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# From the externally augmented soldier to the internally modified soldier: using the genome against chemical and biological weapons

**B.Massoubre [1], C.Boulliat [2]**

[1] Military pharmacist; Hôpital d'Instruction des Armées Desgenettes, Lyon, France

bernard.massoubre19@orange.fr

[2] Head of the Pharmacy Department, military pharmacist; Hôpital d'Instruction des Armées Desgenettes, Lyon, France

## Abstract

The development of molecular biology has allowed a considerable advance in medicine. But applications, both civil and military, can be malicious and must be strictly controlled by the international scientific community. Ethical reflection is necessary to target and circumscribe abuses.

The use of genome editing can protect the soldier in case of biological or chemical attacks. Nevertheless, medical ethics within the armed forces must not be overlooked, even if this genetic modification is an advance in the protection of the combatant in a theater of operations. The soldier is affected in his deepest intimacy, that of his genetic heritage.

Whatever the cause, and even if it is noble, an augmented or modified soldier must not be a dehumanized soldier. We must ensure that the dignity of the soldier, but also of the human being, is respected.

The medical ethics of the armed forces are present to accompany the progress of science and to ensure the respect of its principles.

**Keywords:** Augmented soldier, modified soldier. Genomic editing. CRISPR-Cas 9. Ethics. Chemical and biological weapons. Military health service.

## Introduction

The application of the CRISPR-Cas 9 technique has put the scientific world in commotion because genetic manipulations are infinite: deleting a sick gene, replacing it with a healthy sequence or studying the precise function of a strand of DNA, ... No sector of medicine escapes them (1). They are at the origin of an ethical questioning in the international community because they touch the human being in his cellular intimacy, and tests on the mouse embryo have already taken place (2). The work of the Chinese Jiankiu concerns the modification of the genome, and therefore of embryos. In view of this danger, Lander proposed the adoption of a worldwide moratorium on hereditary genomic modifications. (3)

In the military field, CRISPR-Cas9 has, a priori, no immediate terrorist application. It has not been mentioned in the manufacture of biological weapons that are sufficiently lethal to be considered by the authorities. On the other hand, other techniques have been proposed to protect the soldier from a chemical or bacteriological threat.

The ethical questioning concerns a military application (and implication), whose aim is to fight a chemical or biological attack, and the tool used is the genome.

## Situation of the subject

The increase of human capacities is ancient. The first hunter-gatherers armed with a spear were already augmented men. The evolution continued over the years. But it is really from the middle of the 20th century that the reflection on the augmented man took off, to become a burning subject. Computer science, molecular biology and artificial intelligence have contributed to this development.

In parallel to the civilian world, there have been significant advances in the military sphere. A soldier's outfit in a theater of operations is nothing like the one he wore only 10 or 20 years

ago. The equipment has been adapted to the constraints of the field and conflicts. This exoskeleton, taken in the broadest sense, is a combat aid but it does not modify the internal structure of the human being.

Research on the genome, especially on germ cells and with the contribution of the CRISPR-Cas9 technique, raises important ethical problems. They are, in a way, identical in civilian life and in military life. Molecular genetics has been developed for the battlefield with complementary strategies. The first is to spread increasingly destructive biological weapons. The second is to defend against chemical weapons (such as organophosphates) and bioterrorism.

Initially, the techniques used are biochemical components, enzymes, to destroy the chemical agent. Since 2012, we can act directly on the human genome. This alteration may be transient, according to the researchers. Or not? Indeed, it is not so simple. The cells of an adult individual, whose genome is altered, are permanently altered, but not all the cells of the individual. Thus, during cell renewal, the locally modified cells will disappear little by little.

