#

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**THE ETHICAL CHALLENGES OF NEW TREATMENTS IN CHILDREN:**

**could we do now what we did then?**

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This is a lecture about the core values which should underpin the work of a surgeon. [SLIDE] We should make the patient **safe**, ensure that our treatments are **effective** and give those patients the **best experience** during treatment that we can. We must tell the **truth**; to them, their families, our colleagues and the wider public. If we do not do so, we lose the key relationship which supports good care; that of **trust**. [SLIDE] Trust takes years to build, but only seconds to break, and over the years the medical profession has repeatedly broken that trust, culminating in attitudes not wholly different from those of George Bernard Shaw, [SLIDE] who in his preface to The Doctor’s Dilemma (1909) said *“the medical profession is a conspiracy to exploit popular credulity and human suffering”*.

In my last lecture[[1]](#footnote-2), I described some of the key discoveries and consequent pioneering procedures which have characterised the history of surgery for congenital heart disease. I drew attention to some of the surgeons involved in those early steps, and talked a little about some of their attitudes and behaviour.

I described several of them (but not all) as mavericks. [SLIDE] And a maverick is “*a person who shows independence of thought or action, especially by refusing to adhere to the policies of a group to which he or she belongs*”. You might remember that the first operation for a congenital heart defect (Persistent Ductus Arteriosus ligation) was done by Gross; but only when his boss went on holiday. And everyone describes Lillehei as a maverick.

There can be little doubt that they were taking risks based on the premise that they believed passionately that they could treat congenital heart defects. The risks they were taking were reputational and professional. But the risks taken by their patients and their families were of a different order; not only were the patients’ lives on the line, but no one could predict what those lives would be like if they were to live.

As humans, we often take risks when making decisions despite being uncertain about their effects on our future lives; for example in choices of education, occupation or partner. [SLIDE] Risk can imply something ‘undesirable’, but it can also imply ‘lack of knowledge’ - something that has an unknown outcome1. The surgeons we discussed last time cannot have *known* the outcome of what they proposed to patients and they certainly cannot have known the potential *total* consequences of their actions. We can only guess at what was said to those patients in advance of the surgery. [BLANK SLIDE] But times were different then, and medicine was certainly more paternalistic than it is now. What we can be sure of was that the *surgeons*’ lives were not at risk.

The surgeons I named instituted changes and procedures that have had a profound impact on patients’ lives and the speciality itself. Subsequent refinements have dramatically improved survival. But at what cost were those advances made? Were there others out there trying to do the same, but not successfully, or surgeons copying the strategies of these innovators and failing to report the outcomes? Do we only hear about success? It is well known that Journals prefer to publish positive results, and researchers are prone to ‘search for significance’, (this has become known as publication bias)2,3 . Have the total consequences of these strategies on patients, families and society been fully reported and understood?

And if these individuals had been trying to introduce their innovations in the current regulatory framework, would they have been allowed to do so by ethics committees, their institutions or their peers? Or more importantly, well-informed parents and patients?

[SLIDE] Perhaps it should be not ‘could we do now what we did then’, but ‘*should* we have done what we did then?’

It is human nature to want new stuff, to seek new ideas and to try new ways. But, there is often confusion between the terms *invention, innovation* and *research.* [SLIDE]

**Invention** is the *creation* of the idea or method itself.

**Innovation** is the *use* of something new (drug use, process or procedure) to alter the course of events. It must be based on existing science, knowledge and where possible practice. In a medical context it has usually come to mean the application of a new idea to a specific patient for whom there is no available tested alternative.

**Research** is creative work undertaken on a *systematic* basis and in the context of medical science the accumulation of relevant data. In medicine, a hypothesis is usually being tested by conventional scientific method such as comparing one set of patients treated the new way, with one not treated at all or with either a placebo or the old way. The answer as to which is better will be found in the data generated by the study.

Medical science is founded on these definitions, all aimed at improving the lot of patients.

In theory at least, innovation should be in the interests of everyone, patients and doctors alike. Humans generally want to live disease free, for longer and with a good quality of life. Who wouldn’t support an innovation in patients for whom there is no available effective treatment for their condition and who otherwise might look forward to distress and suffering, in addition to a shortened life? The rewards for the patient if the innovation proves to be successful are obvious.

[SLIDE] In fact, doctors and nurses innovate every day in small ways; by varying treatment by altering doses or combinations of drugs, or (as in my case) carrying out operations in a slightly different way to reflect the specific needs of that patient. Sir Robert Francis QC has argued4 that the public *expects* that, *wants* that and indeed the staff may *have a duty* to do just that.

It is not just the patients for whom the rewards for innovation may be considerable. The medical staff also benefit [SLIDE]. Obviously, the human benefit of seeing an innovation work for a patient to improve their health should be the primary reward. But careers and reputations are built on these individual successes, by publication, presentation, merit awards, potential financial gain and certainly kudos. Doctors have been very effective over the years in putting themselves and their success ‘out there’, and there are media hungry for such stories. Sadly these temptations have proved too great for some, and innovative treatments have been tried without adequate agreement from the patients, or maintained in the face of contradictory or inadequate information. Supporting the view of GBS [SLIDE] that ‘*most doctors, like other Englishmen, have no honour or conscience’* [Preface to the Doctor’s Dilemma again]The power of opinion over fact.

