GCSP
Geneva Centre for Security Policy

NOVEMBER 2026 | ISSUE 49

Strategic Security Analysis

Synthetic Biology and Antimicrobial Resistance: Engineering a Systemic Security Threat

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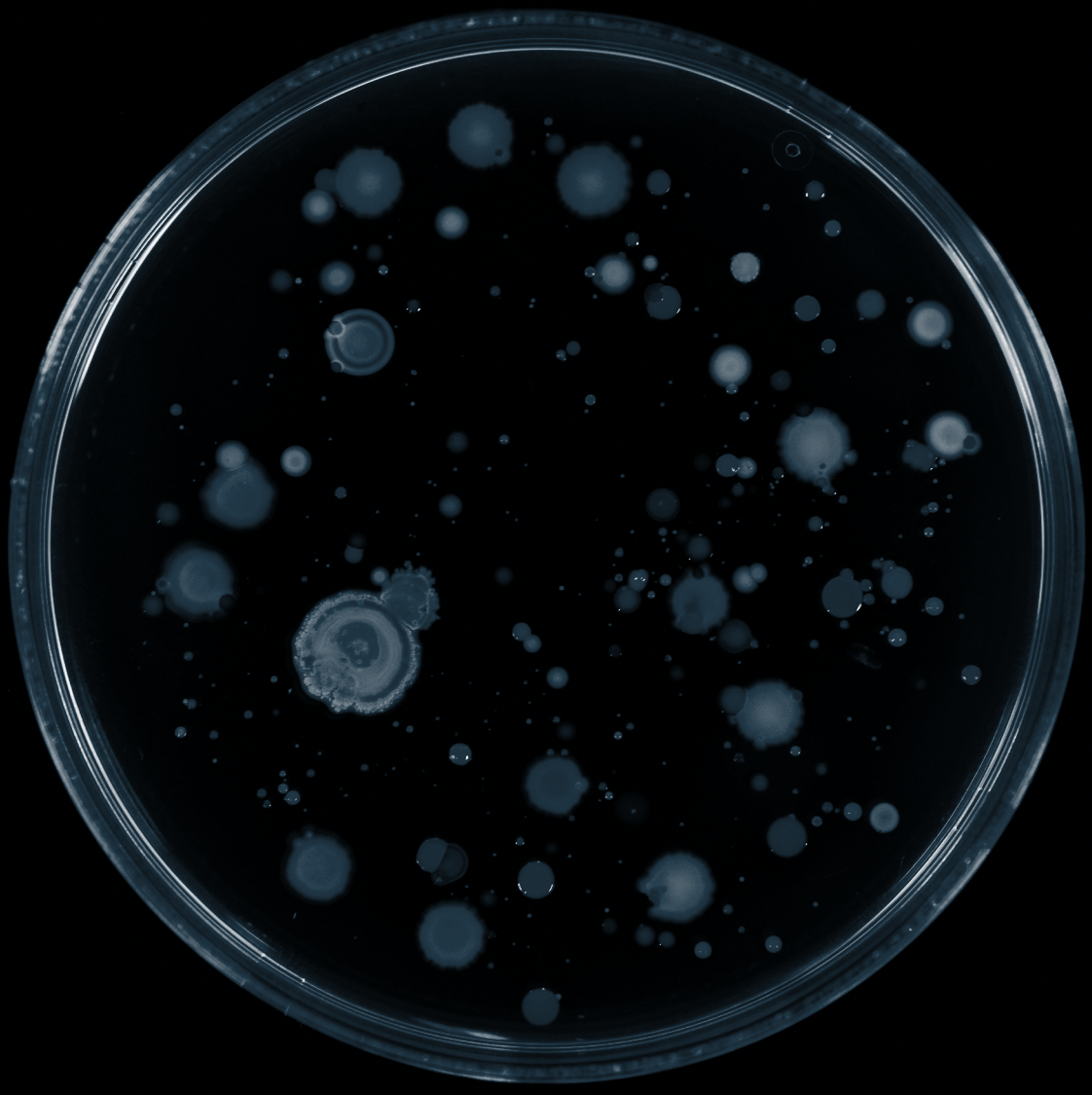

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This series is edited by Dr Jean-Marc Rickli, Head of Global and Emerging Risks.

