



DIVISION OF MEDICAL ETHICS
HIGH SCHOOL BIOETHICS PROJECT

Teens and Children in Clinical Research and Care

Overview

This module provides insight into the ethical challenges of involving children and teens in decisions about clinical research and medical care. It encourages students to think about what types of ethical issues adolescents face in medical and research contexts and how doctors, researchers, and parents/guardians consider medical ethics in specific situations. Students will be exposed to information concerning IRB regulations, FDA regulations, and the various pillars of medical ethics that researchers and doctors must adhere to whenever adolescents are involved in clinical research. This module relies on current statistics as well as the analysis of theoretical situations, both of which are explained in depth so that students can follow and comprehend accordingly.

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Learning Outcomes

1. Understand principles of informed consent and how they present unique challenges for children/adolescents in research and medical care
2. Evaluate the potential risks and benefits that can result from children and adolescents participating in research
3. Understand therapeutic misconception and the tension it causes between the goals of the researcher and the participant, particularly if the participant is a child or adolescent with a life-threatening illness
4. Understand the specific ethical concerns raised by pediatric cancer and epilepsy research and treatment

Procedures and Activities

This unit uses a student-centered and interactive approach to teaching. Activities are designed to allow for student participation and are marked as an individual, partner or group activity.

The following terms are used to designate the different types of activities:

- Teacher-Directed Class Discussion
- Individual Activity
- Partner Activity
- Group Activity

1. What Is Research Ethics?

Research that involves the participation of humans, especially those under the age of 18, raises unique and complex ethical, legal, social, and political issues. Research ethics is concerned with the welfare and rights of participants in research studies, particularly those that test new drugs. The main three objectives of research ethics are: 1) to protect human participants, 2) to ensure that the research is conducted in a way that serves the interests of the individuals who participate, and 3) to examine specific research activities and projects for their ethical soundness, looking at issues

such as the management of risk, protection of confidentiality, and the process of informed consent.

2. Introduction

This module will address both adolescents and children and their ability to provide consent. An adolescent is defined by the World Health Organization as “any person between ages 10 and 19,” and this definition will be used hereafter. Individuals younger than 10 years of age will be referred to as “children.” Adolescents specifically face unique considerations regarding their ability to consent or assent because they are in a transitional phase in their lives. Each year, thousands of children and adolescents in the United States, ages 0–18, are afflicted with diseases that have no known cure or treatment including epileptic disorders and fatal cancers. While medical journals boast the discovery of new treatments spawned from innovative clinical trials, many fail to recognize that a majority of these clinical trials focus only on the adult demographic and fail to properly cater to adolescents who may be afflicted with the same or a similar disorder. This is due to a major misconception in the medical community that has prevailed for decades: that adolescents are “small adults.” This misconception was brought to the forefront during the COVID-19 pandemic, as vaccines were authorized first for adults, then for adolescents ages 12 and older, with authorization for use in children 10 and younger lagging far behind. The thought process behind this misconception stems from the scientific hypothesis that adult dosages of clinically tested medications can simply be modified for children depending on factors like height, weight, age, etc. Upon first consideration, this method seems logical, and is why researchers did not feel an urgency to enroll adolescents into clinical trials for several decades before the early 2000s. Unfortunately, the truth is that children are *not* small adults and cannot rely on dosages established by adult clinical trials. There remains an urgent need to include children and adolescents in clinical trials that study deadly diseases and disorders, for if this does not occur, the field of medical research will have failed the adolescent population in its promise of fair participant selection.

