BIOETHICS NEWS

Universidad Católica de Valencia San Vicente Mártir

PUBLISHED BY: OBSERVATORIO DE BIOÉTICA

SPONSORED BY: Fundación Ciencia, Cultura y Vida Humana

nº 27, november 2014

correspondence: justo.aznar@ucv.es

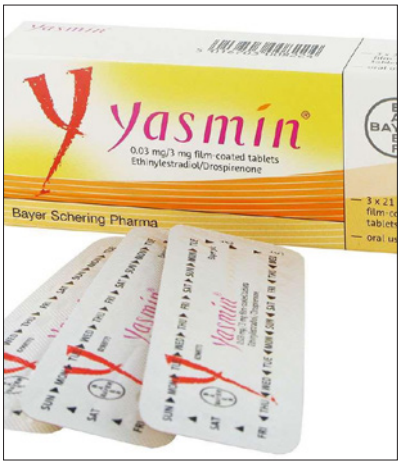
Reports

Yasmin: Contraceptives and thrombosis. Are patients well informed of the risks of using certain contraceptives?

Serious ethical problems

It has recently been reported that the multinational drug company Bayer has had to pay out 1800 million U.S. dollars in damages to 8900 women in the United States who suffered medical problems (including death) as a result of having used some of their contraceptive products, namely Yasmin or Yar, which contain drospirenone.

In a financial report to their shareholders in the second trimester of 2014, the company acknowledged that those affected had indeed suffered personal health conditions (some of them fatal) after using this type of contraceptive, particularly thromboembolic events, which were clearly the most prevalent.



In addition to the 8900 lawsuits that have already been settled, on the 9th of July, Bayer stated that they had a further 5000 lawsuits pending.

However, the most surprising thing about this news, which is terrible in itself, is that the risk of thromboembolic effects due to the use of Yasmin has been known for more than a decade.

Yasmin is an oral contraceptive containing ethinyl oestradiol and drospirenone that was launched on the market by Bayer and approved by the European Union in 2000 (BMJ,2002;324,869).

Paradoxically, its use was promoted because the German pharmaceutical company believed that it might have fewer thromboembolic side effects than other contraceptives hitherto used.

However, as far back as 2003, five cases of thromboembolism were described in women, only a few days after they had started taking Yasmin (BMJ 2003; 326,257).

That same year (2003), we also described the case of a young 21-year-old woman who, 15 days after having begun to take Yasmin for contraceptive purposes, felt discomfort in her right arm, with decreased sensitivity. These symptoms persisted for over 24 hours, and were related with a possible stroke. This may have been the first time that the use of Yasmin was associated with a cerebral ischaemic event (Thrombosis Research 2003; 112,121).

What seems remarkable is that when the first thromboembolic events secondary to the use of Yasmin were detected in 2003, the drug continued to be prescribed and used, as evidenced by the fact that in the United States alone, around 14,000 women had problems after taking it, a figure which could rise, since only those who filed lawsuits against Bayer were counted.

In this case, we can see two major ethical problems here, among others. The first is that women have almost certainly not been informed of the risks of using Yasmin, and the second is the laxity of the health authorities for permitting the continued use of this drug, although it has been known since 2003 that it could have major health risks, mainly thromboembolic events.

Are we to believe that if we used another Bayer

product, for example aspirin, in which such serious side effects had been found, that it would not have been quickly taken off the market?

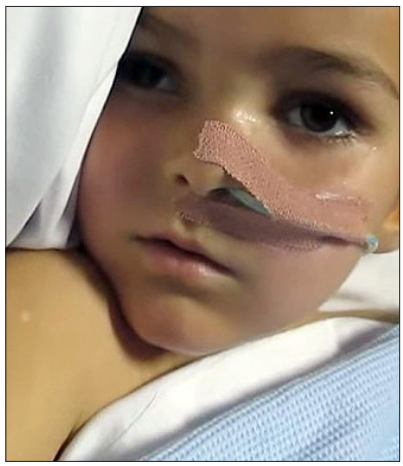
We consider that, ultimately, it is not only the pharmaceutical company - in this case Bayer, which with a distinct lack of business ethics continues to distribute a hugely profitable drug - that is to blame, but also society in general, which has shown itself to be very reluctant to speak out against the use of a contraceptive. This is almost certainly because to do so would be considered as going against the sexual freedom of women, when the only aim is to protect their health.