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About this publication

This publication is part of a special series of papers under the GCSP's **Polymath Initiative** supported by the Didier and Martine Primat Foundation and the EA Funds Long-Term Future Fund. For more information, please visit the Polymath Initiative website:
www.gcsp.ch/the-polymath-initiative

ISBN: 978-2-88947-337-3

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Key points

- Antimicrobial resistance is usually treated as a public health problem. Synthetic biology adds a further dimension: resistance can be engineered in a pathogen.
- Modern medicine depends on antibiotics to treat a wide range of health issues, so engineered resistance could remove effective treatment as a key factor of human security.
- Armed conflict exposes this vulnerability particularly clearly. Recent wars have repeatedly produced casualties infected by highly resistant pathogenic bacteria.
- Modern military medicine presents a paradox: technological advances increasingly allow severely wounded personnel to survive injury, yet their subsequent recovery may depend on antimicrobial therapies that have advanced far less dramatically.
- Efforts to circumvent antibiotics by modifying classic biological warfare agents have already been exposed, but contemporary synthetic biology makes the manipulation of microbial genomes increasingly accessible and difficult to attribute.
- Preparedness should therefore treat antimicrobial efficacy as part of critical defence infrastructure.

Introduction

Antimicrobial resistance (AMR) is generally described as a slowly developing global health emergency, sometimes referred to as "the silent pandemic".[1] Bacteria evolve under antimicrobial pressure, resistance genes circulate among microbial populations, and treatments that were once reliable progressively lose efficacy. However, this framing is incomplete: it treats AMR primarily as an evolutionary and epidemiological process resulting from excessive antibiotic consumption. Advances in synthetic biology introduce another possibility: resistance can increasingly become a designed and intentionally disseminated property.

Antibiotics are not simply one category of medicines among many: they are enabling technologies on which much of modern medicine depends. Surgery, intensive care, transplantation, cancer therapy, neonatal medicine and the management of major trauma all rely on the assumption that bacterial infections can ultimately be controlled. When this assumption fails, the consequences extend beyond the individual infection. Medical procedures become riskier, hospital stays become longer and more resource intensive, and interventions that depend on successful infection control become harder to perform.

Making an otherwise treatable pathogen difficult or impossible to treat could be sufficient to undermine one of the central technological advantages of modern medicine.

The relationship between antibiotics and military medicine is unusually deep. Penicillin was transformed from a laboratory discovery into a mass-produced medicine starting in the Second World War, with military demand helping to accelerate its development and deployment.[2] Antibiotics subsequently became integral to modern combat casualty care. As a result, infection became far less likely to determine the outcome of otherwise survivable wounds. But after eighty years of extensive antibiotic usage, AMR threatens to erode part of this achievement.

Modern armed forces have developed extraordinarily sophisticated systems for keeping wounded personnel alive: haemorrhage control, rapid evacuation, resuscitation, reconstructive surgery, intensive care and increasingly capable battlefield diagnostic technologies. Yet these systems ultimately converge on a comparatively old biological requirement. If a severely wounded patient develops a bacterial infection, clinicians must still be able to control the spread of the pathogenic agent. Recent conflicts demonstrate how fragile this assumption can become. War casualties frequently suffer blast and penetrating injuries involving extensive tissue destruction, repeated surgery, and prolonged exposure to multiple health-care environments. Conflict simultaneously disrupts sanitation, laboratory capacity, infection control, pharmaceutical supply chains and antimicrobial stewardship. These conditions create an environment in which resistant organisms can emerge, circulate and become concentrated among the most severely injured patients.

This Strategic Security Analysis argues that this naturally occurring phenomenon also exposes a potential synthetic-biology security vulnerability. A biological threat does not necessarily need to acquire radically increased virulence to create strategic disruption. Making an otherwise treatable pathogen difficult or impossible to treat could be sufficient to undermine one of the central technological advantages of modern medicine. The security concern that we are now facing is therefore not simply resistant pathogens, but the possibility of intentionally engineering organisms to exploit antibiotic dependency.