Over the centuries doctors have not exactly covered themselves in moral glory [SLIDE], as so many have been exposed as charlatans peddling unsuitable or unproven treatments to the weak and vulnerable, raising false hopes, causing pain and even death5. As Roy Porter states5, *‘before the 19th Century, traditional medicine was, and was widely seen to be, a ‘dad’s army’ in the face of invasions of epidemic sickness. Desperation created an insatiable demand for a multiplicity of healers: amongst them were quacks’*. Medical men of all sorts competed for custom, recognition and reward. Margaret Pelling (1987), (quoted by Porter), said *‘each in his own way…made his bid to seize the moral high ground in a medical arena in which the law was acknowledged to be dog-eat-dog.”*

In the 18th Century, quackery was common [SLIDE], [SLIDE] trading on both the desperation of patients and the need of physicians to make an income. [SLIDE] Samuel Johnson in his *Dictionary* (1755) defines A Quack as (1) *a boastful pretender to arts which he does not understand,* (2) *a vain boastful pretender to physic, one who proclaims his own medical abilities in public places,* (3) *an artful, tricking practitioner of Physic.* [SLIDE] Here are some excellent examples of quackery in action, and not just from that century.

Patients at their lowest ebb need to be protected from such people. It must be incredibly tempting to accept the offer of a new therapy if there is little hope elsewhere. “I’ll try anything doctor”. Or, “I’ll go anywhere to get the best doctors” [SLIDE] As Levin has pointed out6, there is a certain status that comes with treatment by a doctor who is ‘*at the cutting edge*’, and this is perhaps even truer when the stakes are high.

Patients **are** at their most gullible, and sadly some physicians have always been willing to exploit that.

Nowadays, ethics committee approval and informed consent have become widely accepted as prerequisites for any treatment, but it is salutary to consider for a moment how these rather obvious restrictions came about.

The role of the doctor is generally assumed to be that of healing and support. This is an understanding going back to ancient times, made manifest in the Hippocratic Oath and largely practiced over the centuries.

[SLIDE] “Trust me, I’m a doctor”. But how we have let down that trust.

[SLIDE] Torture has been a terrible stain on human history almost from the beginning of time. Used by all regimes, it became systematic in the Spanish Inquisition at the end of the 15th century. Unfortunately, in 16th Century it became clear7 that doctors had strayed from their traditional roles of care and healing and become involved in the very opposite, namely torture. [SLIDE] In *Constitutio Criminalis Carolina* in 1532 (in the reign of Charles V), clear reference was made to the complicity of doctors in torture. Maio7 reports that in the 16th century there were ‘torture physicians’, present at the time of torture, and whose job was to advise when to stop the torture to avoid death, to assess when unconsciousness was real or simulated, and to treat fractures to allow the torture to continue. [SLIDE] This practice is still going on in 2015, as the case of Raif Badawi in Saudi Arabia demonstrates [http://www.bbc.co.uk/news/world-middle-east-30847692].

 In reality, torture was regarded as legitimate right up until the 18th Century, and doctors who at the time could do little more than alleviate pain, were considered part of the ‘authorities’. There was a basic fear that courts would have difficulty convicting criminals without torture, and it was thought to be a pre-requisite for ‘internal security’. [SLIDE] Although the utilitarian philosopher Jeremy Bentham (1748-1832) questioned the use of use of torture, he actually recommended its use, ‘especially where the whole state may be endangered’. He described torture as a weapon of ‘inestimable power’. For the doctors involved in that era, torture was not a *moral* problem, although many did criticise it on the basis of its *effectiveness*.

It was not really until the 20th century [SLIDE] that there is disturbing evidence of a more direct role for physicians. They began to take an active part in torture, devising new methods and using observational science to determine just how much pain and suffering humans could endure. At least since the second world war we have real evidence of medical involvement, although I find it difficult to imagine that doctors and nurses had not been involved in torture in earlier conflicts.

Of course, the role of doctors in a military role is fraught with difficulty. As Michael Gross put it8 *“medical personnel are not in any way neutral or above the fray. Quite the contrary, medical care is an adjunct of war; it does not speak of easing the pain and suffering of individual soldiers as an end in itself, but of conserving manpower, maintaining military capabilities, and preventing, as one military manual put it “adverse effects of unevacuated casualities on combat efficiency…by providing adequate medical care and rapid evacuation” [Army Field Manual, FM8-10, 1951, 195].*

[SLIDE] The second world war was a turning point. Horrific though that is to hear, it was the discoveries of what doctors had been doing in the camps [SLIDE] [SLIDE] associated with the Nazi regime, exposed in detail at what became known as the ‘Doctor’s Trial’ at Nuremburg [SLIDE] that both brought the potential cruelty of doctors most directly to public attention, and fundamentally altered the balance of trust between physician and patient. Most of you will know of these notorious doctors, and at least something of what they did, either directly as torture or in the name of medical research.