There is a lack of adolescents in clinical trials for myriad reasons, including the many protective regulations set for children, the lack of adequate numbers of adolescents suffering from rare diseases who are willing to participate in research, and the financial implications concerning the lack of funding for research into a rare

disease as opposed to a well-known one such as breast cancer or HIV. The developmental stages of adolescent bodies also play a major role; there are “dynamics of growth and maturation of organs, changes in metabolism throughout infancy and childhood, changes in body proportion, and other developmental changes that affect how drugs are metabolized in children” (Center for Drug Evaluation and Research). These reasons are coupled with the three major ethical issues concerning the involvement of adolescents in clinical research: consent, confidentiality, and the protection of adolescents from harm. These reasons have served as legal and biological barriers for medical researchers who have made active efforts to discover cures for fatal diseases or disorders. It is important to note, however, that instead of avoiding pediatric research because of its challenges, it is much more crucial to build up support for such research so that future pediatric research can advance. Without such support, adolescents remain at heightened risk.

The primary concern that looms in the minds of healthcare providers and researchers who work with adolescents is obtaining adequate informed consent. There is very little consensus in the literature about the way researchers should go about doing so. Consent, confidentiality, and protection from harm are three major pillars to which all medical practitioners must adhere, and the most vital of these three is consent. Commonly cited issues with consent involve articulating clear criteria for obtaining truly informed consent, establishing an age at which a person can consent to treatment or research participation, and knowing to what extent parents and guardians should be involved. U.S. law does not consider most children to have the competency necessary to consent to medical treatment. And because the risks of involving children in research studies—in which the risks and benefits of an experimental intervention are not yet known—may be high, children are also not considered competent enough to consent to participation in medical research under the law. Consent thus becomes an issue of convincing parents of the safety and efficacy of a particular medical treatment or trial. However, because it’s not clear at what age children are able to fully consider the consequences of their ages, it is possible that some children are able to consent to participate in research without a parent intervening. Indeed, voluntary consent is a hallmark of ethical research conduct. This raises a number of questions: How can a medical practitioner or researcher determine the level at which an adolescent can comprehend the information required to provide consent? Moreover, should the adolescent trial participant be presented the same information as his or her parent or guardian, and

should the researcher rely on consent from the patient or the guardian? ? Can the safety and efficacy of the trial be guaranteed so as to protect the adolescent from harm so that adolescents and parents can give true consent? These are questions that researchers and medical practitioners must answer so that adolescents can be fairly included in medical research.

These questions are not just crucial, they can intimidate parents and adolescents. This is evident by the fact that 22.3% of the U.S. population is under the age of 18 (73,197,412 people) but only 1,265 ongoing clinical trials involving adolescents were being conducted in the U.S. as of June 2021. In 2020, an estimated 16,850 of these children and adolescents ages 0–19 were diagnosed with fatal cancers, and an estimated 1,730 died of a disease. Thus, the research ethics community must determine how to safely include adolescents in research, balancing their safety and their need for new treatments.

3. Definitions

Vulnerable Subjects

Vulnerable subjects are those whose ability to autonomously decide to participate in research may be compromised. Vulnerable subjects require special protections when giving consent to research participation, and precautions must be taken to preserve the voluntary nature of their consent. Federal regulations specify additional protections for four classes of vulnerable subjects: pregnant women, fetuses and neonates, prisoners, and children.

Institutional Review Board (IRB)

The institutional review board (IRB), also known as the ethics review board, is a committee that is formally designated to approve, monitor, and review biomedical and behavioral research involving human subjects. Each institution in the U.S. that conducts research with human participants has IRB oversight, except in cases of minimal risk. The IRB reviews and approves research involving human subjects to ensure that it is conducted in accordance with all federal, institutional, and ethical guidelines.

Informed Consent

Informed consent is the process by which a patient learns about and understands the purpose, benefits, and potential risks of a medical or surgical intervention. Many medical procedures, like undergoing an MRI or having surgery, require that patients sign an informed consent document. To participate in medical research, a potential participant must agree to receive the experimental treatment or otherwise participate in the study. Informed consent generally requires the patient or responsible party to sign a statement confirming that they understand the risks and benefits of the procedure or treatment.