Justo Aznar y Julio Tudela
Institute of Life Sciences
Catholic University of Valencia

An ethical reflection on the Ashya King case

Media coverage of the case of Ashya King, a 5-year-old English boy who was diagnosed with a malignant brain tumour, has done little to clarify the drastic measures taken by the English authorities, after a complaint was filed against his parents by Southampton General Hospital, for having deprived a minor with a life-threatening condition of proper medical care.

The parents had stated since the child had been diagnosed with meduloblastoma (a type of serious brain cancer) that they did not wish to subject him to the intensive radiotherapy treatment proposed by the hospital, as they considered it very aggressive; moreover, they also believed that the most serious side effects could be avoided with proton therapy. When the hospital told them that they could not receive any other treatment apart from the one they could offer, they decided to flee the country without seeking medical approval in order to avoid further delays, taking advantage of temporary approved leave while the child recovered satisfactorily from an operation. Hence, they came to Spain on 28th August this year, with the intention of selling their house in Malaga, to meet the very high costs of the chosen treatment and to be able to go immediately to Prague so that the boy could undergo the aforementioned therapy.



As a result of the European arrest order imposed on the parents following the complaint by the English health authorities, they were arrested by Spanish police in Malaga and kept in isolation for several days, during which time, the child remained in hospital. The English authorities also withdrew the couple's parental rights.

Following intensive efforts made by the child's parents, Brett and Naghemeh King, and the Spanish lawyer who took the case, the English authorities eventually suspended the measures taken against them.

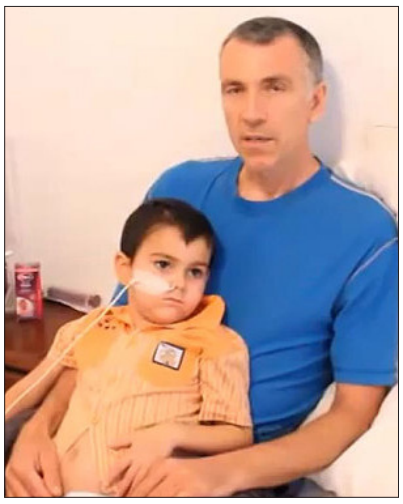
On 9th September, 11 days after leaving England, Ashya arrived with his parents at the Proton Therapy Center in Prague. On Tuesday 16th, the press released a statement from the director of the Centre on the health of the child, saying: "More and more smiles and now he's moving, he's improving slowly, because more time has passed since the operation" (Czech press "CT24", 15/9/2014). Beyond these facts, we believe it is important, in order to make an ethical evaluation of the case, to determine if proton therapy can be as effective as conventional radiotherapy, and if the case of Ashya really was life or death, as the hospital reported.

With respect to endangering the life of the child, unless there are any other circumstances that have not been made public, and in view of the fact that the parents were allowed to leave the hospital with the child, the danger of imminent death alleged by the English hospital appears to have been overstated.

For all these reasons, and also taking into consideration information on the child's health that was published while the was in hospital in Prague, it seems ethically unacceptable that the English hospital could not allow the parents to use the therapy that they preferred and could pay for (which was not available in the United Kingdom) and furthermore,

made the complaint against them in such over-the-top terms.

Proton therapy appears to be more specific than conventional radiotherapy. Due to its characteristics, the proton beam can selectively reach the tumour area, scarcely damaging nearby tissues, which seems crucial in a treatment of this type. Along the same lines, the specialists at the Czech clinic state that, "Proton therapy is a treatment than enables the highest doses possible to be given without affecting the surrounding tissue. A very important characteristic if we consider than in the vicinity of the tumour are the centres that regulate the heart, lung, liver and intestines. Proton treatment reduces the risk of damaging these brain centres and unwanted side effects." (Czech press "CT24", 15/9/2014).



Our ethical opinion regarding this specific case is sufficiently explained in the text above. However, a further reflexion may be useful on how patient autonomy should be reconciled with medical knowledge to determine which type of treatment should be applied in each case.

There is no doubt that on specific occasions, like this one, they may be a conflict between the views of the patient or their representatives, as regards the type of therapy they wish to apply and what the doctors think.

From an ethical point of view, patient autonomy should of course always be respected, but it is a fact that the patient does not always know what is the best treatment for him or her. In this respect, we believe that the most important, and therefore critical factor, is that the medical staff have sufficient ability and knowledge to convince the patient of the advantages of the treatment that he or she requires, to thus be able to apply it. However, if they cannot come to a mutual agreement, we believe that the patient's autonomy should be respected.

It is interesting to highlight that the press officially reported that the English health authority had agreed to assume the costs of the 5-year treatment of Ashya King in Prague, which we believe is a very positive change of attitude.