To quote again from Gross8, *“like Elie Wiesel, we are apt to believe that a medical degree ought to ‘shield’ doctors from evil”*. The acts of the Nazi doctors clearly demonstrated that it does not. These doctors[SLIDE] [SLIDE] [SLIDE] carried out, in concentration camps, a series of medical (so-called) ‘experiments’ on large numbers of prisoners, mainly Jews (including children) from across Europe, but also in some cases Romani, ethnic Poles, Soviet POWs and disabled non-Jewish Germans. Prisoners were forced to participate; they did not volunteer and there was no consent. And typically,the experiments resulted in death, disfigurement or permanent disability. This was true medical torture.

Among the doctors involved were assistant and tenured professors, clinic directors, the personal physician of the Chancellor, the head of the German Red Cross, the highest ranking physician in the German army and air force and biomedical researchers for industry, the military and the universities[SLIDE]9. These were people like my peers and I; physicians, surgeons, researchers, colleagues. What made them able to do that? And more worryingly could I, or any of my peers, have done it in the right circumstances? It seems so far away from what medicine is all about that it is really hard to believe, and does prompt consideration of the concept and definition of evil.

Is what is ethical a product of the time in which we live or the company keep? It is clear that the physicians involved in these concentration camp horrors had all bought into the Nazi dream of Aryan domination and racial purity. How they might have arrived at that view has been very well reviewed by Hartmut Hanauske-Abel9, who considered whether the behaviour of the Nazi doctors carrying out the experiments was the result of some sort of moral decline, ‘a slippery slope’, or the result of ‘sudden subversion’ brought about by their new masters, the National Socialists. This latter view was held for years by the German Chamber of Physicians, which in only 1986 acknowledged that they had “unfortunately” destroyed potentially embarrassing documents relating to their collusion with the Hitler administration. Hanauske-Abel was not convinced by these arguments and set out to review the evidence set out in German medical journals in 1933 to see if that would give a clue as to what was being read and studied by the 52, 518 doctors then practicing in Germany. He considered the political, scientific and economic arenas of the time.

In 1932, the 3rd International Eugenics congress met in New York[SLIDE] and elected as its President Professor Ernst Rudin of The Kaiser-Wilhelm Institute of Psychiatry in Munich, famous for its research into the genetics of mental illness. Hanauske-Abel helpfully defines9 eugenics as a metascience combining population statistics, genetics, anthropology, psychometrics, history and religion into a form of preventive medicine that endeavours to define and eradicate inherited illness. The social impact of this was defined as “*rassenhygiene* – racial hygiene”, building on the ideas of Ploetz and Schallmeyer [SLIDE][SLIDE]from the turn of the 19th century10. Within months, the two biggest German medical societies sent a petition to the ministry of the Interior in the Weimar Republic requesting that it should draw up legislation to permit sterilisation on eugenic grounds ‘to guarantee the integrity of the population’s gene pool’.

Hitler came to power in January 1933, and in March the leaders of these two main German medical societies, The Hartmannbund and the Deutscher Artzvereinsbund held intimate talks with National Socialist colleagues in Munich, after which [SLIDE] Dr Alfons Stauder president of the Hauptmannbund telegraphed Hitler with this message *“the principal professional organisations in Germany gladly welcome the firm determination of the Government of National Renewal to build a true community of all ranks, professions and classes, and they gladly place themselves at the service of this great patriotic task.”* Stauder met Hitler on the 5th April, and a week later [SLIDE] the Deutches Artzteblatt announced the meeting with Hitler on its title page and published Hitler’s manifesto of racial purity and the elimination of Jews form cultural and spiritual life, and his call to physicians to ‘*build a firm foundation for the genetic development of the nation*’ and to participate in this work through scientific research and practical assistance.

On the 19th April, the German Society for Surgery also telegraphed a homage to Hitler, and its 57th Annual Meeting was held under ‘the symbol of the New Germany, the Swastika. By July 26, 700 people had been placed in ‘protective custody’, and by the end of 1933, several dozen concentration camps had been established, including Dachau and Sachsenhausen. [SLIDE] Advertisements for lucrative positions for doctors at these camps soon appeared. Physicians went on certify on government forms that tortured prisoners are in excellent health, that emaciated inmates could work if discharged, and that ‘natural causes’ led to death in detention. Within short order physicians falsify the medical records of victims and suppress physical findings of torture.

In July, the regime enacted, as part of its racial purity agenda, and as the doctors had asked, the Sterilisation Act, paragraph 12 of which instructs that the operation “*must be performed even against the will of the person to be sterilised*”. Force could be used, and amongst the ‘genetic diseases’ listed were alcoholism and psychiatric disease.

Physicians asked for this, catalogued the patients and carried out the procedures. By August 1933, the Deutsches Artzeblatt published an article by Lommel 11 lauding these phrases:-

 ‘legally enforced sterilisation’

 ‘creating a new, biologically cased nobility’

 ‘extermination of life not worth living’

This last became part of continuing medical education and a standard technical term.

[SLIDE] Doctors applied the new sterilisation laws with zealous enthusiasm, so much so that the Nazis even reined them in in 1938 after they greatly exceeded their targets. In 1939, the sterilisation program was halted, and replaced by [SLIDE] the T4 euthanasia program; “*a nationwide, centralised and peer-reviewed programme to murder adult and paediatric patients clinically classified as futile or terminal cases*”.