## Critical analysis of the literature: the concept of anthropotechnics

Jérôme Goffette defines anthropotechnics as "an art or technique of extra-medical transformation of the human being by intervention on his physiology". He proposes to use a more adequate noun, "the modified", and to give it the following definition: "state succeeding the ordinary state of the individual, by the intervention of an artificial and decided change of his physiology. In short, between the ordinary and the modified, is the space of the modification of the individual by intervention on his biology." (4)

Enhancement and anthropotechnics are synonymous terms, the latter being understood as "the application of techniques to improve human performance without medical purpose" by technology applied to humans. For the sake of simplicity, the concept of reversibility of anthropotechnics is based, in this article only, on the examination of the durability of its positive effects, and not on the durability of all its consequences (notably negative ones, which would allow for subdivisions such as probable sequelae, no sequelae, etc.). (5)

Goffette places anthropotechnics in the context of medical ethics and Beauchamp's principles (6). Anthropotechnical practice, by putting certain risks at risk, does not respect the principle of non-maleficence. The principle of beneficence can be expressed in two ways: positive

beneficence (providing a benefit) and estimated beneficence (maximizing benefits). Since there is no medical benefit, anthropotechnics is rejected. The author defines autonomy by appealing to Kant because he finds Beauchamp's definition too restrictive. For the German philosopher, autonomy is the foundation of his ethical imperative and his goal. In the anthropotechnical perspective, two points are crucial. This principle brings legitimacy to anthropotechnics. The person expresses a request, and sometimes a decision, matured and guided by a rule of conduct (Kant's "free will"). Respect for autonomy leads to the rejection of alienating demands, and to the acceptance of demands that promote freedom. Concerning justice, anthropotechnics does not serve the purpose of medical ethics, which is based on the fair distribution of care, and on the concepts of equality and equity. The question shifts to the regulation of access to the anthropotechnical service: what should be allowed and what should be prohibited?

At the legislative level, it is crucial to follow the following rule: only what is authorized by the legislator is lawful. It is necessary that each act be the object of a collective deliberation and decision before its authorization. In the event that it is difficult to see, the legislator can set up limited authorizations, limited in time, as preliminary experiments.

## Study material and methodology

The work of Mangeot (2) has shown that it is possible to obtain white mice from embryos fertilized from black mice and modified before reimplantation. But we also obtained chimeras, white and black.

The catalyst for this article was Jiankiu's presentation at a conference. This Chinese scientist reported that he had created the first genetically modified babies, the twins Lulu and Nana, designed to be immune to HIV. In response to this news, Lander proposed the adoption of a worldwide moratorium on hereditary genomic modifications (3). This article is co-authored by the future Nobel Prize winner Emmanuelle Carpentier.

In our study, we are interested in a particular, targeted use of a molecular biology technique. The framework is that of the genomic modification of the soldier in order to protect him from a chemical attack in a theater of operations.

CRISPR was the first technique discussed. But it is only a tool, a vector. It is important not to crystallize on CRISPR to conduct an ethical reflection on the modified soldier. Other techniques are used, in biochemistry and molecular biology.

The methodology is situated at three levels: ethical reflection on the modification of the genome, bearing in mind that our study does not involve a modification of the germ line. Then, the specificities of genetic manipulation in the soldier. And finally, what are the ethical problems posed by this new situation?

The analysis will be of interest if it is done in its entirety, with the combatant, the military institution, biological and medical research, the hostile environment... (7)

Jiankui's work reveals the institutional failure of ethics governance, which depends largely on the self-regulation of scientists. It is necessary to improve this governance as soon as possible through the application of technical and ethical guidelines, and the establishment of laws related to these bioethical issues. (8)

Sand M. (9) discusses the concept of moral hazard in medicine and its impact on the limits of judgments such as "anything that ends well is good" or "someone broke the rules and is therefore to blame". The risks associated with scientific research are often put aside when it is successful. This is the case for our example.

The moratorium, and more generally international controls, have a cost in logistics and personnel. Pedagogy requires time, to explain that scientists evolve within a society, in which values are involved. Neuhaus CP et al (10). The lack of knowledge, or mistrust, of ethics also exists in the military. For some, ethics remains superfluous or "out of touch.

Are these provisions applicable in the armed forces? Yes, because international bans have been put in place for certain technologies, particularly in the CBRN field. The question concerns the application of these laws, especially by countries where human dignity is not a priority.