For children to participate in research, researchers must consider both the legal and developmental aspects of competence and capacity to give informed consent. By law, most children (individuals under the age of majority in the state where the research is being conducted) are not considered competent to give consent to medical treatment, let alone to consent to participation in medical research. Thus, researchers must provide information to both parent and child. The parent or guardian provides the *consent* while the adolescent provides the *assent*, or agreement to participate (see below).

Adolescents generally fall under the category of “vulnerable subjects.” Because of this, federal regulations establish specific, special protections for them and children to ensure that adequate, voluntary, non-coerced informed consent is provided. Details of the basic requirements for informed consent for research are displayed below.

Table 1. Requirements for informed consent (Title 45 Code of Federal Regulations Part §46.116)

Basic elements

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental
2. A description of any reasonably foreseeable risks or discomforts to the subject
3. A description of any benefits to the subject or to others which may reasonably be expected from the research
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained
7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject
8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled

Additional elements to be provided when appropriate

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent
3. Any additional costs to the subject that may result from participation in the research
4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject
5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject
6. The approximate number of subjects involved in the study

Consent and Assent

Legally, adolescents are not permitted to provide informed consent (defined above). However, researchers and healthcare providers often request that they provide *assent*, which is an adolescent's verbal agreement to undergo treatment or a procedure or to take part in clinical research. Though assent is not always required for treatment or research to begin, IRBs may require it depending on the type of research and how much harm it poses to the adolescent.

To provide assent, children must be mature enough to understand the trial and what they are expected to do in said trial. Children younger than 7 are usually not considered eligible for clinical trials, but the age varies depending on the maturity of a specific child and the policies of the institution running the trial. This may mean that a child under the age of 7 can give assent to participate in research.

The Assent Process:

1. Parents or a guardian provides the informed consent required for the adolescent to be treated or join a clinical trial.
2. The provider or research team explains the trial to the child in simple, comprehensible language that he or she can understand, including the potential risks and benefits and expectations placed on the child.
3. The child is encouraged to ask questions and is given the decision to provide assent or dissent (basically, a “yes” or “no” response).

Risks Related to Pediatric Research: Federal Regulations

Federal regulations have different designations for pediatric research depending on the level of risk inherent for participants, especially those that are aimed at developing new cancer treatments. These four categories are displayed below:

§46.404. Research not involving greater than minimal risk
§46.405. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects
§46.406. Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition
§46.407. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children

Standard of Care

The legal term “standard of care” mainly falls under the definition of “the degree of care and skill of the average health care provider who practices the provider’s specialty, taking into account the medical knowledge that is available to the physician” (Goguen). Put another way, the standard of care describes treatments that an average physician would customarily or typically offer to a patient with a particular disease, such as penicillin for strep throat. In many studies, participants receive the standard of care so that researchers can compare the safety and efficacy of an experimental treatment against that to determine whether the experimental treatment might be more effective.

Teacher-Directed Class Discussion

1. Are the IRB restrictions placed on adolescents reasonable? Do they accomplish their job in properly protecting adolescents from the dangers of clinical research?
2. Is it morally correct to have the parent/guardian provide the consent while the adolescent patient only provides the assent? Should the patient provide consent? If so, at what age is it safe to begin providing consent?
3. Should the severity (fatality or rareness) of the disease experienced by the patient affect whether the adolescent patient can provide consent?

4. Adolescents in Oncology Research

A particular field of research where ethical concerns are raised concerning the treatment of adolescents is oncology, or cancer research. This is because cancer therapy itself can be toxic, leading to painful or harmful adverse effects (Berg, Stacey L.). Since such toxic therapy is currently the standard of care, oncology researchers testing new therapies hope that the safety and efficacy of these new treatments could potentially reduce the harmful effects of a variety of medicines that are currently in use. According to Dr. Archie Bleyer, clinical research professor at Oregon Health and Science University and the Knight Cancer Institute, “Cancer in children, adolescents, and young adults are so different that each age group needs its own research effort.” He says that “adolescents and young adults have had low clinical trial participation levels in the past, but that’s changing.”

