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Geographical Incidence of Antimicrobial Resistant Gonorrhea

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Abstract

Evolving throughout the last century, Gonorrhea has become a superbug, becoming difficult to treat. As the second most commonly reported notifiable disease, gonorrhea rates have been increasing, despite efforts in prevention and treatment. Populations at risk are mainly MSM and FSW. In 2015, men's gonorrhea rates in the United States were higher compared to women, at 140.9 and 107.2 per 100,000 population, respectively. Illinois has consecutively had higher rates of infection compared to the US, at 133.5 per 100,000 population compared to the US rate of 123.9 per 100,000 population. The surveillance of gonococcal isolate resistance to current antimicrobials began in the 80's and has continued since, collecting isolates from 25 sites nationwide. These isolates assist researchers in finding susceptibility levels and resistance rates as they emerge. Over time, however, resistance began emerging with every treatment recommended, and gonorrhea is now resistant to most, if not all previous treatments utilized. Through each classification of treatment; sulfonamides, penicillin's, spectinomycin, tetracycline, quinolones, and other macrolides, have once succeeded at curing gonorrhea. However, once resistance is built, gonorrhea then becomes untreatable. Currently, there are only two medications recommended in the treatment of gonococcal infections: Ceftriaxone injection and oral Azithromycin. These two medications are the last of many that show efficacy in treating gonorrhea, despite increasing resistance. Continued work researching geographic incidence similarities and correlations between geographical location, population demographics, and spread of resistance over time, may allow further insight into more evasive ways to manage prevention efforts against resistance.

Keywords: Antimicrobial Resistance, Gonorrhea, Geographical Incidence

Geographical Incidence of Antimicrobial Resistant Gonorrhea

Gonorrhea is a sexually transmitted infection, caused by the bacterium Neisseria Gonorrhoeae, with the capacity to develop resistance to previous and current antimicrobials used to treat the infection (Unemo & Shafer, 2011, 2014). Due to this bacterium's ability to evolve, Gonorrhea has become increasingly difficult to cure in the most at-risk populations, especially among re-infection (Unemo & Shafer, 2011, 2014). If untreated, Gonorrhea can develop into serious conditions, such as pelvic inflammatory disease (PID) in women, and epididymitis in men. Moreover, Gonorrhea has also been associated with facilitating the acquisition of Human Immunodeficiency Virus (HIV) (Centers for Disease Control and Prevention [CDC], 2011; Unemo & Shafer, 2011, 2014; World Health Organization [WHO], 2016). More serious risks can lead to infertility, as well as the potentially life-threatening risk of disseminated-gonococcal infection (DGI) (CDC, n.d.).

The prevalence of Gonorrhea infection in at-risk populations has become a global burden and the focus of public health concern (Unemo & Shafer, 2011, 2014). Treatment of Gonorrhea is the responsibility of each nation, as antimicrobial resistant (AMR) Gonorrhea has been internationally reported (WHO, 2016). The World Health Organization (WHO) determined in 2008 that Gonorrhea AMR is no longer a future concept, however, occurring in the present, threatening the health of people around the globe (WHO, 2016). Additionally, WHO has determined that without an appropriate action plan to combat the prevalence and incidence of antimicrobial resistance, gonorrhea will become untreatable (WHO, 2016). Knowing this, WHO has developed a draft global action plan to guide countries in the fight against AMR Gonorrhea (WHO, 2016).

Epidemiology, Testing for Gonorrhea, and Treating Gonorrhea.

Epidemiology

On a global scale, there were over 106.1 million cases of Gonorrhea reported in 2008, according to the World Health Organization (WHO, 2016). The WHO Western Pacific Region had just under 40% of those cases, with a total of 42 million cases reported in 2008 (WHO, 2016). In the US, Gonorrhea is the second most commonly reported notifiable disease (CDC, n.d.). In 2015, the rate of infection for Neisseria Gonorrhoeae was 123.9 per 100,000 population, with 395,216 total reported cases nationwide. This was an increase of 12.8% from 2014, with the highest reported cases from the South (CDC, n.d.).