For the reasons stated above, in the case of Ashya, we believe that the parents' decision was correct as regards taking the approach that they believed best for the well-being of their son; in this respect we believe that the London hospital should have arranged things so that this decision could have been taken without any further problems.

Manuel Zunín and Justo Aznar
Bioethics Observatory
Catholic University of Valencia

First child born after a uterus transplant

On 5th October this year, the birth of the first child born to a woman who had received a uterus transplant was published in medical journal The Lancet (doi:10.1016/S0140-6736(14)61728-1).

The birth occurred on 4th September. From a medical point of view, this is clearly an important event, as it made it possible for a woman who had no uterus (as a result of Rokitansky syndrome, in which women are born without a genital tract, including the uterus) to have a child, which she could never have achieved naturally.

News of uterus transplants have been discussed previously in Provida Press (Nº 434, 439, 440), but at that time it was not yet known whether the recipients would be able to become pregnant, and above all give birth to a child, which of course has now been achieved.

In the aforementioned articles in Provida Press, we discussed how the first uterus transplant was performed in Saudi Arabia in 2000, and the second in Turkey in 2011, neither of which had a successful outcome.

After these first two transplants, Matts Brännström and his team from the Department of Obstetrics and Gynaecology at the University of Gothenburg, together with various colleagues from other universities, obtained the required permission to perform this type of transplant in Sweden. They were

authorised to carry out nine transplants, the last of which was completed in Spring 2013. In five cases, the donors were the mothers of the recipients, and the rest were relatives or friends. Of the nine transplants performed, two failed because of thrombosis or infection in the recipient. The second phase of the project was to be the transfer of embryos produced by in-vitro fertilisation in the remaining seven women. Now the birth of the first child from one of these pregnancies has been achieved.

The patient was a 35-year-old woman with Rokitansky syndrome. The uterus was donated by a 65-year-old woman who had had two previous pregnancies. One year after the transplant, 11 embryos were produced by IVF using the patient's eggs and sperm from her partner, one of which was transferred. As in all transplant cases, the woman was placed on immunosuppressants, which she continued to take during the entire pregnancy. It is important to highlight that during the pregnancy , she suffered three episodes of rejection, which were resolved using corticosteroid treatment. She also suffered pre-eclampsia at 31 weeks and 5 days, for which an emergency caesarean section was performed. A premature boy was born, weighing 1775 grams. This is the case description so far.

From a medical and social point of view, an initial evaluation of the case merits only a positive assessment. That a woman without a uterus can manage to have a child cannot be viewed any other way. However, we believe that this case also requires an additional ethical reflection.

The same year, Farrell and Falcohe from the Cleveland Clinic published an article in Fertility and Sterility (2014; 101: 1244-1245) in which they assessed the ethics of uterus transplant, mainly from a medical point of view, essentially referring to the risks-benefit for the donor, recipient and newborn.

As far as the donor is concerned, say the authors, there are serious considerations to take into account, namely the surgical difficulty of harvesting the uterus (a procedure that can last between 10 and 13 hours) with its inherent risks, especially as regards dissection of the pelvic veins, which is technically difficult and also the possibility of damaging the patient's ureters. Moreover, there may also be complications derived from infections or haemorrhages, which in some cases have required reparatory surgery.

All donors are normally menopausal, but if they are not, we would also have to consider that they will lose the chance to have any further pregnancies.

As regards the uterus recipient, the patient should first be informed of the risks of the surgery itself, and in particular that she must take immunosuppressants after the transplant, both during the pregnancy and after, as not to do so could result in rejection of the transplanted organ.

Possible damage that she may suffer as a result of the pregnancy must also be taken into consideration. In this sense, it is now known that the woman in question suffered three episodes of rejection and one of pre-eclampsia, as we mentioned in the case report.

Another medical problem, also unavoidable, is that the transplanted uterus must be removed after the birth of the child, so that the patient no longer has to continue the aforementioned immunosuppressant treatment, which undoubtedly is an additional problem for her.

In relation to the child, only the fact that he was born prematurely is noteworthy. However, it is difficult to issue an ethical opinion about the well-being of the child born, without evaluating his medical progress in the longer term.

In any case, we believe it can be said that when the results of only one of the nine transplants are known, it is very premature to make an ethical assessment of this surgical procedure.