But this article deals with the modification of the soldier's genome to protect him from a chemical or biological attack. This is a defensive application, not an offensive one. In this case, one cannot, as the authors advocate, "encourage nations to commit to transparency, public engagement, international consultation, and control of behavior within their own borders." The antinomy, between civilian and military applications, is even stronger when Lander states that the moratorium "would also allow other nations to discourage a country from engaging in ill-conceived uses."

## The results

### Ethics and military research

#### *Framing research*

The Nuremberg Code does not define what it means by "research. Implicitly, it concerns only healthy subjects. Therefore, free and voluntary consent is always required. The Helsinki Declaration of 1964 broadened the scope of research. (11)

In France, successive laws have regulated medical research. We can cite the Huriet-Sérusclat law (1988), relating to the protection of persons involved in biomedical research. Or the Bioethics law (2011), for elements of the human body.

Research carried out within a Defence structure has evolved over time while respecting the French regulations in force. The "clinical research action plan for the armed forces health service" 2012-2014 has made it possible to boost the research effort, in particular with an operational aim, with practical applications or recommendations. (12)

At the end of the study, a summary for the patients must be written by the project team to inform them of the overall results. Regulatory, administrative and financial follow-up is required, with the investigators and the "Research Steering" office of the DCSSA and the BGRC. Finally, all research documents are archived, according to a specific filing plan, for a period of at least 15 years, depending on the type of document and study. (13)

The article by Greene and Master (7) reviews the use of CRISPR in military research in the USA. It would seem that American intelligence services attach more importance to the bioterrorist threat than French services, at least at the present time. This is also true for the chemical risk, as increasingly asymmetric conflicts, with the use of non-lethal weapons, raise the level of this threat.

Nevertheless, this assertion must be put into perspective because French military doctrine once again envisages the possibility of high-intensity conflicts.

The public dissemination of experiments in the United States and elsewhere that were deemed unethical led to the publication of the Belmont Report (14). The "Common Rule" is intended to protect individuals involved in research. DoD is moving toward greater transparency, accountability, and protection for military, and civilian, participants in research.

### *Ethics of Research for Military Genetic Enhancement*

In bioethics debates, a distinction is made between genetic modification for therapeutic (treating or preventing) and non-health purposes. The fear is to install a new, softer form of eugenics, which would reinforce inequalities for secondary traits (such as eye color). And which would be accepted more for the improvement of human development or intelligence (15).

Scheufele published an interesting study on the sentiment of the American population about genome editing. A minority favors somatic lineage augmentation/enhancement (40%) and even more so when it comes to germline modification (26%). In the article, the authors also took into account the level of religious belief and culture of the respondents. The question asked was: "Should scientists consult the public before applying genome editing to humans? There were no significant differences between the two groups, the majority of whom answered in the affirmative. (16)

**Benefits and risks for soldiers**

The benefit/risk balance would be in favor of genomic enhancement, as it would increase the chances of survival during armed conflict (17). However, care must be taken to ensure that combatants are not exposed to unnecessary harm.

The most concerning thing about CRISPR is the potential for off-target effects, due to the large number of repeats and the highly homologous genome. It can unintentionally cleave sequences causing mutations, with probable development of cancers. (18)

The consequences are difficult to predict, and further research should be conducted. However, it would appear that the deleterious effects are limited, especially if a reversible mode of action is used. Furthermore, if a metabolic enzyme is modified to resist chemical attack, its functionality cannot be fully predicted.

### *Informed Consent*

Command structure affects informed consent for research. For the military, because of the superior-subordinate reporting relationship, DoD research policy wants to minimize command influence, ensure informed consent in advance, and limit waivers of informed consent (19). DoD could request a waiver in emergency situations to protect military personnel from chemical or biological agents. Especially since with CRISPR-Cas9, genetic modifications can be temporary. This exception is known as the interim rule. It was authorized by the FDA

during the first Gulf War, and passed by the US Congress in 2017. To date, there are no specific laws to prohibit military enhancement, although the focus is on optimization.

The military all adheres to a single command structure. The Code of Military Justice makes it a crime to disobey a lawful order, given by a superior officer, because such refusal to obey would endanger operational safety (20) Also, DoD Instruction 3216.02 excludes senior officers in charge of the chain of command, recruiting, or administration from consenting to the solicited soldier. The research team is responsible for obtaining consent. The research team must ensure that the exclusion, autonomy, and voluntariness of the research subject is enforced.