[SLIDE] **These were doctors**. A whole raft of them. Senior physicians in positions of authority. They were respected and trusted. They managed their professions, edited their journals, upheld the professional standards of their peer groups taught their students…and yet, and yet, within a very few years they had fundamentally deviated as a group from what for centuries had been regarded as the core elements of the profession. They had become murderers and torturers, apparently insensitive to the needs of other human beings. [SLIDE] By the end of the 30’s there were virtually no Jewish doctors practicing openly in Germany, but the rest of the doctors were making more money. Hanuaske-Abel concluded his in depth review of the papers of the time that it was the convergence of political, scientific and economic factors that resulted in the quantum change observed in the medical profession in 1933. It happened once, and could happen again, and we must always be on our guard.

[SLIDE] Trust takes years to build, but only seconds to break. And that is what happened as a result of public awareness of what the Nazi doctors were capable of. The public realised it needed protection from the doctors.

After the Nuremburg Doctors Trial, the concept of medical ethics developed rapidly and was manifest in the Nuremburg Code [SLIDE] and the subsequent Helsinki declaration. The Nuremburg Code was originally made up of six main points drawn up by Dr Leo Alexander (one of the military lawyers at the trial) to define legitimate medical research. These were adopted in the Trial Verdict and four more added. I reproduce it here in full.

***THE NUREMBERG CODE***

*1. The voluntary consent of the human subject is absolutely essential.
This means that the person involved should have legal capacity to give consent; should be*

*so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved, as to enable him to make an understanding and enlightened decision. This latter element requires that, before the acceptance of an affirmative decision by the experimental subject, there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person, which may possibly come from his participation in the experiment.*

*The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.*

*2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.*

*3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study, that the anticipated results will justify the performance of the experiment.*

*4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.*

*5. No experiment should be conducted, where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.*

*6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.*

*7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.*

*8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.*

*9. During the course of the experiment, the human subject should be at liberty to bring the experiment to an end, if he has reached the physical or mental state, where continuation of the experiment seemed to him to be impossible.*

*10. During the course of the experiment, the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgement required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.*

*["Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10", Vol. 2, pp. 181-182. Washington, D.C.: U.S. Government Printing Office, 1949.]*

You would think such events and such a code would strengthen the moral behaviour of clinicians. Not so I am fraid, as the recent CIA report has demonstrated.

The Nuremberg code was superseded by the Helsinki Declarations (<http://www.wma.net/en/30publications/10policies/b3/>) and the Good Clinical Practice rules (<http://www.therqa.com/committees-working-parties/good-clinical-practice/regulations-and-guidelines/>), but remains highly relevant and the essential source of the four basic principles of modern medical ethics [SLIDE] 12 , namely;-

**1. Beneficence**

a. Medical practitioners should *act in the best interests of the* *patient*

b. They should prevent harm, remove harm and promote good *for the patient*

**2. Non-Maleficence**

a. Medical practitioners *must not harm the patient*

**3. Respect for Autonomy**

a. Capable patients must be allowed to accept or refuse recommended medical interventions

*b. Voluntary, informed consent*

**4. Justice**

*a. Health care resources should be distributed in a fair way* among the members of society

There is clearly often a balance in these issues between the status of the individual and the needs of society. As we saw in 1933, concepts of what is right ethically vary over time and in relation to the society in which they are evolved. That is why some authors13 have suggested that respect for *individual* *dignity* and a principle of *veracity* (which requires the complete truth to be shared with patient) be added. This latter has been reflected in the Duty of Candour described in the Francis Report (http://www.midstaffspublicinquiry.com/report).

[SLIDE] The ethics of innovation when children are concerned are even more complex than those core principles described above. The child is often not competent to make the decision for itself; the parent or guardian has to act as their agent, which imposes a huge load on them at a difficult time. They feel pressure to treat from the physicians, and often from peers, relatives or religious advisors. In the context of early cardiac surgery, there was little concept of the long-term consequences, good or bad, of the interventions being planned. The treatment might turn out to be worse than the disease, and the family has to consider their role not just in giving life to a child, but also to protecting it from future harm. Any family agreeing to surgery was entering into a contract built on uncertainty. If the surgeons or their team are less than honest about this uncertainty, or if the parents feel pressure from the treating team to proceed, this can create a very bad situation indeed.

This was the background against which cardiac surgery was developing in the immediate post-war period. [SLIDE] There was a ‘hot-house atmosphere’ in cardiac surgery. The need for surgery of the heart was obvious. Without surgery for many congenital conditions, the affected children would die. And if they did not die immediately, their death was likely to be unpleasant for both them and their families. [SLIDE] That surgeons, teams and institutions were willing to offer pioneering and often radical therapies must have seemed like a beacon of hope [SLIDE] to such families.