Men are disproportionately at higher risk, especially among the men who have sex with men (MSM) population (CDC, n.d.). Additionally, female sex workers (FSW) are also considered to be a high-risk population (CDC, n.d.). In 2015, the rate of infection for men in the United States was estimated to be 140.9 per 100,000 population, compared to women at 107.2 per 100,000 population (CDC, n.d.). The burden falls mostly on the age groups of 15-19, 20-24, and 25-29, with rates for men at 252.7, 438.7, and 262.9, respectively, while rates for women in the same age groups are 567.7, 596.6, and 236.0, respectively (CDC, n.d.).

Gonorrhea in Illinois

Illinois has consecutively reported higher rates of Gonorrhea infection, from 2001 to 2015 (Illinois Department of Public Health [IDPH], 2016). In 2001, the rate of gonorrhea per 100,000 population was 193.4, (IDPH, 2016). In 2016, the reported number of gonorrhea cases in Illinois was 17,130, with a rate of 133.5 per 100,000 population (IDPH, 2016). The city of Chicago makes up more than half of the reported cases, with a total of 8,786 cases (IDPH, 2016). Cook County (including City of Chicago) was 11,082 cases (IDPH, 2016).

Testing for Gonorrhea

There are multiple ways to test for a gonococcal infection, however, only two tests are considered appropriate, and are recommended by the Centers for Disease Control and Prevention (CDC). The first test, Nucleic Acid Amplification Test (NAAT), is performed by testing either a first catch urine sample or culture sample from the anatomic infection site or both (CDC, n.d.). The second testing type is Isolation and Identification (also known as Gram Stain) which is typically recommended when the anatomical site of specimen collection is urethral for men or vaginal for women (CDC, n.d.). NAAT is considered to be the most effective diagnostic test available, however, gram stain is recommended in settings where optimal testing is not available (CDC, n.d.).

There is also a third test, which is less of a feasible option. This method is not testing a sample for a diagnosis of gonorrhea, however, is used for antibiotic susceptibility testing. This test is performed to determine the efficacy of a specific treatment of Gonorrhea. These tests are typically performed when there is a known treatment failure (CDC, n.d.). The test involves assessing the gonococcal isolates for antibiotic susceptibility to multiple available treatments. When the sample is considered susceptible, the antibiotic can be used in treating the infection. If susceptibility diminishes, then the treatment is less effective, or not effective, after a level of susceptibility has been diminished (CDC, n.d.).

Treating Gonorrhea

Current CDC treatment recommendations of uncomplicated gonococcal infections consist of a combination of a single injectable dose of Ceftriaxone 250mg intramuscularly and a single oral dose of Azithromycin 1gm (CDC, n.d.; Unemo, del Rio, & Shafer, 2016; Workowski & Bolan, 2015). Alternative therapies exist, such as Gentamicin or Gemifloxacin in lieu of

Ceftriaxone, when allergies to Cephalosporin's are present (CDC, n.d.; Workowski & Bolan, 2015). This therapy has been used for the treatment of Gonorrhea as well as concomitant Chlamydia infections for the last few decades. However, decreasing susceptibility and rising resistance to the ESC's have increased the minimum inhibitory concentrations (MICs) required to treat Gonorrhea to increase (Unemo et al., 2016; Unemo & Nicholas, 2012; Unemo & Shafer, 2011, 2014; Workowski & Bolan, 2015).

Antimicrobial therapy for Gonorrhea treatment is typically given empirically during the first visit, requiring the physician to prescribe treatment based on physical examination, and reviewing symptoms (Unemo et al., 2016; Workowski & Bolan, 2015). This process follows the guidelines for treating Gonorrhea, however, may also be contributing to the rise in AMR Gonorrhea (Bala & Sood, 2010; CDC, 2011; Contie, Defibaugh, Steinberg, & Wein, 2014; Katz et al., 2012; Kidd et al., 2015; Kirkcaldy et al., 2013; Unemo & Shafer, 2011, 2014; Walsh, 2000; WHO, 2016; Workowski & Bolan, 2015).

The problems that exist are the current testing procedures required to measure susceptibility and resistance to gram-negative cultures obtained require certified laboratories and usually take weeks. Culture staining of samples obtained from the patient can be done in a clinic, however, are only available a day following the visit (Unemo et al., 2016; Workowski & Bolan, 2015).