Another factor is that the military is trained to act as an entity. Sometimes recruitment targets an entire unit. In this case, researchers can organize group meetings. It is difficult for a soldier, under group pressure, to not participate in an activity. It is then important to give the information to the soldier in written form, in addition to discussing the research project and answering questions. The goal is to accurately inform the service member of the procedures, risks, and benefits, and that the service member has the opportunity to withdraw.

Military members may be encouraged to participate in research if they believe they will gain an advantage over the enemy. But some volunteers will have difficulty understanding the basics of genetics. There are also misconceptions about the intent of these types of trials, and deaths in gene therapy trials have not cleared the air. (21)

The main purpose of early human studies is to ensure their safety. But there can be a "therapeutic misunderstanding" on the part of the soldier who thinks the technique can protect him from the dangers of combat. Military authorities must also verify that the presentation of performance enhancement has not been exaggerated in the application for informed consent.

A final point concerns issues of individual autonomy and informed consent. In 1990, during the first Gulf War, the DoD sought, and ultimately received, a waiver from the FDA allowing the use of experimental compounds in soldiers without their informed consent. (22)

In 1990, issues of individual autonomy and informed consent came to the forefront when the U.S. Department of Defense sought and ultimately received a waiver from the Food and Drug Administration (FDA) authorizing the use of experimental compounds in soldiers without their informed consent.

This article reviews the concepts of autonomy and informed consent within the military, and examines the history and ethical debate surrounding the interim rule. The author suggests that

an ethical impasse will continue to exist as long as human subjects are exposed to chemical agents for research purposes. Yet, definitional constraints should not prevent the development of beneficial compounds in appropriate circumstances.

The author proposes criteria for establishing an investigational agent as a standard of care. Using this set of criteria, he examines the use of pyridostigmine bromide during the 1991 Persian Gulf War. This was a notable decision given the strong association between the agent and Gulf War illness. A detailed review concludes that the agent in question cannot be considered a standard treatment, and that the compulsory administration of the compound without informed consent was a violation of the principle set forth in the seminal bioethics documents of the 20th century. (22)

It is difficult to predict the timing of an attack. Thus, obtaining informed consent shortly before deployment is complicated. Under current regulations, the "product" could be used in emergency situations, and/or in cases of accelerated "Research and Development." If refused, soldiers could put themselves at risk, and compromise the mission. Premature administration of a substance, in the broadest sense, would threaten the safety, autonomy, and consent capacity of the military.

Smaller scale testing should be conducted, in a controlled research setting, prior to large scale use and application in the field. Military command, IRBs, and the FDA must target the unknown risks to soldiers, and the risk of mission failure if adequate human subject research using the technology has not yet been conducted.

***Unequal Access***

Uniformity in armies is a necessary means of instilling discipline and following instructions. It is intimately linked to the structure of the chain of command. Because of the risks associated with genome research, early human studies may be limited to those with risky missions, such as special forces. If some members, in an operational situation in a conflict zone, benefit from genetic enhancements and others do not, this is a source of dissension. For example, soldiers could refuse to be deployed because they did not receive the same level of protection. The consequences would be dire. Temporary or permanent assignments would be required, with the risk of creating inequalities within the forces, and disrupting the chain of command.

The status of the service member, active duty or not, may have an impact on unequal access. DoD regulations prohibit active duty service members from being paid for participation in

testing. A DoD-paid soldier may not receive any ancillary income. Compensation would be considered an unfair incentive to furloughed service members. And if participation is limited to only furloughed soldiers, in order to obtain fair compensation, It will be necessary to determine whether this contradicts principles of fairness for all military research. (7)

Greene suggests two lines of action. Encourage public and stakeholder engagement on the ethics of using these techniques. Opinions may differ if the applications are military. And to promote discourse, several strategies could be employed, such as public meetings, citizen juries, consensus conferences, surveys, and focus groups. (23)

There are several considerations that must be taken into account to ensure the protection of frontline combatants. For the DoD, it is paramount to ensure that military personnel receive the best possible protection in a war zone. But this creates many ethical questions about the violation of individual rights and autonomy. Consideration could be given to incorporating these risks into discussions during enlistment and recruitment. In 2003, the President's Council considered the risk of using modified genomes to be too high. It is not clear that the same conclusions are being drawn today, given the scientific advances on the subject. (7)

In 2010, the Defence Ethics Committee was set up in France by Florence Parly, Minister of the Armed Forces. The first reflections focused on the augmented soldier (24).