War as an amplifier of antimicrobial resistance

The association between armed conflict and difficult-to-treat wound infection is not new: what has changed is the microbiological landscape. Combat wounds combine several conditions favourable to infection: extensive contamination, devitalised tissue, foreign material, delayed closure and repeated surgical intervention. Patients may move through several levels of care and across borders, receiving broad-spectrum antibiotics along the way. This strongly favours hospital-associated organisms and the selection and transmission of drug-resistant strains. Several important hospital-associated bacterial pathogens, including *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, are major causes of difficult-to-treat wound and health-care-associated infections.

Armed conflicts unusually amplify AMR.

Cases from battlefields in Iraq and Afghanistan drew international attention to this problem, particularly through multidrug-resistant *Acinetobacter baumannii*.[3] Studies of casualties from Iraq documented frequent multidrug resistance in trauma-related infections, considerably narrowing therapeutic options.[4] The phenomenon subsequently became an important issue for deployed military health services, and stimulated interest in infection-control systems and diagnostic technologies better suited to military care.

Ukraine provides a striking contemporary example. Beley et al. analysed 1,441 wound cultures from 478 Ukrainian servicemen treated between 2022 and 2024.[5] The most common pathogens were *K. pneumoniae*, *A. baumannii* and *P. aeruginosa*. Almost all *K. pneumoniae* isolates were classified as multidrug resistant, highlighting a striking difference from the rates in non-conflict zone. Other studies of Ukrainian war casualties similarly report highly resistant organisms, including carbapenem-resistant strains, while genomic studies pre-dating the February 2022 full-scale Russian invasion of Ukraine had already demonstrated diverse resistance determinants among *A. baumannii* isolated from wounded personnel.[6]

These manifestations should not be interpreted as evidence that war somehow creates resistance *de novo*, nor can resistance alone be separated easily from injury severity, hospital exposure, and antibiotic consumption. Rather, armed conflicts unusually amplify AMR by bringing together susceptible hosts, severe tissue injury, antimicrobial pressure, disrupted infrastructure and multiple health-care environments.

Antibiotics as infrastructure

The strategic significance of this phenomenon becomes clearer if antimicrobial therapy is viewed not merely as pharmaceutical treatment, but as medical infrastructure. The success of modern trauma care depends on mutually reinforcing technologies. A casualty who would once have died from haemorrhage may now survive. Devastating injuries that once required immediate amputation may be treated with complex surgical reconstruction. Intensive care can sustain patients through prolonged unstable physiological states. Each improvement increases survival – but survival also creates a new population of patients exposed to infection. A person with extensive soft-tissue damage, open fractures, implants and repeated operations may require antimicrobial protection for weeks or months. The more surgical prowess advances, the more critical infection control becomes to the success of post-operative recovery.

This creates an asymmetry in technology. Military medicine has invested extensively in operating at or close to the battlefield, developing and refining techniques such as rapid casualty evacuation, physiological monitoring, and imaging and sophisticated point-of-care diagnostic platforms, including microbiological diagnostics. However, diagnostics do not cure infection. A modern military health system may therefore identify a resistant pathogen more rapidly than ever while still confronting essentially the same question: is there a drug that can treat infection? Recent reports on war casualties demonstrate the extraordinary treatment burden that resistant infections can impose, including repeated operations, prolonged hospitalisation and highly individualised antimicrobial regimens, which nevertheless can ultimately lead to amputation.[7] This highlights the limits of modern medicine.

This does not mean that increased AMR has caused higher amputation rates. Injury patterns, survival rates, evacuation systems and clinical definitions vary dramatically between conflicts. Indeed, improved trauma survival creates substantial survivor bias: patients who would have died in previous wars now survive long enough to undergo repeated attempts at limb salvage.

Recent reports on war casualties demonstrate the extraordinary treatment burden that resistant infections can impose.