Timeline of Resistance, Decreased Susceptibility, and Surveillance

Timeline of Antimicrobial Resistance

Antimicrobial resistance was observed in the late 1940's when greater than 90% of gonococcal isolates showed signs of resistance to Sulfonamides (Unemo & Shafer, 2011, 2014). Although Penicillin and Sulfonamides were discovered in 1928 and 1935, respectively,

Sulfonamides became the first antimicrobials used in the treatment of gonorrhea (Unemo & Shafer, 2011, 2014). It was not until 1943 when Penicillin was appropriately documented as appropriate treatment of gonorrhea. With a higher cure rate (95% of cases with Penicillin treatment, versus 80% to 90% with Sulfonamide treatment) and rising resistance to Sulfonamides, Penicillin became the new recommended treatment of gonorrhea (Unemo & Shafer, 2011, 2014).

Within 2 years of introduction, Penicillin began showing signs of decreased susceptibility (Unemo & Shafer, 2011, 2014; Walsh, 2000). Accumulation of chromosomal resistant detriments caused the Minimum Inhibitory Concentrations (MIC) of Penicillin against gonorrhea to rise, causing a decrease in susceptibility to Penicillin treatment (Unemo & Shafer, 2011, 2014). Although MIC's were on the rise, and resistance started emerging, Penicillin was still widely recommended as the treatment for Gonorrhea, until 1987, mostly due to high-level resistance caused by the emergence of β-lactamase-encoding plasmids (CDC, n.d.; Unemo & Shafer, 2011, 2014). As time progresses, and newer antibiotics are introduced, decreased susceptibility and resistance occurs, creating the need for newer antibiotics, and the inability to treat bacterium that develops resistance to current therapies, including Gonorrhea (Bala & Sood, 2010; CDC, 2011; Contie et al., 2014; Katz et al., 2012; Kidd et al., 2015; Kirkcaldy et al., 2013; Unemo & Shafer, 2011, 2014; Walsh, 2000; WHO, 2016).

Plasmid- and/or chromosomally-mediated resistance to Penicillin is the main contributor to Penicillin resistance, and over the last 70-80 years, antimicrobial agents, such as Tetracyclines, Fluoroquinolones, Macrolides, and early-generation Cephalosporin's, have become less effective in treating Gonorrhea (Bala & Sood, 2010; CDC, 2011; Contie et al., 2014; Katz et al., 2012; Kidd et al., 2015; Kirkcaldy et al., 2013; Unemo & Shafer, 2011, 2014; Walsh, 2000; WHO,

2016). Through research, locating how and where these chromosome mediations occur has been noted, however, new mutations are often occurring, making it difficult to develop equipment to specifically target known mutation sites (Bala & Sood, 2010; CDC, 2011; Contie et al., 2014; Katz et al., 2012; Kidd et al., 2015; Kirkcaldy et al., 2013; Unemo & Shafer, 2011, 2014; Walsh, 2000; WHO, 2016).

Surveillance

In 1986, the Gonococcal Isolate Surveillance Program (GISP) was formed to establish the selection of therapies based on a rational basis, by monitoring antimicrobial susceptibility trends in N.G. strains in the US (CDC, 2016; Kirkcaldy et al., 2013). GISP collaborates with the CDC Division of STD Prevention (DSTDP), the Surveillance and Data Management Branch (SDMB), the Laboratory Reference and Research Branch (LRRB), the Program Development and Quality Improvement Branch (PDQIB), regional labs, selected public health STD programs, and associated specialty care clinics in the US (CDC, 2016; Kirkcaldy et al., 2013). GISP analyzes demographic and clinical data from positive urethral cultures from the first 25 male patients presenting to the sentinel reporting sites, and data for antimicrobial susceptibility (CDC, 2016; Kirkcaldy et al., 2013).