What information does this report provide on the ethics of research?

In the guiding principles: "It is imperative not to inhibit research on the augmented soldier, as in the field of defense innovation in general, in order to avoid any risk of our armies losing their capabilities"; and "If research in the field of augmentation is to be open, it must respect the rules of medical ethics and benefit from the guarantee of the Ministry of the Armed Forces' Committee for the Protection of Individuals". And in the recommendations: "Prohibit eugenic or genetic practices for the purpose of augmentation of military personnel"; "Prohibit the use of augmentation that has not been the subject of prior research on the impacts and undesirable effects". These recommendations set a red line. This was the meaning of the statement made by the Minister of the Armed Forces when the report was presented: "Yes to Iron Man's armor and no to the augmentation and genetic mutation of Spider-Man". The guiding idea is clear, it is to avoid the possible drifts of the augmented soldier, without harming the operational capabilities of our armies.

Although the opinion is consultative, France is at the forefront of international ethical reflection on the augmented soldier.

## Medical ethics in the army

"Medical ethics in times of armed conflict are the same as in times of peace". This is the first statement of the World Medical Association (WMA) regulations. However, in practice, the Army Medical Corps knows that it is difficult to have identical standards in times of conflict. This would include the allocation of limited resources, dual loyalty conflict, the concept of military necessity, medical eligibility rules for establishing treatment, two-tiered care, and complications related to impartiality and neutrality. (25)

Recent research has shown that ethical decisions, in combat and humanitarian deployment, are not easy to make. (26, 27). Military medical practice often leads to conflicting ethical stances. (25)

Vollmar had given a clear and unambiguous opinion, on medical ethics in peacetime and wartime, specifying that "the demands of battle pose unique challenges incomparable to the civilian context because of the magnitude of threats to life, unpredictability, and levels of violence." (28)

## Biological applications used to modify the soldier

Certain products (here enzymes) can be administered to reduce or block the effect of nerve agents (organophosphates). These agents are the most toxic and deadly chemical warfare compounds. They induce a cholinergic crisis by irreversibly inhibiting acetylcholinesterase, and require rapid medical attention. However, this treatment also has its limitations. The enzymes do not remain in the circulating blood for long, and must be given just before a possible attack, and several times. Current antidotes prevent death, but they are ineffective against complications and have side effects.

Molecular biological techniques, such as gene therapy, are being developed (29). Gupta et al (30) have worked on the catalytic efficiency of PON1, which is able to hydrolyze nerve agents into inactive substances in the blood. These advanced variants, and the screens developed, provide the basis for prophylaxis against other G-type agents. But the military would have to produce, and stockpile, large quantities of "bio-protectants" to inject into soldiers. It would also have to find a way to protect the proteins of the immune system to make them effective.

Betapudi (31) has developed an alternative approach, with pretreatment with a therapeutic protein capable of hydrolyzing nerve agents into biologically inactive products. Paraoxonase 1 (PON1) shows promise in providing prophylactic protection for animal models.

The authors showed that gene therapy was a viable approach by expressing PON1 (and its IF11 variant) using adenoviral vectors (AAV8) in mice. A single administration of AAV8 carrying the PON1-IF11 gene (AAV8- PON1-IF11) resulted in high expression, and secretion, of recombinant PON1-IF11 protein into the circulation. Protection is asymptomatic against multiple lethal doses of all G-type nerve agents for at least 5 months.

AAVs have a preferential tropism for certain organs. But the AAV8 vector has a predisposition for the central nervous system, the heart, the liver, the pancreas...It will therefore be difficult to use this type of AAV in a healthy individual. The team also showed that PON1 concentrations remained high in the intramuscular setting, a more practical route of administration in a theater of operations.

