

## **Antimicrobial Drugs and Bacterial Amyloid Peptide Induce Toxic Manifestations in Chronic Diseases**

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**Received:** November 28, 2017; **Published:** January 04, 2018

**Keywords:** *Antimicrobial; Drugs; Bacterial; Lipopolysaccharides; Amyloid Peptide; Diet; Amyloid Beta; Oligomer; Cholesterol; Antimicrobial Peptides; Antibiotic Resistance*

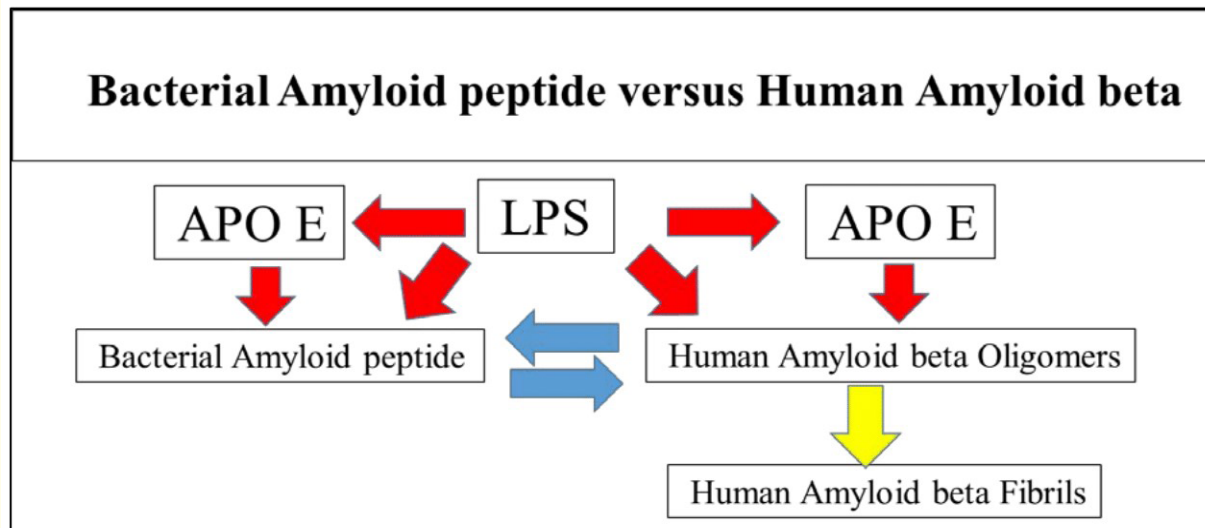
### **Abbreviations**

LPS: Lipopolysaccharides; Sirt 1: Sirtuin 1; apo E: Apolipoprotein E

The global problem of antimicrobial resistance is particularly relevant to the developing countries where the infectious disease and costs have accelerated with infectious disease regarded as a major problem in the world [1,2]. Management of infectious disease has been critically compromised by the appearance and rapid spread of antibiotic resistance [3]. Antimicrobial is an agent that kills microorganisms or inhibits their growth. Antibiotics are used either against bacteria or antifungals against fungi with the global antibacterial market to cost the global community 36 billion dollars. Antimicrobial agents such as antibiotics (Beta Lactam Derivatives, Penicillins, Cephalosporins, Macrolides, Tetracyclines, Metronidazole, Clindamycin, Antifungal Agents, Aminoglycosides, Vancomycin, fluoroquinolones) destroy microorganisms in the body by targeting bacterial cytoplasmic membranes but the debris from the bacteria such as gram negative organisms may release lipopolysaccharides (LPS) and amyloid peptide into the blood plasma.