Besides the risks-benefits that this intervention may have for the donor, recipient and child, we must also consider the high cost of these types of procedures, in addition to the costs of all the previous work that had to be done in order to ensure the safest surgical approach to the transplant. Similarly, another ethical aspect to consider is that these types of surgeries are in a very experimental phase, so they could be included within so-called "compassionate therapy", a practice which, as we know, can be applied without the required previous studies on safety and possible negative effects.

Finally, something that should not be ignored is that to obtain the desired child, IVF must be used,

with the moral difficulties inherent to this practice, not least the many embryos lost (Medicina e Morale 4; 613-616, 2012).

Besides these considerations, it is clear that on the positive side of uterus transplant, we must include the satisfied desire of the recipient to have a child. Nevertheless, a child is always a gift, not a right of the woman may want it, which certainly must be taken into consideration when ethically assessing the risks-benefits of this type of intervention.

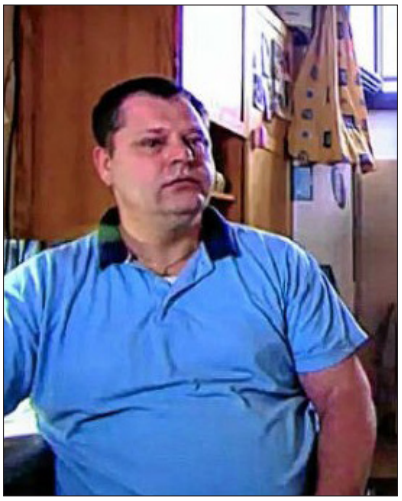
Justo Aznar MD, PhD,
Director of the Institute of Life'Valencia
Catholic University of Valencia

News

Euthanasia has been granted to a prisoner condemned to life imprisonment in Belgium

In Belgium, a prisoner condemned to life imprisonment has requested - and finally obtained - that he be released early by euthanasia from a life that he considers meaningless and which brings him only mental anguish.

Frank van den Bleeken is a Belgian prisoner who was condemned to life imprisonment when he was 20 years old for the rape and murder of a young 19-year-old woman. Now 50-years-old, van den Bleeken does not suffer physical pain, nor is he in the terminal stage of any illness. However, after spending three decades in prison, he considers that his life is not worth living, and for this reason requested euthanasia, arguing unbearable mental anguish.



The Federal Commission on euthanasia told him that they would not respond to his request until all the therapeutic possibilities had been exhausted. Van den Bleeken asked to be transferred to a psychiatric penitentiary in Holland, where he could be treated, by virtue of an agreement between both countries. However this was denied by the courts, so he presented a complaint against the Justice minister, requesting the transfer or euthanasia. Three doctors have certified that van den Bleeken suffers permanent anguish, which cannot be cured. His lawyer eventually reached an agreement with the Ministry of Justice to permit the euthanasia.

Although exceptional, his case is in line with the drift of euthanasia in Belgium, which led first to justifying it for physical suffering and then mental, from the terminally ill patient to the incurable patient, and from the conscious adult to the minor. With these increasingly lax criteria, the rate of euthanasia has not stopped growing since its legalisation in 2002, and according to the official report of the Commission on Euthanasia, "it tends to escalate significantly since 2011". Last year, 1,807 cases of euthanasia were officially reported.

It is not surprising that, in the light of these criteria, a prisoner condemned to life imprisonment thinks that he too has the right to have access to euthanasia. If the notion finds its way that certain situations prevent living with dignity, how do we oppose his desire for a "dignified death"? If some people consider that death is preferable to leading a life without independence, can those who do not have any better prospects in life than to be locked up forever in a hostile environment not think the same? If the only criterion is individual autonomy, we must respect the decision of those to prefer to serve their sentence with a rapid death instead of with a slow one.

We could even say here that euthanasia could also be applied "out of mercy". This is how Jacqueline Herremans, Belgian president of the Association for the Right to Die with Dignity" sees it, declaring that van den Bleeken "is considered a danger to society" and, bearing in mind that prisoners live in poor conditions, "euthanasia was the lesser evil".

But it shouldn't be such an exceptional case. As a result of this authorisation, around fifteen Belgian

prisoners have also requested euthanasia, as they would rather die than live the life they currently lead.

Although euthanasia has in practice become a right in Belgium, other prisoner's rights leave a lot to be desired. In 2013, the European Court of Human Rights condemned Belgium for not having provided adequate treatment to prisoners with psychiatric problems.

Euthanasia for prisoners condemned to life imprisonment can be presented as the answer to their wish to have a "dignified death", but it can also be a return to the death penalty dressed up in humanitarian motives. Lethal injection whether on death row in Texas or in a Belgian hospital is exactly the same way of eliminating troublesome subjects. That one is classed as undignified death and the other as dignified is one of the mysteries of newspeak (El Sonar, 16-09-14).