This study supports the development of AAV8-based prophylactics for soldiers and dogs, as well as for people working in military, medical and homeland security operations.

But other researchers, such as Oksana Lockridge, point out that the increased expression of PON1 is likely to provoke a stronger immune response in humans (it contains parts of rabbit, rodent and human PON1), and thus reduce its effectiveness. It can cause serious (cardiac) health effects (29). Betapudi acknowledges these warnings, but says it has not sought to solve all the problems with gene therapy. "It is a proof-of-principle study of sorts.

Other work has been published, this time on anthrax. The transmission of the bacterium (bacillus anthracis) is by inhalation of the spores. Within a few days, the release of toxins leads to a respiratory illness, with fever, malaise, fatigue and shortness of breath. This form is 80% fatal.

Martchenko (32) shows that the capillary morphogenesis gene 2 (CMG2) encodes a major membrane protein receptor for anthrax toxin. Human genetic variation in this gene significantly alters susceptibility to the toxin.

Arévalo reports that antibiotics are not effective because they do not remove high levels of toxin. The authors worked on two anthrax toxin receptors: the CMG2 and the endothelial tumor marker 8 (TEM8). They used another molecular biology technique: RNA interference (RNAi). Silencing the CMG2 receptor with targeted RNAi provides near-complete protection against toxin cytotoxicity in human and murine macrophages, but also in human kidney cells. (33)

The RNA-guided DNA recognition platform enables genome-wide selection of gene expression. (34)

## Discussions

### Military research in the service of medicine

The need to frame research is fairly recent. In 1966, Beecher, an anesthesiologist and professor at the Faculty of Medicine at Harvard University, published an article entitled "Ethics and Medical Research." (35). He described 22 unethical experiments.

In response to these scandals, a commission was created in 1973, the "National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research." It was interested in questions such as the right to information, research on children, prisoners, mentally handicapped people or foetuses. On each of these issues, it published a report, and ultimately the Belmont Report. It had a considerable impact.

In 1976, the Medical Research Council (MRC) set up a "working group on human experimentation" in Canada. In France, clinical research distinguishes between interventional and non-interventional research. (36)

The Commission established three principles: respect for persons (which it preferred to autonomy), beneficence and justice. Initially, these three principles were concerned only with research ethics. (11)

Greene and Master's article (7) provides a solid foundation for the protection of combatants from biological or chemical weapons.

Informed consent involves autonomy, respect for the individual. The patient is offered to adhere, after being properly informed about the proposed research. In the military, it is more difficult to define and establish. The hierarchical relationships, strong and accepted by all, risk biasing the free will of the soldier. It is necessary to place the combatant in the singularity of his function, for which "Military personnel must obey the orders of their superiors and are responsible for the execution of the missions entrusted to them" (37)). Non-obedience to superior authority could jeopardize a mission. (20)

The notion of informed consent implies a clear and loyal explanation of the subject of the research for which the patient, in this case the soldier, is going to give his approval. But who would be responsible: the operational command, the Army Medical Corps or both? What should be the content of the information, in what form, on what medium, at what time? What is the influence of the research team? ....

The questions are multiple, especially since the situation on a battlefield is not fixed, and not always controllable. The DoD has proposed and adopted a waiver authority for emergency situations: the "interim rule". Before large-scale military use, it is necessary to have certainty about the results of published studies.

In the examples selected, consent would be favored by several parameters. There are no specific laws to prohibit military enhancement in the US or France. "It is important to seek and improve the operational capacity of the armed forces, while respecting the principle of respect for the dignity of the human person. (24) The substance offered to the soldier is a drug in the sense that its administration protects against the effects of a chemical or biological attack. And the effects on the genome are temporary.

For a soldier to refuse would mean to oppose the group of which he is a member, to disassociate himself from it and marginalize himself. And to put it at risk. Such a choice would not be defensible in front of his fellow soldiers. Steps must be taken to reduce group pressure to improve the pedagogy of consent. It would allow soldiers to understand the risks and purpose of interventions. Identical training is given to every soldier who is going to intervene in the same conflict zone, and the command ensures that the information delivered has been retained.