Synthetic biology changes the threat

Resistance naturally emerges through mutation, selection and gene transfer. These processes continue to dominate the global AMR crisis, and synthetic biology does not replace them. Rather, it changes the security landscape by making biological traits increasingly amenable to deliberate manipulation. Resistance determinants are particularly relevant because many are genetically very well characterised. Resistance can occur when bacteria produce enzymes that destroy or modify antibiotics, alter the targets of drugs, decrease permeability, or activate efflux. Genes encoding such functions circulate naturally on and between bacterial chromosomes. Modern molecular biology has consequently accumulated an enormous catalogue of resistance mechanisms.[8]

From a scientific perspective, introducing a resistance determinant into a bacterium is a routine procedure. Antibiotic-resistance genes have been commonly employed as selection tools for decades. Laboratory biosafety regulations impose containment precautions, and introducing resistance genes in a pathogen does not increase the biosafety level of an organism. From a biosecurity perspective, the important distinction lies in which resistance phenotype is generated, in which organism, and for what purpose.

This technical tractability has already been recognised as a biosecurity concern. The US National Academies' 2018 report *Biodefense in the Age of Synthetic Biology* identified the modification of existing pathogens to overcome medical countermeasures, including AMR, as an important synthetic-biology threat.[9] More broadly, the report emphasised that synthetic biology expands the range of biological characteristics that can potentially be deliberately designed rather than simply selected through natural evolution.

The biodefence literature has described decades-old, genetically modified variants of classic threat agents as "improved agents", engineered to circumvent established countermeasures.[10] Former Soviet biological-weapons programmes aimed at incorporating antibiotic-resistance genes into classic bacterial pathogens such as *Brucella* (causative of brucellosis), *Bacillus anthracis* (causative of anthrax) and *Burkholderia* (causative of glanders). The goal of these modifications was to produce agents against which existing therapies would be ineffective.

A review of AMR among major bacterial biothreat agents documents that resistance has been experimentally generated in a group of notorious

pathogens considered to be potential biological weapons, either through the introduction of resistance determinants or through laboratory selection.[11] The authors consequently emphasise that the susceptibility profile of a micro-organism encountered after an intentional release could not safely be assumed from the normal characteristics of that species.

These historical examples require careful interpretation. Claims regarding former offensive programmes are partly based on defectors' statements and open literature, and cannot all be independently verified. Furthermore, demonstrating that resistance can be generated experimentally is very different from demonstrating that an organism can be developed into an effective biological weapon. Successful weaponisation involves numerous additional biological, engineering, and operational barriers, including biological containment, dissemination, and the survival of the pathogen upon release. Nevertheless, the underlying principle is established: resistance is a desirable property from the perspective of an offensive biological programme because it acts directly against the defender's capacity to respond effectively.

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Synthetic biology strengthens this logic, thereby expanding the security threat. In recent years, the development of genome sequencing, inexpensive DNA synthesis, genome editing, and increasingly sophisticated computational approaches to gene and protein design have progressively shifted biological engineering from the manipulation of individual genes towards the deliberate construction and modification of larger genetic systems. Contemporary scientific literature describes the synthesis of chromosomes, genomes, and viruses and the continuing expansion of biological design capabilities.[12] This has created many opportunities to develop new therapies, including ones that tackle AMR pathogens.[13] On the other hand, however, commercial nucleic-acid synthesis has made custom DNA broadly available, prompting the development of sequence- and customer-screening systems specifically because synthetic DNA could potentially be misused to construct dangerous biological agents.[14] However, such screening is inherently less effective for antibiotic-resistance determinants, which are ubiquitous, widely used as routine laboratory tools, and therefore difficult to flag without generating large numbers of false positives. A more effective screening strategy could therefore focus on contextual combinations of sequences rather than individual resistance genes, e.g. orders that suggest the addition of resistance determinants to already recognised biological threat agents.