This claim has proven to be true. In recent years, there has been a doubling, even tripling, in the number of adolescents participating in clinical trials for cancer, which provides a beacon of hope for the thousands of patients suffering from different cancers. Looking at only the U.S. in 2021, it is estimated that 10,500 children younger than 15 will be diagnosed with cancer as well as about 5,000 to 6,000 adolescents between the ages of 15 and 19. An estimated 1,190 deaths will occur for children under 15 and an additional 600 for those between 15 and 19. According to ClinicalTrials.gov, in July 2021 there were 5,571 clinical trials being conducted in the U.S. for children with cancer ages 0 to 17; 507 of these trials were active, meaning that they are no longer recruiting and have begun to collect data.

It is important to remember that adult cancer treatments given to children at lower doses are not optimal therapeutic options, chiefly because there are so many types and subtypes of pediatric cancers and because the immune system of a child is not strong enough to withstand the intense adverse effects of adult cancer treatments. Many available therapeutic options, particularly radiation, actually do more harm than good. Children will experience severe adverse effects, such as hair loss, nausea, weight loss, weakened immune system, etc., and there is still no guarantee that the cancer will completely disappear.

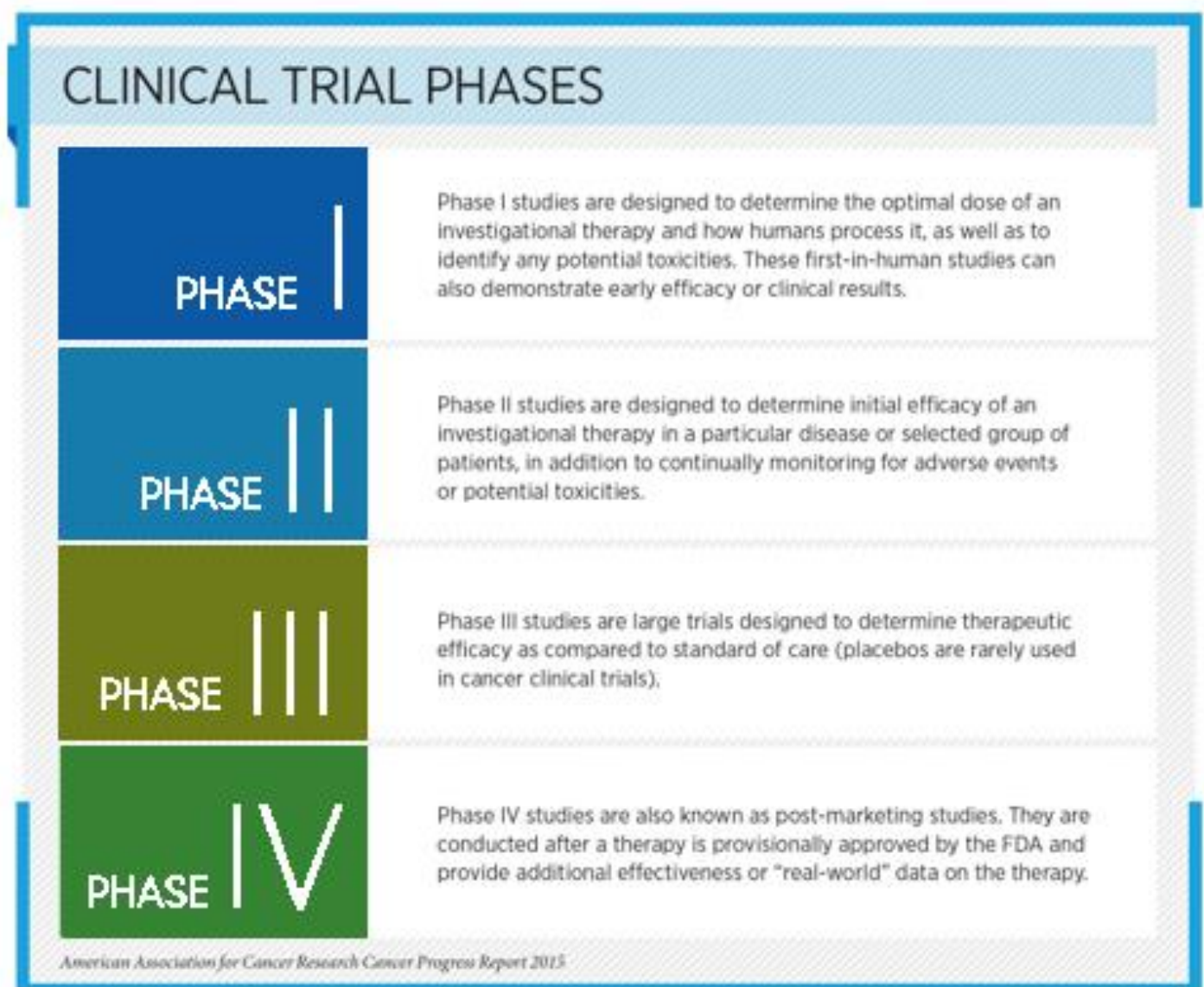
The ethics of oncology research has three specific challenges: obtaining informed consent and assent from children/parents, therapeutic misconception, and concerns related to the unknown safety and efficacy of these new, experimental treatments.