But there is always hope, and much of what medicine is built on is hope. This has been most clearly expressed by Gil Wernovsky, a paediatric cardiology colleague of mine from Philadelphia (now in Miami) who wrote in 2008, in the context of the value of treating hypoplastic left heart syndrome; - *“By not intervening for HLHS, we deprive today’s patients of today’s results, but more tragically, we deprive them of what is to come in the future.”* In other words, even if the outcome turns out to be bad something will turn up which helps sort it out. Medical Micawberism perhaps, but it is what sustains many of us carers and families alike, through difficult times. It is also the case that parents may, understandably, ‘grasp at straws’ and be unable objectively to weigh up the risks and benefits proposed to them14,15.

[SLIDE] The question I posed for this talk is whether it would be possible to do now what was done then, in the development of cardiac surgery. It is useful to test out the early developments against the ETHICAL framework. Before I do so I want you to think for a moment about the dilemmas that faced those involved at the time, and which recur frequently in modern practice.

Is a child’s life to be valued above all else, even if the quality of that life is so poor that it involves permanent suffering, not only for the patient but for all those who care for them?

For the parent of a child being put forward for innovative surgery, does the hope of life overpower the possibility of suffering?

Might not everyone’s life be better if the newborn baby were allowed to die, rather than go through such complex, unpredictable surgery with unknown consequences?

Perhaps the weight of risk might be better managed by trying to have another child; allowing grief, but creating life.

[SLIDE] Al Eyadhy and Razack recently outlined16 the current ethical framework appropriate for innovative treatment in children:-

 *Patient’s autonomy*; The parents or guardians have the right to refuse treatment. Paediatricians should *help* the parents decide, taking into account capacity, perspectives, culture and values. They should use language that can be understood easily and focus on long-term goals as well as technical issues. They should answer questions fully and honestly.

 *Professional Consensus;* if there is little evidence so far that a therapy might work, expert opinion can be used to support a decision.

 *The Role of the Institution*; the host organisation must maintain quality assurance, risk management and ensure appropriate resource allocation. Institutional ethical review

 *Evaluation;* innovative treatments should be evaluated and reported.

This is consistent with the advice of the IDEAL group17-19, and outlined on this [SLIDE]. This has been taken a bit further with a simple aide memoire from Jenny Schwartz in Washington. The ETHICAL model. [SLIDE]

There is no significant literature about how patients felt about their involvement in these early developments, although my good friend and colleague, Dr Kate Bull is currently working on a book [*personal communication*]to collate these patients’ perspectives. For the moment we can only speculate on what they felt and what they were told.

So, [SLIDE]let us apply Schwartz’ ETHICAL framework to Lillihei’s cross circulation experience.

1. Would Lillehei have been able to demonstrate adequate **Expertise** in his field? I don’t think there is any doubt about this. He understood××× the physiology, anatomy and basic science as much as or better than any of his peers.

2. Did he possess the **Technical** skill and have the correct **Technical** equipment and training to do the procedure? Again, there is little doubt about this. He is often described as an excellent technical surgeon, and certainly was involved in developing the necessary equipment.

3. Did he assess fully the probable **Hazards** of both performing and not performing the operation? The ‘net hazard’ must be much less with the chosen procedure. Did he consider the risk of iatrogenic injury as a result, and could he even begin to anticipate any long-term consequences? This is much harder to know. His papers imply that he had considered all this, but he was the dominant personality in the institution and it is unclear whether, even if he had asked for significant peer review, anyone would have stood in his way.

4. Did Lillehei obtain adequate **Informed consent** before proceeding? Again, how can we really know. Even in my working lifetime the concept of consent has changed enormously. In the early days of my training, there was a tacit assumption that patients would be unable to grasp the complexities of what was involved, and anyway, why should they? The surgeon had many years of complex training and was bound to know better than the patient what was good for them. Why worry them with what might go wrong when we are trying to make them ‘better’?

5. Was Lillehei free from **Conflicts of interest?** Almost certainly he was not. Schwartz gives as examples of conflict of interest the use of equipment or materials from which the surgeon would benefit financially, prestige, career advancement, honours and awards, CV enhancement or just the desire to be first. Lillehei fits all these. And the political and cultural backgrounds to the developments were important. *The achievement of the open heart repair of a blue child was a realisation of American virtues: the Minneapolis Heart Hospital itself had been built by the philanthropic efforts of the Variety Club and in 1952, President Truman had declared “war against heart disease” and made Federal funding available for heart research.  Here was a dividend that would go down in world history [Bull,C. personal communication].* We also know that he was developing very close links with colleagues in Industry, and he later went on to develop the first Pacemaker with Earl Bakken and joined Medtronic. He held many commercial patents and it seems extremely unlikely that he was not involved with at least thoughts of commercialisation at that time. Of course, that may have been the only way to get things done, but conflicts of interests would be watched very carefully these days.

6. Did he devote adequate time and effort to the **Analysis** of the outcome and relevant endpoints? And was it planned that this work should lead to more robust trials? Probably, but again we cannot be completely sure. The whole Minnesota practice was devoted to making heart surgery work, and did so. Trials of surgical practice remain controversial20-23.

7. Did he publish the results in peer-reviewed **Literature** or registries regardless of the outcome? He did publish24, and he and his team continued to do so.