Currently, there are approximately 25-30 sentinel sites located throughout the US, that collect urethral isolates obtained from men, to test for antimicrobial susceptibility, and resistance. (CDC, 2016; Kidd et al., 2015; Kirkcaldy et al., 2013). Sentinel sites are required to collect urethral cultures from the first 25 male patients to be sent to the GISP Laboratories for testing (CDC, 2016; Kidd et al., 2015; Kirkcaldy et al., 2013). In addition to GISP, the Gonococcal Antimicrobial Surveillance Programme (GASP) was established by WHO to coordinate gonococcal antimicrobial resistance surveillance, monitor longitudinal trends in antimicrobial

resistance and provide data to inform treatment guidelines (WHO, 2016). This program has been implemented globally and works with GISP and local and national departments in the surveillance of emerging resistant infections.

Decreased Susceptibility and Antimicrobial Resistance

Gonorrhea is currently becoming untreatable due to decreased susceptibility and resistance to first-line antimicrobial therapy (Bala & Sood, 2010; CDC, 2011; Contie et al., 2014; Katz et al., 2012; Kidd et al., 2015; Kirkcaldy et al., 2013; Unemo & Shafer, 2014; Walsh, 2000; WHO, 2016). There has been isolates collected in the recent years that are showing decreased susceptibility and resistance to the current treatment regimen (Bala & Sood, 2010; Camara et al., 2012; Contie et al., 2014; Katz et al., 2012; Kidd et al., 2015; Kirkcaldy et al., 2013; Ohnishi et al., 2011; Starnino et al., 2012; Tanaka et al., 2002; Tanaka, Furuya, Irie, Kanayama, & Kobayashi, 2015; Unemo et al., 2012; Unemo & Shafer, 2011, 2014; Walsh, 2000; WHO, 2016; Workowski & Bolan, 2015). The first cephalosporin-resistant strain of Gonorrhea was reported in Japan, then spread internationally (Bala & Sood, 2010; Camara et al., 2012; Ohnishi et al., 2011; Starnino et al., 2012; Tankaka et al., 2002; Tanaka et al., 2015; Unemo et al., 2016; Unemo et al., 2012; Unemo & Shafer, 2011). This resistant strain caused Japan to discontinue the use of Cefixime, and replace it with treatment with Ceftriaxone and Spectinomycin, which are both injectables (Bala & Sood, 2010).

Currently, there is an emerging endemic of decreased susceptibility and resistance to current extended-spectrum cephalosporin's, as well as Azithromycin, in the treatment of gonococcal infections (CDC, n.d.; Kidd et al., 2015; Kirkcaldy et al., 2013; Starnino et al., 2012; Tanaka et al., 2015; Unemo et al., 2012; Unemo & Shafer, 2014). The MSM population have been frequently found to have strains of gonococcal infections associated with an elevated MIC

level, resulting in decreased susceptibility, and resistance to current antimicrobial therapies (CDC, n.d.; Kidd et al., 2015; Kirkcaldy et al., 2013; Starnino et al., 2012; Tanaka et al., 2015; Unemo et al., 2012; Unemo & Shafer, 2014).

Scope of Project

GISP Collaboration Project

The GISP project began as a partnership between the University of Illinois, Urbana-Champaign (UIUC) and Southern Illinois University School of Medicine (SIU) to determine if specific mutation profiles matched a specific resistant microbial. In order to study this, UIUC received 130 isolates from the Illinois Department of Public Health, which were collected by the Chicago Department of Public Health. The PenA gene would then be sequenced for mutations, and matched with a known resistance, to determine if a match could be made.

The GISP collaboration project then stalled, due to a few factors. The first major factor was the lack of funding for the project. Since the project was mostly probative, the work being performed was not being funded. The second was due to the priority and importance of additional funded projects. Although work has temporarily stopped, the idea and prep work is not lost.

Research Questions

The next direction for the GISP project was to look into the geographical incidence of antimicrobial resistance, as well as the direction in which AMR spread. Recently, antimicrobial resistant strains have first been discovered in the Western Pacific or Asian areas, before spreading eastward towards Hawaii, Western United States, and the Eastern United States. Additionally, what types of populations are being identified in the first AMR strains, and are there any similarities among these populations with each incidence of resistance? With this in

mind, the following research questions were identified: 1) Where is the geographical location of the first reported case of resistance to each line of treatment, and, 2) What are the demographics of the population involved in the first reported resistance?