Advances in artificial intelligence (AI) may further expand this design space. Future systems could enable the design or optimisation of resistance proteins that do not simply reproduce resistance mechanisms already found in nature. More immediately, AI-assisted protein design is beginning to decouple biological function from recognisable sequence: proteins can increasingly be designed to adopt structures or functions resembling known proteins while sharing limited sequence homology with them.[15] This creates a potential blind spot for nucleic-acid synthesis screening systems that rely heavily on sequence similarity to known hazards, particularly if such novel functions could be introduced into bacterial backgrounds that already possess substantial intrinsic or acquired AMR.

The result of the convergence of synthetic biology and bioweapons is not that creating an effective biological weapon has become trivial.[16] It has not. Rather, the space of possible modifications has widened, and some modifications, particularly well-understood traits such as AMR, are conceptually much simpler than designing fundamentally new forms of pathogenicity.

This distinction is important for threat assessment. Security discussions around synthetic biology often focus on spectacular, seemingly high impact possibilities with uncertain outcomes: the creation of novel pathogens, major increases in virulence, altered host range or entirely synthetic organisms.

Engineered resistance represents a less exotic and less intimidating strategy, but a potentially more credible and feasible path that is harder to detect. The pathogen may already possess the characteristics necessary to infect humans. The engineered intervention need only reduce the effectiveness of the defender's medical response, i.e. the efficacy of antibiotics.

Engineered resistance as an attack on medical dependency

This leads to a different way of conceptualising AMR, i.e. as a biological security threat. The traditional question is: Could synthetic biology make a pathogen more dangerous? For AMR, a more relevant question may be: Could synthetic biology make the defender less capable of treating an otherwise familiar pathogen? The distinction matters because biological effects and strategic effects are not equivalent.

Could synthetic biology make the defender less capable of treating an otherwise familiar pathogen?

A resistant organism need not replicate faster, transmit more efficiently or cause intrinsically more severe disease. Its strategic impact could instead arise from prolonging illness, increasing demand for surgery and intensive care, complicating medical evacuation, consuming scarce drugs, forcing isolation measures, and reducing confidence in standard prophylaxis and treatment protocols. Individually, these effects increase pressure on health-care systems. In combination, they could temporarily overwhelm local or deployed medical capacity. This applies to civilian settings, but is particularly relevant to armed forces. Military organisations depend on the expectation that wounded personnel can enter a medical system capable not simply of keeping them alive, but offering a credible path to recovery and, ideally, back to combat. The effectiveness of this system contributes to operational resilience and society's willingness to tolerate military casualties. Highly resistant infection attacks this system at a vulnerable point.

The biological weapon envisaged here therefore differs somewhat from the classic model centred on mass lethality. The objective need not be to maximise immediate deaths, but rather to overwhelm both the civilian and military health-care systems. A pathogen that predictably generates complex, persistent, and difficult-to-treat infections could instead impose disproportionate demands on evacuation networks, surgical capacity, specialist personnel, and hospital beds. An infection that turns one casualty into a patient requiring months of medical treatment may create effects far beyond its direct mortality.

This logic also bridges naturally occurring AMR and deliberate biological threats. The war in Ukraine demonstrates what resistant wound pathogens can do without deliberate engineering. Synthetic biology raises the possibility that some of the same treatment problems could be intentionally reproduced or amplified. The natural phenomenon is therefore a warning of vulnerability, not evidence of hostile manipulation.

Detection is necessary, but not sufficient

The problem is further complicated by uncertainty. When a resistant organism appears during a conflict, the default explanation will usually be natural evolution and transmission. Conflict zones already generate powerful conditions for AMR, so distinguishing an unusual natural resistance pattern from deliberate engineering would therefore be extremely difficult. An unusual AMR profile could constitute a possible epidemiological indicator of deliberate biological release, and modern microbial genomics now offers considerably greater ability to reconstruct pathogen evolution and epidemiology, identify

unusual genetic elements, and search for signatures of engineering. Work on genetic-engineering attribution suggests that sequencing and forensic analysis may eventually help determine whether an organism has been modified, and potentially provide information about its origin.

