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Radical Solutions Needed for Antibiotic Resistance

Antibiotic resistant infectious diseases have created a public health crisis worldwide. The conventional reductionist approach is failing to cope. **Sam Burcher** and **Mae-Wan Ho** argue for the revival of traditional healthcare systems, and for the many safe and effective anti-microbials now documented among indigenous plants that have been tried and tested for millennia.

Infectious diseases are responsible for one-quarter of all the deaths in the world, second only to cardiovascular diseases ^[1]. They are associated with the new strains of bacteria and viruses emerging within the past twenty-five years, which are also highly resistant to drugs and antibiotics. Infections become more difficult to treat, the severity of illness increases, as does the duration of infectiousness, adverse reactions, the length of convalescence and costs.

Drug and antibiotic resistant infectious diseases have created a public health crisis worldwide, and this was the subject of a series of high level international conferences in 1998, such as the World Health Assembly and the European conference "The Microbial Threat".

In Britain, the House of Lords Select Committee on Science and Technologies and the Standing Medical Advisory Committee (SMAC) each produced a special report on antimicrobial resistance ^[2]. These resulted in an Antimicrobial Resistance Strategy and Action Plan in June 2000 ^[3], which will cover work for the next two years and will be

advised by the new Expert Advisory Committee on Antimicrobial Resistance.

The proposed strategies include,

1. Surveillance -- to monitor and provide data on resistant organisms, illnesses associated with them and antimicrobial usage.
2. Prudent antimicrobial use -- to slow down evolution of resistance by reducing unnecessary and inappropriate exposure of microorganisms to antimicrobial agents in clinical practice, vet practice, animal husbandry, agriculture and horticulture.
3. Infection control -- to reduce the spread of infection in general, thereby reducing the use of anti-microbial agents and the spread of anti-microbial resistant microorganisms.
4. Infection controls within hospitals and the community -- promoting collaboration between the European Union and the World Health Organization.
5. Research into the basic mechanisms of resistance -- to find out how resistance spreads, and how to prevent, treat and overcome resistance with novel agents/technologies.

These strategies seem sensible, but there are already signs that they may not be enough to combat antibiotic resistance. For example, although the overuse and abuse of antibiotic have contributed to the evolution of high levels of resistance among bacteria associated with disease, a growing body of evidence now indicates that phasing out antibiotics or reducing use will not necessarily reverse the situation ^[4]. Essentially, the functional complexity of genes frustrates any attempt to make predictions based on the simplistic assumption that one gene is responsible for one function. An antibiotic resistance gene often has multiple functions, while many different genes may contribute to resistance against a single antibiotic. There is now overwhelming evidence that antibiotic resistance genes spread by horizontal transfer among different strains of bacteria, which is almost impossible to control.

It is also becoming widely recognised that designing ever more deadly drugs to kill bacteria is no longer a viable option, both financially and clinically. Resistance to new drugs is appearing with increasing rapidity, often within a year of introduction. That means little or no return to drug companies that develop the antibiotics. Furthermore, drugs that are toxic to bacteria are often toxic for human beings as well, and the 'side-effects' may become much worse than the cure.

Some scientists are now rethinking the failed conventional model of killing pathogens with new, ever more deadly antibiotics as bacteria become resistant to the old ones ^[5]. They are designing drugs that aim to physiologically 'tame' the bacteria, rather than kill them. This is an important approach, which acknowledges the accumulating literature on the flexibility of micro-organisms. Bacteria can change drastically according to ecological conditions. They not only look different but behave differently as well. In particular, bacteria can stop proliferating and become non-virulent but remain metabolically active under appropriate ecological conditions. A logical extension to designing drugs that physiologically tame the bacteria is to find how ecological balance could be restored, so bacteria need never become virulent ^[6]. It is time to stop waging war on nature.

Another strategy that has not yet been considered in Britain is to integrate traditional or alternative medicines more broadly into the National Health Service, especially in the search for more effective, low risk, less costly antimicrobial agents. Other countries have made serious efforts at incorporating holistic medical practices into national health, with notable success especially in China where traditional and western medicine are practiced and taught together [7].