The first research question requires further research into the timeline of antimicrobial resistance, to discover the first reported case of resistance, and follow the timeline for two years after, in order to establish a timeline of resistance both in time and geographical manners. This allows for a deeper understanding of when and where resistance is beginning, and whether the geographical location of infection determines the direction in which resistance is spread over time.

The second research question requires observation of the populations affected by first reported antimicrobial resistant gonorrhea, and whether there are any similarities between populations during each incidence of first reported resistance. Additionally, over time, are the same populations being infected with gonorrhea, and subsequently, the populations becoming the first with developing antimicrobial resistant gonorrhea.

Agency Overview

The agency included in the fieldwork experience was under the supervision of Wiley Jenkins, Ph.D., MPH, Office of Population Science and Policy (OPSP; formally the Population Health Science Program) at SIU, located in Springfield, IL, This office sets out to acquire and study data to identify disease risk, design and implement strategies to improve health, formulate legislative, clinical, and educational policies to provide sustainable solutions, and educate current and future health professionals in population health (SIU School of Medicine - Office of Public Affairs, 2012).

The population reach of SIU is considered to be mostly rural and urban, with a reach of about 66 out of 102 total counties in Illinois. These counties are all located within the central and southern portion of the state. Illinois has a population of over 12 million, with only about 3 million residents within this reach (United States Census Bureau, 2010).

Preliminary Findings and Significance

Findings

Reviews published by authors Unemo and Shafer (2011, 2014) that detailed the history of Gonorrhea and provided preliminary information to determine a timeline for antimicrobial resistance. The authors detailed the history of gonorrhea in a pre-antimicrobial era, as well as after microbials were introduced (Unemo & Shafer, 2011, 2014). With this information, other specifics around resistance could be used, such as the articles the two authors referenced, particularly when specifying when and where first resistance was noted.

Antimicrobials used in the treatment of Gonorrhea.

Sulfonamides and Penicillin's

Sulfonamides were introduced in the mid-1930's, and according to first reports, began producing resistance to treatment by the mid-1940's, as found in studies testing sulfonamide susceptibility (Dunlop, 1949). By the late 1940's, however, greater than ninety percent of gonococcal isolates showed resistance *in vitro* to sulfonamides (Unemo & Shafer, 2011, 2014).

Penicillin's were first introduced prior to the sulfonamide treatment era, however, were not widely used as primary treatment for gonococcal infections until 1943, in time for the sulfonamides to soon be phased out as primary treatment (Unemo & Shafer, 2011, 2014). Over time, penicillin had a success rate of more than ninety-five percent, which was more than the ninety percent once found with sulfonamides, however, over time gonococcal isolates began

developing resistance to lower doses of penicillin, thus requiring higher doses to achieve cure rates (Amies, 1967; Unemo & Shafer, 2011, 2014).

Over time, penicillin's continued to be utilized as the first line therapy for treating gonococcal infections. Due to increased numbers of isolates showing signs of decreased susceptibility, and later, resistance to penicillin's, the United States experienced increasing numbers of chromosomally mediated penicillin-resistant gonorrhea. This increase was first seen sometime in the mid-1970's, causing the US, and many other countries, to change the recommended treatment for gonococcal infections by the mid-1980's (Unemo & Shafer, 2011, 2014).

Tetracycline and Spectinomycin

Tetracycline was used for the treatment of gonorrhea that showed resistance to penicillin and was used beginning in the mid-to-late 1940's. After some time, however, gonococcal isolates began showing resistance to tetracycline, and by the mid-1980's, tetracyclines became excluded from all treatment guidelines (Unemo & Shafer, 2011, 2014). First reported in the United States and the Netherlands in 1986, tetracycline resistant gonorrhea became widespread internationally (Roberts, Wagenvoort, van Klingreren, & Knapp, 1988; Unemo & Shafer, 2011, 2014).

Spectinomycin, synthesized in the 1960’s, was used as gonorrhea treatment in isolates that showed resistance to penicillin and tetracycline. By 1967, however, gonorrhea isolates began showing decreased susceptibility, and eventually resistance, were reported in the Netherlands and then in the Philippines by 1981, and in London thereafter (Ison, Littleton, Shannon, Easmon, & Phillips, 1983; Stolz, Zwart, & Michel, 1975; Unemo & Shafer, 2011, 2014). Due to increasing reports of spectinomycin throughout the 1980’s, this therapy was abandoned internationally, even though high-level resistance was exceedingly rare (Unemo & Shafer, 2011, 2014).