But attribution will remain challenging. Resistance genes move naturally between organisms, and many of the molecular operations used in engineering mimic processes occurring in nature. A pathogen carrying a familiar resistance determinant may provide little evidence about intention. This creates another reason for preparedness to prioritise phenotype (observable traits, such as antibiotic susceptibility) and genotype (DNA sequence and resistance genes). Uncertainty also creates opportunities for plausible deniability. An actor accused of deliberately engineering resistance could point to natural evolution, laboratory contamination or the actions of another party as alternative explanations, making attribution contestable even when suspicion is high.

A health-care system needs both the ability to recognise an unexpected pathogen and the therapeutic flexibility to act on this information.

Weigel and Morse emphasise that the presence of a resistance gene does not always reliably predict clinical resistance,[17] a feat that is widely documented in the field of infection biology.[18] Conversely, unexpected resistance may emerge through mechanisms not covered by targeted molecular assays. Rapid genomic diagnosis is therefore essential, but rapid phenotypic susceptibility testing remains equally important when immediate treatment decisions must be made.

The broader lesson mirrors the technological asymmetry described earlier: information alone is insufficient. A health-care system needs both the ability to recognise an unexpected pathogen and the therapeutic flexibility to act on this information.

From an AMR problem to a security problem

Not every resistant infection is a national-security event. AMR becomes a security issue when resistance begins to interfere with functions essential to the stability or operational capacity of a state, be it in military or public health care. Several characteristics are therefore particularly relevant when assessing pathogen-resistance combinations.

1. *Clinical dependence:* How strongly does treatment of the infection depend on a limited number of antimicrobial classes?
2. *Medical-system amplification:* Does the infection disproportionately affect patients requiring intensive care, surgery, implants or prolonged hospitalisation?
3. *Conflict compatibility:* Is the organism well suited to wound infection, environmental persistence or transmission within stressed health-care environments?
4. *Dissemination potential:* Can the resistance determinant or organism move efficiently through health-care networks or across borders?

Classic agents such as anthrax and plague remain important because of their established biological-warfare potential. But from the perspective of military trauma, organisms already causing major contemporary health-care-associated infections, including *Klebsiella*, *Acinetobacter* and *Pseudomonas*, deserve attention precisely because they exploit the medical environments generated by modern warfare. The relevant question is therefore not simply Which pathogens are most lethal? but, rather, Which combinations of pathogen, resistance and context could most effectively degrade medical capacity?

The systemic consequences of AMR would extend well beyond health-care delivery itself. When medical capacity is constrained, the resulting consequences are unlikely to be distributed evenly. Communities with poorer access to care, fewer financial resources, greater dependence on public services, or higher sensitivity to illness are less able to absorb interruptions in diagnosis, treatment, and surgery. Prolonged hospital stays, shortages of effective drugs and delayed procedures could therefore generate secondary effects well beyond infected patients. Recent public health crises have shown how quickly such inequalities can arise and erode confidence in institutions responsible for managing such crises.

These pressures could also interact with an increasingly contested information environment. Visible treatment failures, uncertainty over the origin of resistant infections, and unequal access to scarce therapies could provide fertile ground for misinformation, conspiracy narratives, and accusations of institutional failure. In turn, declining trust could make public health measures harder to implement and deepen social polarisation, creating a feedback loop in which the informational and political consequences of AMR amplify the medical crisis itself. In this sense, the strategic significance of AMR lies not only in the infections it causes, but in its potential to trigger cascading effects across health-care capacity, social cohesion and institutional legitimacy.

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The international-security implications of AMR also extend beyond individual states. Resistant pathogens and resistance genes move across borders through travel, migration, and patient transfers. This creates a collective-action problem: weaknesses in surveillance, antibiotic stewardship or treatment capacity in one country can generate consequences elsewhere. In an engineered or unusually resistant outbreak, uncertainty over origin could also complicate attribution and fuel interstate tensions, making international coordination a core part of AMR security preparedness.