In this way, the French soldier, subject to a possible chemical risk, will be provided with adequate equipment. But who should be included in the research groups? The soldiers who will be going into action, officers, administrative staff, non-commissioned soldiers, reservists? And how do you select the two groups, including the placebo group?

Expected beneficial results can mobilize many staff. On the other hand, disappointing or pejorative results will drive them away. In this case, how can they be selected without creating major tensions within the armed forces, which would be detrimental to effective cohesion? Another problem is that of the volunteer's remuneration. What would be the "basis for discussion"? Whatever the form (cash or other), the risk of inequity is important. In the U.S., the DoD prohibits active duty military personnel from being paid for research trials. A fair possibility would be to limit participation to soldiers on leave. But in this case, it would have to be verified that this distinction does not undermine the principles of fairness for military research. (7)

## Medical Ethics in the Military

Is the recent arrival of this discipline in the military an added value? Initially, we must consider the benefit of the general contribution of ethics in the military. A priori, it is not mandatory. Indeed, under fire, ethics will be less useful to the soldier than a heavy helmet and a machine gun. At least at first. (38)

For a very long time, in fact, we were content with the "habits and customs of war". The oldest formulation dates from the Middle Ages, with the "jus ad bellum" (right to wage war) and the "jus in bello" (right in war), which decline the concept of "just war" inherited from Saint Augustine (39). Today, Royal prefers to speak of "justified war".

The soldier's moral code is included in the codes of honour. It is a value shared by all French army personnel, and therefore by SSA caregivers. Morality is for all soldiers, and ethical reflection is adapted to the situation and the corps.

The particularity of a conflict zone is to erase the differences between combatants, to create a brotherhood of arms. A dangerous situation, in a vacuum, strengthens the bonds and encourages exchanges, also of an ethical nature.

"An ethic of behavior in combat is more than ever indispensable to the soldier, actor and victim of war. It will protect him from the consequences of his actions, both with regard to the law and to his own psychological and moral health. It will also meet the expectations of the population: that of his own nation, from which he derives his legitimacy, but also that of the nation whose support and respect he must earn.

The SSA is a military entity. It is therefore subject to an ethic of responsibility. But is it only that and can we speak of an ethic of conviction? Is the SSA in the camp of science whose goal is the search for truth? The politician has to make compromises," Weber points out, "the scientist cannot cover them up. In some respects, yes. Medical support is not action in the strategic sense. (38)

In armies, the individual exists within the group that he feeds and strengthens. Is this the same for SSA personnel? Indeed, the military responsibility is collective, but the medical act is individual.

## The soldier's genomic package

We have reviewed the ethical issues raised by medical research, the impact of SSA ethics in the military. In this last part, the ethical approach reflects on the impact of the modification of

the soldier's genome, in order to protect her (from a terrorist threat). Presented in this way, it is difficult to oppose it, especially if the action is reversible and will not affect the return to civilian life.

Thus, the DoD and the Defense Ethics Committee of the French Ministry of the Armed Forces have given their agreement. The latter body writes that "All military personnel, whatever their training and speciality, are called upon to fight and may, in certain cases, be concerned by an increase in their capabilities". Among these, the committee retains: "practices that prevent a health risk". The opinion is homogeneous up to the following recommendation: "Prohibit eugenic and genetic practices for the purpose of augmenting the military". (24)

Why such apparent inconsistency? The semantics retained concern the terms "augmented" and "modified. The DEC does not use the English word "enhancement" because it indicates, according to the DEC, an increase coupled with an improvement. It prefers to use the French word "augmentation", and will therefore speak of an augmented soldier. Aware that this term is not without ambiguity either, the committee wished to define "the augmented soldier" by placing it in its own singularity. For this dissertation, we preferred to use the term "modified" because it corresponded better to the situation analyzed.

The applications, and the ethical reflections that follow, are recent and are not clearly mentioned by the Committee. However, the Committee indicates that the augmentation of the combatant in an operational situation could concern "commitments on national territory relating to public order". It cites, for example, the case of a bacteriological or chemical threat (biological defence of armies). 31/(CED) 24

The ERC report is clear. It addresses the ethics of the augmented soldier from every angle, and it makes recommendations. But it is difficult to be comprehensive.