Obtaining Consent and Assent:

Clinical trial researchers often question the quality of consent they are provided because adolescent patients may not fully comprehend the risks, benefits, and potential outcomes of the study in which they are being asked to participate. Because adolescents are usually deemed to be lacking in “competence” and “mental awareness” as they have not reached full cognitive development, two forms of consent have been established: **consent and assent**. Consent comes from the parent, who signs off on any legal requirements so that neither the medical researcher nor the facility conducting the research faces legal consequences. This consent is in turn dependent on the assent provided by the adolescent, which is the agreement to participate in the trial after the details of the trial have been clearly explained to the adolescent. An ethical concern with using parental consent and patient assent is the question of whether there should be “limits to parents’ ability to give permission for a child to participate” in clinical, nontherapeutic research. Adolescents have a right to their bodies and minds as all other human beings do; medical research is, however, one of the many places where the validity of such a statement is questioned. It is difficult to determine whether a parent of an adolescent knows what is truly best for the adolescent. And if the adolescent does provide assent, it is unclear as to “how this affirmative agreement can be measured, how seriously dissent should be taken, and at what developmental stage the child’s wishes should take precedence over all else” (Berg, Stacey L.). This means that each case is unique, for the medical researcher would have to determine, based on his or her perception of the adolescent, whether the patient can grasp and process the information necessary to provide assent. There is no standard method of obtaining

consent, which makes it particularly difficult when one asks whose opinion takes precedence over the other: the adolescent or the parent.

After consent/assent is provided, the issue of dealing with the risks that accompany each study phase arises. Clinical trials are usually conducted in three phases, although the FDA may require an additional study, Phase IV, after a drug has been approved. Each phase focuses on a different scientific question, with the ultimate goal of having the medication or treatment under testing to be approved and adopted for use in the general population. Below is a graphic of what each phase entails:



Ethical concerns about study phases often revolve around “which components of the treatment actually represent research and how much potential risk and benefit those individual components represent” (Berg). This claim compares risk and potential benefit. If one doctor, for instance, claims that a certain procedure presents more harm than benefit but another doctor disagrees, this conflict can sway the IRB against approving that particular study. It is basically a question of how much risk the doctor (or researcher) is willing to place the patient in for the sake of research. Since few are willing to put their daughter or son’s life on the line for the sake of research, this concept raises special concerns in clinical research.