Recommendations

National strategies already provide a strong foundation for reducing the emergence and spread of AMR. For example, Sweden's 2026-2035 strategy and Germany's DART 2030 emphasise prevention, surveillance, antimicrobial stewardship, diagnostics, access to effective drugs, research, and international cooperation.[19] These measures are essential, but are designed primarily around naturally emerging resistance in civilian and agricultural settings. They do not yet fully address AMR as a deliberate security threat, including issues like the possibility of engineered resistance, its exploitation against military and civilian health-care systems, the challenges of attribution, or preparedness for treatment failure under conflict conditions. The recommendations below are therefore intended to complement existing AMR strategies by adding a biosecurity and defence dimension to them.

Recommendation 1: Treat antimicrobial efficacy as critical defence infrastructure

Military preparedness should treat access to effective antimicrobial therapy as a strategic capability rather than solely a pharmaceutical issue. Threat assessments should explicitly examine scenarios in which standard antibiotics fail against organisms associated with combat wounds and health-care transmission.

Recommendation 2: Build diagnostics for unexpected resistance, not only expected pathogens

Investment in rapid battlefield and hospital diagnostics should continue, but systems should be designed to identify resistance phenotypes that fall outside standard expectations. Genomic sequencing, resistance-gene detection and rapid phenotypic susceptibility testing are complementary rather than interchangeable technologies.

Recommendation 3: Integrate conflict-associated AMR surveillance with biosecurity surveillance

Military, civilian, and humanitarian surveillance systems frequently treat naturally emerging AMR and deliberate biological threats as separate domains. However, they should be more closely connected. Genomic surveillance of resistant organisms in conflict zones can simultaneously support clinical treatment, infection control, epidemiology and the detection of anomalous events.

Military, civilian, and humanitarian surveillance systems frequently treat naturally emerging AMR and deliberate biological threats as separate domains.

Recommendation 4: Develop therapeutic resilience rather than relying on fixed antibiotic stockpiles

Stockpiling antibiotics assumes that the susceptibility of the threat organism is broadly predictable, but engineered resistance directly challenges this assumption. Preparedness should therefore emphasise diversified antimicrobial options, rapid access to reserve agents, alternative therapeutic approaches and the capacity to update treatment protocols quickly when resistance patterns change.

Recommendation 5: Strengthen microbial forensic and international attribution mechanisms

Because resistant organisms arise naturally, any allegation that AMR has been deliberately engineered during conflict would have enormous political consequences and carry substantial risk of misattribution. Internationally credible scientific mechanisms for microbial forensic analysis are therefore important for both deterrence and preventing premature accusations. This should be supported by stronger international and cross-sectoral coordination in the form of an “AMR diplomacy” linking health, defence, biosecurity, research, and foreign-policy communities around surveillance, attribution, and response.[20]

Conclusion

AMR already represents one of the clearest examples of how biological evolution can undermine technological progress. Modern medicine has built increasingly sophisticated systems around an implicit assumption: bacterial infection is treatable.

War exposes the fragility of this assumption. Recent conflicts demonstrate that severely injured personnel can become infected with organisms resistant to multiple, sometimes nearly all routinely available antimicrobial options. Synthetic biology introduces an additional security dimension. The genetic basis of many resistance mechanisms is understood, resistance genes can be moved between organisms, and the experimental creation of resistant biothreat agents has long been documented. Historical biological-warfare programmes reportedly recognised precisely this strategic value: resistance can be used to circumvent the defender's medical countermeasures. The most consequential engineered pathogen may not be the organism with the most exotic and dramatic toxicity; rather, it may be an otherwise familiar pathogen modified so that modern medicine can no longer reliably control it. Seen in this way, AMR is more than a public health burden: it is a potential attack on the technological infrastructure of medicine itself. For armed forces personnel whose ability to survive severe injury increasingly depends on that infrastructure, protecting antimicrobial efficacy should be regarded as an element of national and international security. The path forward is therefore not only to slow the emergence of resistance, but to build resilience against the possibility that resistance could be deliberately engineered or strategically exploited. This will require closer integration of AMR policy with biosecurity, military medicine, genomic surveillance, rapid susceptibility testing, microbial forensics and international coordination.

The path forward is therefore not only to slow the emergence of resistance, but to build resilience against the possibility that resistance could be deliberately engineered or strategically exploited.

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ISBN: 978-2-88947-337-3

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