Gupta's early results had drawbacks, regarding storage of bioprotectants and effects on the immune system (30). Using gene therapy for prophylaxis, Betapudi has shown promising results. In mice, the recombinant PON1 protein provides protection, asymptomatically, against multiple lethal doses of all G-type nerve agents for several months. The treatment is also effective in IM, a route of administration more suitable for the battlefield. (31). Yet Lockridge points out that PON1 causes significant immune responses, and other serious health effects. (29)

This work highlights the concept of benefit/risk. Soldiers deployed in a theater of operations have to protect themselves from an attack, which may or may not be fatal in the short term. The answer is obvious. And this modus operandi is all the more guiltless for the combatant, who is suggested to administer (or to administer to himself) a product to escape death, and this, without taking the life of the enemy.

These results are experimental and need to be completed. The "proof-of-principle study" is not enough. Finally, if the military authorities receive marketing approval, the package insert must be as complete as possible.

The risk incurred by the undesirable effects of the substance must also be brought to the attention of the combatant, and the circumstances of administration and the procedure clearly defined. The French armies can draw inspiration from the protocol for using atropine syringes: where, when and how to inject the product.

The work of Martchenko (32) and Arévalo (33) concerns the anthrax threat. While the molecular biology techniques differ, the purpose is the same: to modify the anthrax toxin receptor(s) to inhibit its action on the organism.

Some authors indicate that the action of genomics is temporary, i.e. reversible. We have seen previously that this notion is relative. Tomorrow, nothing will prohibit targeting other toxic agents of biological or chemical threats, making definitive genetic modifications and touching the germ line. How far and how long will the "modified soldier" be modified? This is where the spirit of the Lander moratorium comes into play.

Another question concerns the possible consequences of the techniques used on bacteria (here the anthrax). Biologists will have to be vigilant, and make sure that this does not encourage selection pressure.

Each technical "advance" should be studied, and analyzed, by competent military, ethical and scientific authorities, and at regular intervals. Aware of this, the CED has established a periodicity of about ten years to take stock.

But if the experimentation of Chinese teams seems to escape control by the scientific community, what about countries that do not respect the laws of war? We know that, despite international bans, some countries, like Syria, use nerve agents against soldiers and civilians.

It is difficult to control the activity of "rogue states" and terrorist groups. What then is the contribution of ethics, referee of a match where one of the two camps does not respect the

rules of the game? This is an essential question, but one that is difficult to answer. Royal does, however, give us an element of an answer: "When the soldier finds only barbarism to respond to barbarism, the conflict tips over into reciprocal violence and it is the very notion of civilization that is affected". (39)

## Conclusion

Since the beginning of time, men have fought wars, and local and international conflicts are still going on. Faced with a threat, the combatant has always adapted by using the technology of his time. Often, there are no structured armies, but mobile groups, with a perfect knowledge of the terrain. The code of honor of armies, and the Geneva Conventions, are denied by these belligerents. We are thinking about the evolution of the augmented soldier with our military values and our culture.

Ethics must adapt to these changes, by anticipating situations and analyzing data provided by the command. Military medical ethics have the same constraints and objectives as in the civilian world. They are not antinomic, they are complementary, and they have the same goal. The particularity of ethics in the armed forces is simply linked to the singularity of situations, whether in overseas operations or on national territory.

Research is recent and benefits from the contribution of new molecular biology techniques, such as CRISPR-Cas9. The authorities seem to accept, in whole or in part, the genetic modifications of the cases mentioned in this article. But even if the use of these techniques is effective, it is an invasion of the soldier's privacy. How will genomic modification evolve in our military? Will science produce chimera soldiers, like Mangeot's black and white mice (2)? The consequences will be worse if genetic engineering falls into the hands of terrorists (if it has not already).

The ontological question concerns the future of the combatant who goes from being an augmented soldier to being modified. What future are we preparing for those who watch over us, the combatants who have chosen to dedicate their lives to the defense of our country?

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