In previous experiments by various laboratories [4] novel information has been provided that indicates the brain and liver human amyloid beta metabolism is integrated and interference with the amyloid peripheral sink clearance leads pathway leads to cellular senescence and neurodegeneration. Diet and drug therapy is essential to prevent defective hepatic human amyloid beta metabolism [5]. In the developing world the release of bacterial amyloid peptide from microorganisms [6-9] need to be carefully considered with relevance to corruption of the amyloid peripheral sink clearance pathway in man [4]. Bacterial LPS mediate the peripheral clearance of human amyloid beta [10] with its neutralization of human apolipoprotein (apo E) [11] and albumin that promote human amyloid beta association interactions. LPS represses the nuclear receptor Sirtuin 1 (Sirt 1) with critical effects on membrane cholesterol efflux and amyloid beta aggregation [10-12].

The effects of antibiotic resistance in the developing world is associated with elevated plasma LPS levels [12] but the increased bacterial amyloid peptide in human plasma needs to be interpreted with relevance to diet and pharmaceutical microbiology [13]. Bacteria and amyloid peptide have become of interest to chronic diseases in man with relevance to bacterial control of membrane amyloid beta proteins [6,8]. In man the brain has been shown to contain bacterial amyloid beta structures and shown to co-exist with human amyloid plaque [6,8]. In figure 1, LPS and bacterial amyloid peptide may interfere with peripheral human amyloid beta metabolism with relevance to regulation of human oligomer and amyloid beta fibril formation.



**Figure 1:** Bacterial LPS and amyloid peptide induce toxic manifestations by neutralization of apo E (cholesterol homeostasis) with generation of toxic amyloid beta oligomers that supersede antimicrobial drug therapy.

Cholesterol in lipid rafts is a critical component required by microorganisms to enter or exit the cell interior [13,14]. Bacterial products such as LPS and amyloid peptide target membrane microdomains of eukaryotic cells that contain cholesterol, sphingolipids, and certain proteins. Cholesterol is the major regulator of amyloid beta production in cells from amyloid precursor protein [10] with microorganisms such as gram negative bacteria (LPS) a critical regulator of eukaryotic cells cholesterol and amyloid beta aggregation (Figure 1). In the current global antibiotic resistance epidemic the promise of new antimicrobial drugs now include antimicrobial peptides (amphipathic structures) with cholesterol specifically involved in bacterial and antimicrobial peptide interactions [15-18]. These antimicrobial drugs may regulate the brain to liver human amyloid beta transport with relevance to brain cholesterol/drug metabolism [15] with induction of Type 3 diabetes [5].

The management of infectious disease by antimicrobial agents has become of major concern with the billion dollar cost to the global community. Hepatic drug metabolism needs to be assessed with relevance to the global non-alcoholic fatty liver disease epidemic that is associated with complete inactivation of drug metabolism and antibiotic resistance. Diets that are low calorie and contain Sirt 1 activators [19] are essential to activate the nuclear receptor Sirt 1 essential for cholesterol efflux, bacterial amyloid peptide and human amyloid beta metabolism. The novel antimicrobial agents that inhibit microorganism growth needs to be carefully consumed early in infections to prevent excessive LPS and bacterial peptide release associated with amyloid beta oligomer formation and cell apoptosis. The major concern with relevance to antibiotic resistance is related in the global chronic disease epidemic and its relevance to the use of antiepileptic drugs that need to be carefully controlled to prevent of epilepsy associated stroke associated with various neurological infectious disorders [19].

**Conclusion**

Novel information indicates the corruption by bacterial amyloid peptide of the amyloid peripheral sink hypothesis in man. A healthy diet and early antimicrobial drug/peptide therapy is essential to prevent toxic manifestations with relevance to bacterial amyloid peptide induced oligomeric amyloid beta toxicity to peripheral and brain cells. In the developing world the increase in plasma LPS and bacterial amyloid peptide needs to be carefully considered to prevent interference with cholesterol specifically involved with antimicrobial peptide therapy. Antibiotics/antimicrobial therapy used either against bacteria or against fungus now are of concern with antibiotic resistance expected to cost the global antibacterial market approximately 36 billion dollars by the year 2022.

### Acknowledgements

This work was supported by grants from Edith Cowan University, the McCusker Alzheimer's Research Foundation and the National Health and Medical Research Council.

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**Volume 6 Issue 1 January 2018**

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