Therapeutic Misconception:

An additional struggle concerning study phases is a phenomenon known as “therapeutic misconception.” When many people consent to research participation, they do so because they believe that they will personally receive a benefit, most often in the form of improved health from receiving an experimental treatment. But individual benefit for individual participants is not the goal of clinical research. The goal of clinical research is to gather knowledge from a representative participant population that can be applied to all people who might benefit from the experimental treatment in development. Indeed, for research to be ethical, researchers cannot know whether the experimental drug will or won’t help a participant. The therapeutic misconception illustrates a tension between the stated goal of the researchers and the motive of the patient for participating in research, particularly a study that has the potential to offer a benefit. Because the patient seeks immediate relief or aid from the agent as opposed to participating for the purpose of gathering generalizable knowledge, the therapeutic misconception can often interfere with the consent process, especially for adolescents. Parents do not wish to cede their children for the purpose of “experimentation.” Thus, parents and adolescents alike are often more likely to retract consent if the immediate purpose of the agent is not to “cure” the patient.

Safety and Efficacy of New Treatment:

One of the remaining ethical challenges relates to establishing the safety and efficacy of the new treatment. Next to consent, this is likely the most prominent ethical concern that pediatric oncology researchers face. Let’s consider the example of a more recent technological breakthrough: molecularly targeted therapy. Molecularly targeted therapy is designed to “specifically target a critical pathway within cancer cells” in order for doctors to tailor treatment to a particular type of tumor (Berg). This removes the issue of excessive tests and screenings to determine

the most effective form of treatment, whether it be chemotherapy or clinically tested pharmaceutical drugs. However, it does present an ethical concern for adolescents. At some point, this technology could be developed to target pediatric tumors without an analogous target in adult tumors, meaning that anticancer drugs and treatments could be developed to first be used in children instead of adults. While it is true that one cannot use treatment meant for adults on children, the fact that the safety and efficacy of a certain treatment was first tested on adults and thus found to be effective has provided some reassurance to doctors and parents for many years. Removing the safety barrier of first conducting research on adults to confirm safety and efficacy makes doctors, parents, and patients extremely hesitant to approach such new technologies like molecularly targeted therapy.

The development of molecularly targeted agents also includes assessments of the drugs on the target. “This brings into sharp focus the problem of more than minimal risk, non-therapeutic components included in therapeutic trials, such as tumor biopsies” (Berg). This again raises the question of consent versus assent. An adult, of course, can consent to trials that pose more than minimal risk, but is it acceptable for a parent to provide consent for an adolescent to take part in such a trial?

The case of *Grimes v. Kennedy-Krieger* in the state of Maryland provides insight into this question. At the end of this 2001 case the court held that “a parent...cannot consent to the participation of a child or other person under legal disability (this includes vulnerable subjects) in nontherapeutic research or studies in which there is any risk of injury or damage to the health of the subject.” “Any risk” was later defined as “greater than minimal risk.”

There is a questionable balance between the positive and negative aspects of adolescent involvement in oncology research. Though their participation is necessary, it can also be life threatening, and the implications surrounding the ethical challenges of oncology research should be first on the agenda of doctors and researchers to deal with before any further advancements are to be made.

Partner Activity

Discussion questions:

1. If the adolescent is willing, should she or he be able to risk her or his life in order to participate in clinical research? Why or why not?
2. Should research be approved if it first tests on adolescents instead of adults? Why or why not?
3. Is the *Grimes v. Kennedy-Krieger* decision a reasonable one? Why or why not?

5. Adolescents in Epilepsy Research

Another prominent field of research that raises ethical concerns is epilepsy research. While cancers are widespread throughout the body, epilepsy deals with, arguably, the most crucial organ of the body: the brain. The brain is the basis for the development of a human being as a person; something like epilepsy, where excessive electrical activity can harm crucial areas of the brain, impairs this development to varying degrees. Extremely severe forms, such as Lennox-Gastaut syndrome or Dravet syndrome, can slow neurodevelopment by years, preventing children from reading, writing, speaking, and carrying out basic functions without the assistance of a caretaker until well past adulthood. Childhood epilepsies are most common among epilepsy diagnoses, thus placing childhood-onset epilepsy in the spotlight of clinical research for this condition.