China began integrating traditional medicine in the National Healthcare system in the 1950's. Health officials trained in modern medicine sought compatibility between traditional and modern medicine by a western science-based approach that emphasized empirical research. Although some feel that this has compromised traditional medicine and that there is room for improvement, the overall result has been beneficial. Hospitals practicing traditional medicine treat 2000 million outpatients and almost 3 million inpatients annually. Over 95% of general hospitals have traditional medicine departments that treat 20% of outpatients daily. This adds up to 40 million people per day! [8]

In other countries such as South Korea and India, where traditional and western medicine operated in parallel but separately, there has been conflict and rivalry and lack of quality control. Increasingly, countries are feeling the need for proper integration of traditional and modern medical practices, and not just the predominance of one over the other.

The Central Council of Indian Systems of Medicines oversees research institutes where treatment is evaluated. The Indian government is adding ten traditional medicines into its family welfare program, partly funded by the World Bank. They cover a range of medical problems such as anemia, nutritional deficiencies and childhood diarrhea. New regulations were introduced in July 2000 to improve Indian herbal medicines by establishing standard manufacturing practices, quality control, authenticity of raw materials and absence of contamination. The government has set up ten new drug-testing laboratories for Indian systems of medicine and is upgrading existing labs to provide rigorous evidence to licensing authorities on the safety and quality of herbal medicines. Randomized controlled clinical trials of selected prescriptions have been initiated. This will help document the safety and efficacy of the prescriptions and provide the basis for their international licensing as medicines rather than simply food supplements [10].

There are many tried and tested antimicrobials and agents that improve the body's resistance to infections within traditional medical systems [11, 12], which have been the subject of hundreds, if not thousands of western scientific studies. These include ginseng, Astragalus, milk thistle, licorice, Echinacea, and garlic.

Anti-microbials continue to be documented among plants that are used in traditional medical systems. Researchers at Lucknow, India, noticed that seedlings of plants used for a variety of infectious diseases predominate on fresh or decomposing cattle dung. Plants don't normally grow on cattle dung as it contains a lot of bacteria, among other things. The researchers reckoned that plant which grow on cattle dung may well have anti-microbial properties protecting them from microbial attack. This was confirmed when the seeds were directly tested against eight bacterial and three fungal strains. The dung seeds turn out to have high levels of anti-microbial activity [13].

In another investigation, 82 traditionally used Indian plants were screened for antibacterial activity. As many as 56 of the plants exhibited antibacterial activity against one or more test pathogens. Five showed strong, broad-spectrum activity against test bacteria. The five alcohol-soaked extracts with the highest anti-microbial activities were then tested for toxicity in red blood cells of sheep, and found to have none [14].

In a study on the tribal use of twenty-seven important Indian medicinal plants in the Bastar district of Madhya Pradesh, people were observed using plants to treat illnesses such as diabetes, debility, migraine and skin infections [15].

So-called complementary or alternative medicines (CAM) in the west are derived from traditional health practices of many cultures. In the United States, around 42% of the population now use CAM. In recognition of the important role played by CAM in healthcare, the US Congress established the National Centre for Complementary and Alternative Medicines (NCCAM) within the National Institutes of Health (NIH) in 1999, with a budget of nearly \$20 million. (Its current budget has increased to \$68 million.) NCCAM's purpose is to conduct and support basic and applied research and research training, and to disseminate health information. Other programs have been set up to identify, investigate and validate CAM, the diagnostic and prevention modalities, disciplines and systems over the next five years. In 1999, the University of Pittsburgh School of Medicine was awarded \$15million to co-ordinate a six-year study on the efficacy of *Gingko biloba* in preventing senile dementia. The study involves a group of 3 000 compared with a control group taking placebos [16].

Following the UK House of Lords report on antibiotic resistance, Lord Walton, chairman for the foundation for integrated medicine said there was "a good case to suggest that the NHS should play a very strong role in developing integrated medicine". Many now believe using more complementary medicine in the National Health Service could lead to lower costs, as well as encouraging more patient-centred approaches [17]. It could also result in more effective and safer treatments. Iatrogenic illnesses associated with conventional medicine [18] are the third leading cause of death in the United States and other industrialized countries sharing the same reductionist model of disease.

We need a comprehensive paradigm change, not just in addressing antibiotic resistant infectious diseases, but in delivering basic healthcare [19].

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