[SLIDE]We know that Gross waited for his boss to go away before ligating and dividing the ductus Arteriosus, to test out an idea that ‘that had been banded about’ [see my previous Gresham Lecture], and whilst he had expertise and technical skill it was clear that the hazards were considered very great by his peers and we were given an inkling in the video of his patient that I showed you last time that informed consent may have been cursory. The result was published, but we do not know of other patients in other places. He certainly had conflicts of interest in the same way as Lillehei, but he did pay a temporary price for his behaviour by being suspended and fired.

 [SLIDE] The palliative operation introduced by Bill Norwood25 for hypoplastic left heart syndrome (HLHS) in 1980 in Boston was highly controversial. At the time, Norwood was said26 by both peers and his the boss, Aldo Casteñeda, to be ‘a frustrated surgeon’, because all the cardiologists wanted to send their patients to the world-renowned Casteñeda. Norwood had time on his hands and started thinking about HLHS. He had enough of an idea worked out on paper to convince Casteñeda to let him try it out in 1979. Casteñeda’s recollection is said to be different26, and he at first said the procedure would take place ‘over his dead body’ and only Norwood’s persistent nagging resulted in the procedure going ahead. Casteñeda left him to it, and eventually a whole system evolved around the procedure. Norwood claims that initial results were ‘good’ from the start, with a 30-35% death rate. Others recall the mortality as ‘awful’ and ‘discouraging’ while they tried to figure it out. Certainly by the time Norwood moved to Philadelphia a few years later, the mortality was 50% in his first 10 cases there (Gaynor, W., *personal communication*).

Many people think that the moral decision to proceed to a Norwood as palliation was not, as Michael Ruhlman put it, ‘gut-wrenching’, because the alternative was certain death. But several studies27-29 have reported the unwillingness of cardiologists and surgeons to consider the treatment in the hypothetical circumstance that their own child had the diagnosis, largely based on the multiple operations required, uncertainty about medium and long term prognosis, and the total ‘disease burden’. For many years, the long term mortality was approaching 50% in most centres, and even now is 20% in the Milwaukee, Wisconsin (Mussatto, K., Tweddell, J *personal communication*), recognised as the best current results.

Norwood had a very strong personality, and a reputation, well-deserved, for wanting things done his, often idiosyncratic, way. This style of work reached its apotheosis in the hospital in Wilmington, Delaware where he became chief late in his career, and which was run absolutely to his rules. He was shown the door in 2006 for ‘failing to comply with hospital policies regarding informed consent and the use of a medical device”. As the Philadelphia magazine put it at the time30, *“had Norwood finally lost the ethical battle he’d been fighting for 30 years – caught in the gap between the human desire for progress and the equally human unwillingness to bear the cost of it”.* This is the key ethical dilemma; is the innovation worth the pain?

Norwood’s story, personality, style and unflinching drive reflect very clearly the ethical issues we address today. He would certainly fail several of Schwartz’ ETHICAL tests. There was a suspicion of poor consent at the time, and certainly in later there is evidence that he did not carry this out to the standards of the institution in which he worked. There was conflict of interest in many respects. But he just pressed on. Eventually the mortality fell in most centres, and the Norwood strategy is very much part of the mainstream of cardiac surgery. Many people are alive today, perhaps because of his persistence. But there was a heavy toll on the way, a cost of human ‘guinea pigs’ seen before in medicine31, and many physicians remain unconvinced even now that the course of treatment is the best option.

[SLIDE] But there is always hope, and much of what medicine is built on is hope. This has been most clearly expressed by Gil Wernovsky, a paediatric cardiology colleague of mine from Philadelphia (now in Miami) who wrote in 2008, in the context of the value of treating hypoplastic left heart syndrome; - *“By not intervening for HLHS, we deprive today’s patients of today’s results, but more tragically, we deprive them of what is to come in the future.”* In other words, even if the outcome turns out to be bad something will turn up which helps sort it out. Medical Micawberism perhaps, but it is what sustains many of us carers and families alike, through difficult times. It is also the case that parents may, understandably, ‘grasp at straws’ and be unable objectively to weigh up the risks and benefits proposed to them14,15.

[SLIDE] I want now to consider the arterial switch operation (the Switch) for Transposition of the Great Arteries (TGA), introduced by Jatene in 1982. It is an important development, different from the others, in that there was a relatively successful alternative treatment in place at the time. [SLIDE] That alternative was atrial redirection of the flow of blood in the heart, using (mostly) the Senning procedure. In the Senning procedure. There were significant theoretical advantages to the switch procedure, because it resulted in the appropriate left ventricle pumping blood around the body (except the lungs) whereas the Senning operation resulted in the right ventricle (RV) in that role. The RV cannot sustain that role over the whole course of a long human life and thus there was a late attrition rate. But the switch, in its early days, and in every new surgeons hands, carried a much higher *initial,* operative, mortality. So the problem was this, should a unit start doing the switch on the basis that it might be better in the future, or was it better for the child and family to stick to the lower mortality of the older, Senning operation?

