



## COMMENTARY ARTICLE

## Delaying Antibiotics: A Cause for the Rise in Morbidity and Mortality from Sepsis?

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### Abstract

A recent report analyzing the global burden of disease shows that the incidence and mortality from severe sepsis has continued to rise across the period 1990-2017. Although the burden is highest among low-income countries, there are more than 5 million deaths recorded annually in high-income countries and this burden is disproportionately high among young persons, being mostly from communicable infections. Despite residing in one of those high-income countries, I have witnessed severe morbidities such as amputations as well as unexpected mortalities among acquaintances and their relatives, along with rather frequent newspaper reports of such events occurring in young people within my community. These cases are invariably due to infections with Group A Streptococcus (*Strep Pyogenes*), Meningococcus or Pneumococcus, all organisms sensitive to penicillin and its derivatives to this day. However, it appears that in each case the appropriate antibiotic is not administered, or there is an inordinate delay in administration, due to a rigid anti-microbial stewardship (AMS) policy resulting from the unwarranted and generalized fear of anti-microbial resistance (AMR). In Australia, there has been an editorial drive from the leading medical journal to constrain general practitioners from prescribing antibiotics until proof of bacterial infection is demonstrated from swabs or blood cultures. Having personally witnessed post-partum deaths of women within 24-hours of delivery from *Strep. Pyogenes* when antibiotics were not given, I encourage that representative medical associations within high-income countries should review and explain what appears to be a lop-sided AMS policy. It appears that the idea of constraining antibiotic use was directed to protect a debilitated segment of the unwell population but the side effect is unnecessary mortality and morbidity among the young and normally healthy segment.

### Keywords

Antibiotics, Severe sepsis, Anti-microbial stewardship AMS, Anti-microbial resistance AMR, Sepsis mortality

### Introduction

I am highly impressed with the recent Lancet article detailing incidence and mortality from sepsis 1990-2017 in an analysis for the global burden of this disease [1]. In particular I noted in Figure 5 from the article that the highest mortality rates among the almost 50 million cases of sepsis recorded annually occur from communicable infections (rather than from injuries or from non-communicable diseases). Furthermore, the burden of deaths from communicable infections is disproportionately high in the very young (< 10 years), followed by the young (10-30 years), thereafter the aged (70-90 years). Although the highest burden occurred in low income countries such as sub-Saharan Africa, Oceania and across all Asian countries, the problem is universal and even seven high-income countries reported almost 20 million cases of severe sepsis with 5.3 million deaths annually.

### Antimicrobial Resistance is not a Universal Problem

Although living in a high socio-economic region of the world, I have been distressed in recent years witnessing mortality and terrible morbidity (meaning limb amputations) among acquaintances and their families, mostly affecting previously healthy children, adolescents and young adults. In most of these cases it appears that the administration of antibiotics was avoided or delayed as a consequence of strong attitudes such as those expressed in recent Perspec-

tives [2] and Editorials [3] in the Medical Journal of Australia concerning antimicrobial resistance (AMR) and its lop-sided viewpoint. In particular it implies that controlling AMR in Australia requires, amongst other strategies, addressing the “unrestrained use of antibiotics”. This includes a demand that general practitioners should avoid prescribing antibiotics until a swab or blood culture reports a specific bacterial infection.

As a practising gynaecologist aged 75-years, enjoying good health and planning to continue in specialist medical practice for at least 5 more years, I thank 3 antibiotic-related aspects to my blessed life; namely

1. As a child of the 1940's and 50's, whenever I was too unwell to attend school, my mother took me to one of our local general practitioners (GP's) in Midland Junction (now Midland) who, upon seeing my red throat and noting tender neck glands, gave me a Penicillin needle “in the bum” and prescribed some oral penicillin mixture. The GP advised my mother to bring me back in 3-days if still “unable” to attend school; an event which was never necessary.
2. As a resident medical officer (RMO) of the early 1970's, I was exposed to 25% pelvic infection rates post-hysterectomy; particularly vaginal hysterectomy hence I eagerly embraced the new concept of prophylactic antibiotics, providing for myself a more relaxed medical career than that experienced by my mentors (and totally avoiding the mortalities as well as major morbidities to which they were accustomed).
3. To this day I cover every gynaecological and fertility-related invasive operation (including male andrological surgeries) with prophylactic antibiotics; using penicillin or the related  $\beta$ -lactam cephalosporins.

