is intolerable, painful, and insufferable to them; however, in some cases this may be unclear (Savulescu, 2017). As such, proponents believe that challenges such as comfort and well-being may be remedied with sedation and analgesia, arguing that many severely disabled individuals value their lives, even with prolonged ventilation (Savulescu, 2017).

Opponents argue that before resorting to desperate remedies, there must be some probability of success rather than merely using the situation as an endeavour to try a new intervention (Ross, 2020). Furthermore, they contend that children undergoing prolonged ventilation, like Charlie, frequently experience discomfort, endure invasive procedures involving needles, and may be distressed, rendering them unable to communicate the source of their distress (Wilkinson, 2017). In such cases, some may question whether subjecting the children to likely futile treatments could exacerbate their suffering. Moreover, in situations where neither the medical team nor parents are able to ascertain the best interest of a minor lacking decision-making capacity, the court assumes responsibility for representing the child's

interests, as exemplified in the legal case of GOSH v Gard (Butler, 2024; Francis, 2017). Consequently, when courts are presented with proposals of experimental treatments, they expect to receive substantiated evidence of their efficacy with respect to the patient. However, if such evidence is limited or theoretical, courts may reject their use, as their primary duty is to decide what is in the child's best interests, not those of scientific research (Francis, 2017).

Ethical Implications of Using Children as Research Subjects

Various ethical considerations arise when involving the pediatric population in research, including, informed consent, potential benefits to future research and medicine, conflicts of interest, and conflicts regarding a minor's best interests. Informed consent can only be given by individuals deemed competent to make autonomous decisions for themselves (Butler, 2024; Field & Behrman, 2004). As assent cannot be obtained from the age group of birth to 3 years of age, parents or guardians may provide informed consent and are entrusted with making decisions about research participation that safeguard their child's interests (European Commission, 2008; Field & Behrman, 2004). To ensure informed consent, a thorough communication process is required. This involves parents and guardians inquiring about the purpose of the research/treatment and procedures their child will endure, potential harms and benefits of the research, their rights, the investigator's role, their child's medical condition and prognosis, other options for care, and the difference between undergoing usual treatment and participating in a trial (Field & Behrman, 2004).

Wouldn't the knowledge gained from the child's treatment be beneficial for other infants?

In Charlie Gard's case, the hospital and the court's stance were consistent with the Kantian principle that individuals should never be used merely as a means to other individuals' ends (Stanford Encyclopedia of Philosophy, 2022). Thus, experimenting on children for the sake of future patients may be deemed immoral and unethical unless there existed a reason that suggested that the child may benefit from the treatment (Butler, 2024). It may be said that the argument of not using individuals as instruments for the common good becomes even more significant concerning newborns and young minors who are dependent on adults for protection. For instance, a preschool ADHD Treatment Study tested Ritalin (methylphenidate) on 3 to 5-year-olds despite diagnostic uncertainties and the limited safety and efficacy data of antidepressants and mood stabilizers in preschool-aged children (Sharav, 2003; Vitiello et al., 2015; Morton & Stockton, 2000). Parents were compensated when the researcher increased doses, yet no validated evidence demonstrated benefits outweighed the risks of this treatment (Sharav, 2003). Long-term consequences were overlooked and later highlighted in follow-up studies, and concerns arose regarding conflicts of interest (Sharav, 2003). Therefore, considerations regarding parental and guardian informed consent are crucial to ensure that children incapable of providing informed consent are not being used as "commodities for commercial ends" (Sharav, 2003).

Do conflicts of interest taint the integrity of research or the experimental treatments being investigated, and why should we care?

Conflicts of interest arise when professional judgments or choices involving a primary interest may be unfairly affected by a secondary interest, like financial gain or a non-financial motive (Romain, 2015). This may lead to conscious or unconscious biases, thereby compromising the trustworthiness of research and impacting professional integrity and patient confidence (Romain, 2015). Conflicts of interest may also result in harm to participants, contradicting the ethical principle of non-maleficence – do no harm. For example, the case of Jesse Gelsinger, a researcher who volunteered himself as a research subject for a condition called ornithine transcarbamoylase that he was mildly suffering from (Butler, 2024; Rinde, 2019; Donovan & Guzman, 2022). After receiving the gene therapy, his health rapidly deteriorated, ending in his unfortunate death and sparking discussion about "overeager and undercautious" researchers (Rinde, 2019). Therefore, it is crucial that researchers fully disclose any secondary interests in the research

or experimental treatment they are proposing for the sake of the research subjects' well-being, especially when involving the pediatric population and their families.

Conclusion

The discussion of the usage of experimental treatments in unique cases like Charlie Gard's is nuanced. Many positions based in ethical principles, including justice and beneficence, arise surrounding the benefits, potential harms, and uncertainties of employing experimental treatments. This encourages an exploration of the ethical implications of using pediatric subjects in research. Issues, such as autonomy, informed consent, non-maleficence, beneficence, conflicts of interest, and Kantian principles come into play, especially when the decision of participation falls on a parent or guardian. Ultimately, as a society it is important to reinforce that safeguarding the well-being of children when considering research participation or experimental therapies is of paramount importance, as exemplified in Charlie's case, illuminating the broader moral imperative.

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