[SLIDE] This was the basis of a brilliant study32 carried out at Great Ormond Street by a very smart cardiologist called Kate Bull, and my colleagues rob Yates, David Sarkar, John Deanfield and Marc de Leval. They looked at the consequences of our team’s decision to change from the Senning operation to the switch operation in anticipation of long-term benefit.

Earlier, in 1985, [SLIDE] Fergus Macartney had developed33 an actuarial model to describe the short, medium and long term hazards of these operations to help guide decision making. The model clearly reflected the anxieties of all of us in trying to work out whether the transition was wise. Bull et al looked at all 325 patients with TGA having either a Senning or switch between 1978 and 1998. There was a period at the start of this time when only the Senning was done, era 1, a period, era2 when both procedures were done, and era 3, when only the switch was done.

[SLIDE] The results are shown diagrammatically on this slide reveal the cumulative mortality for patients over these eras, compared with another complex operation to see if background risks were relevant. The Sennning mortality rate was essentially unchanged over the whole period, but the rate for the Switch was very high at the beginning of the experience, but much better later in era 3. [SLIDE] This can be seen another way in these logistic regression models which directly compare the probabilities of death over the eras. These data clearly show that the switch operation ends up as the better choice (higher early, lower late mortality), but that its introduction was associated with a transient increase in mortality whilst our team and others learnt how to do it better and better. The learning curve.

[SLIDE] This study highlighted the fact that the ultimate success of a new procedure has a very significant cost for those families engaged in the transition period. It is vital that there is appropriate scientific, logistical and ethical assessment of such progress. Children’s lives are involved, and what might be considered the sacrifice of some for the common (long term) good is terribly challenging for all concerned. The Switch has turned out to be successful. Mortality today approaches zero in the UK, but what if it hadn’t? It is crucial that we gather data about the consequences of our work over long periods of time, and that failed treatments are not pursued. [SLIDE] As Buxton’s Law (1987) states “*it is always too early (for rigorous evaluation) until, unfortunately, it is suddenly too late”.* Electronic records, data sharing and improved analytics with excellent follow up should make things better, but surgical innovation continues to be a significant challenge.

I am now a Medical Director, and I used to be chairman of the ethics committee. In this age of increased scrutiny, how many deaths would a medical director, such a committee or an institution tolerate before stopping an innovative procedure? Stop too soon and you prevent potential success. Stop too late, and well, it is too late. Successful treatments are built on the shoulders of the children who died and the grief of their parents. They took part in an experiment to see what was better. They have (and had) the right to know they are part of a big experiment and must be able to opt out. We have an obligation to design our experiments better, and to carry them out in an ethical way, not as mavericks, not as paternalistic decision makers but respecting our patients, treating them as if they were our friends and working with them as partners. Progress might be slower, but it will be fairer and more effectively provable.

There are additional challenges which I do not have time to explore in depth today, but I do want to leave you to think about them. One of the core ethical principles is justice. We need to consider whether what we do is affordable in the economic environment in which we find ourselves, or in which irresponsible bankers and borrowers or ideologically driven governments might have put us. For example, in the US system a patient in a bed receiving treatment equates to income, usually with a margin, for the hospital and as such a new treatment is more likely to be seen as a financial benefit than here in the UK where budgets are being slashed and an innovative treatment may present too much of a challenge to hard-pressed finance directors. There is a real risk that good innovations may never get properly evaluated because the initial costs (which are bound to be higher that later costs) are not tolerated. We need robust, complete and freely available data to form our choices.

The ethics of introducing new treatments in children are complex, and I have only considered a few of those, even in my field. I leave you to imagine the issues associated with organ transplantation, fetal surgery, the treatment of cancer, and the very pre-term baby. These are children loved by others, loaned to us for care. We need to ensure we look after them and their families first, and work with wider society to deliver high quality, equitable and appropriate care. I do think we could have done what we did then, but maybe slower, more openly and with greater engagement. And hope fully with better, data, on all patients, from the start.

When there is pressure to innovate, there is a risk of over treatment, and I want to finish with a quote from a prize winning essay (PAS SIG Essay Prize 2013)by a paediatric resident, Ashley Treece, from Oregon. She works in paediatric intensive care, caring for children like the ones we have been discussing. She writes about deciding when enough is enough. Even if you want to innovate for the greater good, and are prone not to give in, we must care for the needs of the individual child and family in front of us.

*“Perhaps there is something worse than death, something like losing humanity, like perpetual suffering without any hope of redemption.”*

*“Families could use a more candid explanation of procedures and their lifelong implications, earlier in the disease course, because in my experience these conversations often occur when the family is already too committed to contemplate doing less.*

*“Looking at these children I want to humanise them, to give them the grace of making death OK. Instead of hopelessly fighting death, I want to give them back life”.*

Thank you.

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**References**

1. Hansson SO. The Ethics of Risk. Basingstoke, UK: Palgrave Macmillan; 2013.

2. Lehrer J. The Truth Wears Off. Is there something wrong with the scientific method? The New Yorker. 2013 13 December 2010

3. Ioannidis JPA. Why Most Published Research Findings Are False. *PLoS Med* 2005; **2**(8): e124.

4. Francis R. Comments on the Medical Innovation Bill. 2014.

 <http://www.stopthesaatchibill.co.uk/wp-content/uploads/2014/06/Sir-Robert-Francis-QC-Comments-on-Medical-Innovation-Bill-23-June-2014-FINAL.pdf>.