Unfortunately, many childhood-onset epilepsies are refractory epilepsies, meaning that they do not respond to conventional antiepileptic drugs. This means that extremely severe epilepsies can wreak a path of destruction in an adolescent's brain because doctors do not have an effective way to drastically reduce or eradicate the seizures. There is thus an urgent need to find alternative methods to essentially "cure" refractory epilepsy, as at least 1 person out of every 1,000 may die from sudden unexpected death in epilepsy (SUDEP) each year—meaning there are about 3,000 deaths annually due to SUDEP (Thurman).

The ethical concerns with epilepsy research have much more to do with the physical developments of the adolescent rather than federal regulations. The brain is a delicate organ, so childhood epilepsies present a broad range of treatment challenges that are particular to adolescents. Also, there is a wide range of causes of

epileptic syndromes, many of which doctors have yet to pin down. Thus, the possible negative psychological and cognitive consequences of seizures, and the impact on quality of life, the management of children with epilepsy raises four key ethical issues: communication of diagnosis, the decision of starting a treatment after the first seizure, the use of new drugs in children, and diagnostic challenges.

Diagnostic challenges arise for myriad reasons. When an adolescent has a seizure, it must be recorded using an electroencephalogram, or an EEG, which detects electrical activity in the brain through the use of small, flat metal discs (electrodes) that attach to the patient's scalp. The results appear as spiked lines either on paper or on a computer, and any abnormally large spikes will indicate the appearance of a seizure. Seizures and epilepsy are not synonymous; one does not have to have epilepsy to have seizures. This is why "diagnostic challenges" is one of the ethical issues in the childhood epilepsy community, because treatment is dependent on the correct diagnosis and the child will suffer for it if the doctor fails to properly diagnose her condition. The doctor must be able to determine if the patient suffers from something like tonic-clonic seizures, whereby the entire body convulses and the patient may lose consciousness, or something less severe, like absence seizures, during which the patient simply stares off into space without any physical indication of a seizure. These often require additional diagnostic tests, the dangers of which both the patient and guardian must be aware of. Both patient and guardian must also provide the informed consent and assent to undergo these additional diagnostic tests. Explaining its implications is crucial not only for the guardian but also for the patient; a child or adolescent, whether 5 years old or 15 years old, must still have a certain level of awareness of what treatments they must undergo.

Once the type of epilepsy is determined, treatment options are the next biggest hurdle. Does the patient wish to use antiepileptic drugs? For very severe cases, does the patient wish to opt for surgery, or even the ketogenic diet, which is heavy in fats and meant to slow electrical activity in the brain? These are the types of questions that must be addressed once diagnosis is determined. The problem is: Who answers them?

The answer may seem very obvious, but if one has a 5-year-old patient with extremely severe seizures and a parent who is seemingly oblivious about the disorder, the situation becomes very complicated. The doctor must address the patient's guardian, who must make the decision about whether or not he should implement changes into the patient's life, sometimes ones that are very drastic, such

as invasive neurosurgery. While necessary, these changes are not ones that can always be assented to by the oblivious 5-year-old child with refractory epilepsy, who must undergo treatment with very little understanding of what that treatment actually entails. If the child feels uncomfortable and does not want the treatment, is it ethical, humane even, to ignore that protest and tell the child that this treatment is for his own good? Or should both doctor and guardian comply with the patient, who is not even old enough to be considered legally competent? This type of situation is what puts doctors in a bind when it comes to staying within ethical limits of a medical practitioner's job while also ensuring the patient receives the best standard of care possible.

