The ingenious ways in which microorganisms "learn" to evade our antimicrobial pharmacopeia will no doubt continue to astound, at times confound, and perplex us. With patients being subjected to more invasive procedures and immunosuppressive regimes, greater resistance and increase in opportunistic bacteria will be widely seen. We can control this growing menace by encouraging and motivating concerned personnel to follow basic concepts in asepsis and practice of controlling infection. Rapid detection of antibiotic susceptibility pattern that is by applying quick, specific, sensitive and easily reproducible methods will prevent overuse and misuse of broad-spectrum drugs. Detection of such antibiotic resistance pattern could be a valuable epidemiological tool and can be used for guiding therapeutic choices. Restriction of hospital formularies and antibiotic stewardship will control the human, animal and environment reservoirs of resistant strains from developing. Use and development of new antimicrobials, vaccines and probiotics can control the present and future therapeutic nightmare.