In Brief

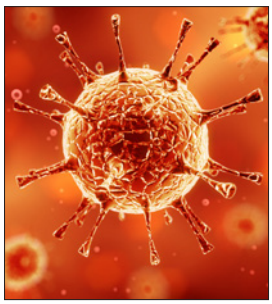
01 In February 2014, the Belgian parliament approved a bill to permit euthanasia for terminally-ill children of any age, with 86 votes in favour, 44 against, and 12 abstentions. This project acquired the force of law when it was signed by the King in March, making Belgium the first country in the world to legalise euthanasia at any age. Until then, the youngest age at which euthanasia could be applied was 12-years-old, in the Netherlands (J Med Ethics 40; 357, 2014).

02 Only 2.3% of the United States population say that they are gay, lesbian or bisexual, according to the National Health Interview Survey, a major federal report that for the first time included a question about sexual orientation. The results have disappointed gay activists, who for years have asked that this question be included in the report.

The report surveyed 35,000 adults in 2013, and found that 96.6% of those questioned declared themselves heterosexual; 1.6% identified themselves as gay or lesbian; 0.7% as bisexual; and another 1.1% answered "something else" or did not answer.

03 The "Saudi Human Genome Programme" is to launch 10 centres to study the genome in Saudi Arabia. It hopes to sequence 100,000 genomes over the next five years, to try to identify both normal and disease-associated genes specific to the Saudi population, all with the ultimate aim of creating personalised medicine in Saudi Arabia (Nature Biotechnology 32; 11, 2014).

04 Even when HIV patients are properly treated, a virus reservoir always persists in their cells, which means that they must always be considered as chronic patients. However, four patients have been discovered, referred to as "the Berlin patient", the Mississippi baby" and two "Boston patients", in whom these HIV reservoirs have completely disappeared after stopping antiretroviral therapy (Nature Biotechnology 32; 315-316, 2014). These facts are encouraging attempts to investigate why this has happened in these patients, to see if this shines a light on new possibilities for the treatment of AIDS patients.



05 A program is being launched in the United Kingdom to sequence 10,000 genomes of patients with "rare diseases" and their parents. The studies will begin next October (Nature Biotechnology 32; 7, 2014).

06 An article has been published in Nature Biotechnology (32; 84-91, 2014) reporting that lung and airway epithelial cells have been generated from iPS cells, which could have a positive application in regenerative medicine where lungs are affected by any degenerative process, to evaluate possible useful drugs in these cases, and to study human lung development.

07 The United States Supreme Court has decided, by a majority of 5 votes to 4, that family companies can object to the Ministry of

Health regulation that obliges them to finance and offer their employees an insurance plan with contraceptives, the morning-after pill and sterilisation. According to the judges of the majority, the so-called "contraceptive mandate" substantially burdens the free exercise of religion (Aceprensa, 3-VII-2014).

08 Unlike what tends to happen in other countries, the French reaction to a confusing sentence from the European Court of Human Rights has been rather strong. The sentence would reconcile the use of surrogate mothers, insofar as it imposes the obligation to inscribe the children in the civil registry, against the jurisprudence of the French Appeals Court. In mid-July, an open letter to French president François Hollande was published, to demand that he not support the euphemistically named "GPA" (from the French "gestation pour autrui") or surrogacy. Among the signatories were well-known figures such as Jacques Delors, Lionel Jospin and several previous ministers or secretaries of state. A famous feminist philosopher, Sylviane Agacinski, also signed. And, should it be necessary, groups as diverse as the co-ordinator for the right to abortion and contraception and some lesbian groups also lent their support. In the document, they stated clearly that "the contract of surrogacy is against the principle of respect to people, both the woman who carries the child, and the child itself, ordered by one or two people, which develops in the womb of the carrier. "Human beings aren't things". There is a "public order" technical criterion that would invalidate any civil contract on this matter (Foro de la Familia, 2-IX-2014).

09 An analysis of the situation of pregnancies that occur during oncology treatments has been one of the points that has aroused most interest among European health professionals. The potential harmful effects of anti-cancer agents are a reason for great concern. In some cases, the treatments are avoided, or the patient decides to interrupt the pregnancy. New studies however have cleared some doubts: foetuses exposed to chemotherapy in the uterus have little likelihood of suffering a negative impact on their mental or cardiac development, according to Frederic Amant of the Lovaine University Hospital (Belgium), who presented the data at ESMO 2014.