5. Porter R. Quacks; Fakers and Charlatans in Medicine. Stroud, UK: Tempus; 2000.

6. Levin AV. The ethics of surgical innovation: More than one answer? *Can J Opthalmol* 2005; **40**(6): 685-8.

7. Maio G. History of medical involvement in torture - then and now. *Lancet* 2001; **357**: 1609-11.

8. Gross ML. Bioethics and armed conflict: moral dilemmas of medicine and war. Cambridge, MA: MIT Press; 2006.

9. Hanauske-Abel HM. Not a slippery slope or sudden subversion: German medicine and National Socialism in 1933. *BMJ* 1996; **313**: 1453-63.

10. Weiss SF. Race Hygeine and National Efficiency: The Eugenics of Wilhelm Schallmeyer. Berkeley, CA: University of California Press; 1987.

11. Lommel F. Volkische Aufartung und Artz. *Dtsch Artztebl* 1933; **63**: 6-8.

12. Beauchamp TL, Childress JF. Principles of Biomedical Ethics. 6th ed. New York: Oxford University Press; 2009.

13. Snyder JE, Gauthier CC. Evidence-Based Medical Ethics: cases for practice-based learning. Totowa, NJ: Humana Press; 2008.

14. Schwartz JAT. Innovation in pediatric surgery: the surgical innovation continuum and the ETHICAL model. *J Pediatr Surg* 2014; **49**(4): 639.

15. Nwomeh BC, Waller AL, Caniano DA, Kelleher KJ. Informed consent for emergency surgery in infants and children. *J Pediatr Surg* 2005; **40**(8): 1320-5.

16. Al Eyadhy A, Razack S. The ethics of using innovative therapies in the care of children. *Paediatr Child Health* 2008; **13**(3): 181-4.

17. Barkun JS, Aronson JK, Feldman LS, Maddern GJ, Strasberg SM. Evaluation and Stages of Surgical Innovations. *Lancet* 2009; **374**: 1089-96.

18. Ergina PL, Cook JA, Blazeby JM, et al. Challenges in evaluating srgical innovation. *Lancet* 2009; **374**: 1097-104.

19. McCulloch P, Altman DG, Campbell WB, et al. No Surgical Innovation without evaluation: the IDEAL recommendations. *Lancet* 2009; **374**: 1105-12.

20. Angelos P. Surgical ethics and the challenge of surgical innovation. *Am J Surg* 2014; **208**(6): 881.

21. Knight JL. The dark side of surgical innovation. *Innovations: Technology and Techniques in Cardiothoracic and Vascular Surgery* 2012; **7**(5): 307-13.

22. Wall A, Angelos P, Brown D, Kodner IJ, Keune JD. Ethics in Surgery. *Current Problems in Surgery* 2013; **50**: 99-134.

23. Wartolowska K. Use of placebo controls in the evaluation of surgery: systematic review. *BMJ* 2014; **348**: g3253.

24. Lillehei CW. Controlled cross circulation for direct vision intracardiac surgery: correction of ventricular septal defect, atrioventricularis communis, and tetralogy of Fallot. *Postgrad Med J* 1955; **1**: 388-96.

25. Norwood WI, Kirklin JK, Sanders SP. Hypoplastic Left Heart Syndrome: experience with palliative surgery. *Am J Cardiol* 1980; **45**: 87-91.

26. Ruhlman M. Walk on Water: The Miracle of Saving Children's Lives: Penguin; 2004.

27. Renella P, Chang R-KR, Ferry DA, Bart RD, Sklansky MS. Hypolastic left heart syndrome: attitudes among pediatric residents and nurses toward fetal and neonatal management. *Prenat Diagn* 2007; **27**: 1045-55.

28. Murtuza B, Elliott MJ. Changing attitudes to the management of hypoplastic left heart syndrome: a European perspective. *Cardiol Young* 2011; **21**(Suppl 2): 148-58.

29. Elliott MJ. A European perspective on the management of hypoplastic left heart syndrome. *Cardiol Young* 2004; **14**(Suppl 1): 41-6.

30. 'Phyllimag'. Did Dr Norwood go too far? (Parts 1&2). The Philadelphia Magazine. 2006.

31. Pappworth MH. "Human Guinea pigs" - a history. *Br Med J* 1990; **301**: 1456-60.

32. Bull C, Yates R, Sarkar D, Deanfield J, de Leval M. Scientific, ethical and logistical considerations in introducing a new operation: a retrospective cohort study from paediatric cardiac surgery. *BMJ* 2000; **320**: 1168-73.

33. Macartney FJ, Spiegelhalter DJ, Rigby ML. Medical Management. In: Anderson RH, Macartney FJ, Shinebourne EA, Tynan M, eds. Paediatric Cardiology. Edinburgh: Churchill Livingstone; 1987: 421-2.

1. <http://www.gresham.ac.uk/lectures-and-events/heart-surgery-for-congenital-heart-defects-science-or-art> [↑](#footnote-ref-2)