### Antimicrobial Stewardship Requires an Adaptive Approach

However, I am concerned by the “lop-sided teaching” now dished out to medical students and vulnerable young medical practitioners who accept the modern mantra indicating they only prescribe antibiotics when there is proven microbial infection, unresponsive to an observational period. It is some years that I faced the oral exam room conditions but, as Medical Director [4], I do face numerous accreditation processes in two Australian states each year (covering laboratory, day-hospital and clinical ART; assisted reproductive technology services) and have to justify my use of antibiotics in a process known as AMS - antibiotic microbial stewardship. So far, I have been allowed to continue this practice as I have been able to present personal horror-story documentation from the 1970's and 80's explaining my pro-antibiot-

ic bias. I certainly do not support the low-value intervention policy [2] promoted in a recent edition of MJA, particularly when it relates to young people and pregnant women.

But younger medical graduates have been “born into” a blissful period of reduced rates of septicaemia hence they are not being stimulated to develop my depth of passion in defence of a pro-antibiotic approach. Is this why I face morning newspaper stories of young people losing limbs or dying from those dreadful scourges Group A streptococcus (*Strep pyogenes*), Pneumococcus pneumonia and Meningococcus (*Neisseria meningitides*)? As I understand it these organisms have almost invariably remained quite sensitive to penicillin or the related cephalosporins and the real problem of antibiotic resistance is more associated with chronic infections, aged care, prolonged hospitalization and debilitation. The current young doctors may have been oversold the idea that they should withhold antibiotics until there is a proven need. Previously healthy young people will continue to lose limbs and even die from this widely promoted policy of delay.

### Delaying Antibiotics in Young Healthy Individuals can be Catastrophic

From my earlier medical life as a busy obstetrician, knowing about the condition of puerperal sepsis and the overwhelming way it could terminate the life of a young, previously healthy young woman; sometimes within 24 hours, affirmed my view that Penicillin or its derivatives was and remains, our best asset in Medicine and works best given prophylactically or in the very earliest stage of a suspected infection (i.e. pyrexia; rather than awaiting an observation period followed by the laboratory reports of swabs or blood cultures). On one occasion where I provided an expert witness opinion, I found myself in major conflict with another expert witness who defended the resident medical staff at a metropolitan obstetric facility who had failed to provide antibiotics to a 38-year-old mother in the immediate postpartum period after the normal delivery of her 4<sup>th</sup> child. She died from Group A streptococcal infection with septicaemia and necrotizing pelvic fasciitis 24 hours post-delivery without a single administration of any antibiotic. I expressed my opinion to the coroner that she would be well today if administered penicillin into her existing IV line soon after her pyrexia of 38 °C was recorded 4-hours post-partum. Unfortunately, the hospital protocols dictated that two separate recordings of 38 °C was required to justify antibiotics; but this woman's temperature continued to slide to 35 °C as her septicaemia raged and renal failure ensued.

### Conclusion

I have spread my pro-antibiotic views to all of the sub-specialist gynecologists and infertility clinicians

who have come under my wing and wonder if the AMR debate is lop-sided. An attempt to publish these views in the leading medical journals of Australia and the United Kingdom was met with “rejected” as being discordant with current views of specialist and academic microbiologists. As a well-published academic, I would request that the subject of AMS be re-visited to explain why medical practitioners should be asked to with-hold their best weapon in reducing deaths from sepsis, namely the rapid administration of antibiotics whenever bacterial infection appears likely or threatening.

### Acknowledgements

As Medical Director of accredited facilities in assisted reproduction in Australia I have the assistance and support of associated consultant colleagues who abide by the protocols which have been established for the respective facilities. These include a pro-antibiotic stance in the AMS which translates to prophylactic antibiotics for all invasive operative procedures, and early introduction of antibiotics for any unwell patient, especially those admitted to hospital.

### Conflicts of Interest

This article is a personal opinion shaped from clinical experiences over a working lifetime from 1970 (MD graduate) and a learning process derived from descriptive articles of historic mentors, particularly those dealing with obstetrics and gynaecology. There was no external funding involved, nor any conflicts of interest to report.

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