There are, of course, individual risks that come with taking standard anti-epileptic drugs, which both guardian and patient must be aware and consent to. There must also be discussion of “potential risks of recurrent seizures, on and off medication,” and other details about changes that treatments either entail or cannot control. As stated before, seizures are not synonymous with epilepsy, so “whether to treat a single unprovoked epileptic seizure becomes an individual decision for each patient, dependent from the possible detrimental effect of AEDs (antiepileptic drugs) on one hand and the risks and consequences of a second seizure on the other” (Barba). If the seizures are not detrimental enough to cause significant change in the patient’s life, or are extremely sporadic, the question of taking AEDs and risking side-effects as opposed to depending on the chance of a second seizure *not* occurring is something the patient must weigh. These implications are also something that the doctor must discuss, even if the patient cannot fully comprehend it.

The use of new drugs is a common ethical challenge in any branch of medicine. For adolescents who do not respond well or at all to standard AEDs, the “clinical goal is to find an optimal balance between the benefits and side effects of any medical treatment” (Barba, Carmen). There are two questions that accompany the topic of new drugs: is it safe enough to be tested in humans, and when should it be administered? Including adolescents in clinical trials to test the safety and tolerability of a new drug is already accompanied by layers of regulations and safety concerns. Even if a medication is approved after a trial has been completed, the question of when it should be publicly administered hangs in the balance. Doctors and researchers must still keep track of trial participants’ responses to treatment and account for any long-term harm. However, financially, the faster a

new drug arrives on the market, the faster revenue will flow in. There is thus an ethical question here about whether financial concerns should trump patient safety.

These are the most prevalent dangers in epilepsy research, but they should not stand in the way of adolescents participating in clinical trials. The most recent breakthrough in support of this claim is the approval, in 2018, by the FDA of Epidiolex, a pure cannabidiol (CBD) plant extract developed by the British company GW Pharmaceuticals. In layman's terms, this is liquid medical marijuana. Under the supervision of GW Pharma, and in conjunction with Dr. Orrin Devinsky, director of the Comprehensive Epilepsy Center at NYU Langone Health in New York City, Epidiolex was studied as a treatment for severe, early-onset, treatment-resistant epilepsies of Dravet syndrome, Lennox-Gastaut syndrome (LGS), tuberous sclerosis complex (TSC), and infantile spasms (IS). Trials included patients under the age of 18, and the approval has provided a beacon of hope for the thousands afflicted with treatment-resistant epilepsy. The positive results from these types of trials should prompt the continuous participation of adolescents in clinical trials, as this kind of participation is what advances the field of science and allows for new, alternative treatment options to become a reality.

Partner Activity

Discussion questions:

1. Should financial implications take precedence over the safety of patients when it comes to the introduction of new antiepileptic drugs, especially in such a highly competitive market? Why or why not?
2. If a child under the age of 7 suffers from very severe epilepsy, should the parent be able to consent to treatment on behalf of that child, even if the child does not fully comprehend the treatment he/she is undergoing? Why or why not? (Remember: 7 years old and under is generally the age where doctors consider children unable to provide consent.)
3. Hypothetical situation: If a patient is diagnosed with epilepsy after seizure but is assured that it is not severe and a second-time occurrence is very unlikely, should the patient still take antiepileptic drugs? Why or why not?

6. Conclusion

Individual Activity

1. List the benefits of parental consent and adolescent assent.
2. List the drawbacks of parental consent and adolescent assent.
3. Should adolescents be permitted to provide consent without a guardian? Why or why not?
4. What should be the minimum age of participation for adolescents to be involved in clinical trials?

Group Activity

1. In what ways can the consent/assent system be improved?
2. Determine what the outcome of this situation should be: A child age 10 is diagnosed with pancreatic cancer. The doctor prescribes heavy doses of chemotherapy and radiation, but the child does not wish to undergo treatment. The doctor is convinced radiation will help the patient. The doctor turns to the parent/guardian for consent. Is it right of the doctor to only address the parent/guardian? Should the parent/guardian provide the consent, given that the child does not wish to undergo treatment?

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