Quinolones and Macrolides

Also in the 1960's, Quinolones were introduced as a treatment for gonorrhea (Unemo & Shafer, 2011, 2014). Decreased susceptibility developed to original dosing of ciprofloxacin by 1990, and resistance developed and spread quickly after the doses for ciprofloxacin were raised (Tanaka, Kumazawa, Matsumoto, & Kobayashi, 1994; Tanaka et al., 2000; Unemo & Shafer, 2011, 2014).

Resistance to quinolone therapy was first reported in the Asian-Western Pacific Region in the mid-to-late 1990's, and by 2000, spread to Hawaii, then further through the west and east coast of the United States (Iverson et al., 2004; Tanaka et al., 1994; Tanaka et al., 2000; Unemo & Shafer, 2011, 2014). This spread of resistance caused the CDC to abandon quinolone therapy as recommended treatment for gonorrhea in 2007 (CDC, n.d.; Unemo & Shafer, 2011, 2014).

Macrolides were introduced in 1952 with the medication Erythromycin, and in 1980, Azithromycin, a synthetic derivative of Erythromycin, was introduced (Unemo & Shafer, 2011, 2014). Early on, erythromycin was found to not be effective in treating gonococcal infections, however, azithromycin had a substantially higher activity in treating gonorrhea (Lewis, 2010; Unemo & Shafer, 2011, 2014).

Resistance to Azithromycin was first reported from 1995-2000 in Latin America and has been seen internationally despite treatment recommendations or prevention efforts (Lewis, 2010; Unemo & Shafer, 2011, 2014). Currently, azithromycin is still used in treating gonococcal infections, however as part of a dual therapy regimen (CDC, 2016; Lewis, 2010; Unemo & Shafer, 2011, 2014).

Expanded-Spectrum Cephalosporin's

Cephalosporin's were discovered early on, during the Sulfonamide era, in 1948, and the first useful antibiotic was launched in 1964, Cefalotin (Unemo & Shafer, 2011, 2014). Quinolones were no longer recommended for gonococcal treatment, third generation expanded-spectrum cephalosporin's (ESCs) took their place (Lewis, 2010; Unemo & Shafer, 2011, 2014). The two most common used were injection Ceftriaxone, and oral Cefixime (Lewis, 2010; Unemo & Shafer, 2011, 2014). Due to limited availability of oral cefixime, other oral cephalosporins were used in Japan, Europe, Hong Kong, and the United States (Lewis, 2010; Unemo & Shafer, 2011, 2014).

By 1995, Japan began reporting decreased susceptibility to cephalosporin's used, and by 1999 and 2002, resistance was being reported (Akasaka et al., 2001; Ito et al., 2004; Lewis, 2010, Unemo & Shafer, 2011, 2014). Resistance to ESC's spread globally, being reported from Japan, France, Spain, eventually to United States (Akasaka et al., 2001; Camara et al., 2012; Ito et al., 2004; Lewis, 2010; Unemo & Nicholas, 2012; Unemo & Shafer, 2011, 2014). Although there has been increasing reports of resistance incidence to ESC's, the use of Ceftriaxone intramuscularly is recommended by the CDC in the dual-therapy treatment of gonorrhea, along with azithromycin orally (CDC, 2016).

Significance

The significance of all the reviews covering antimicrobial resistance over time allows for a detailed timeline of when and where resistance developed, and allows for public health officials to navigate the changing world of infection treatment. This timeline allows further research into the many variables of resistance emerging, such as geographic location, population demographics, treatment recommendations, and spread of resistance. This is important to

continue into the future, as well as take a further look into the past, in order for public health officials to continue the fight against AMR gonorrhea.

Although prevention efforts are already in place, there needs to be some consideration when placing the prevention efforts, so they are not lost among the ever-changing population. Currently, the CDC and WHO both have recommendations for preventing and treating gonococcal infections and are continuously monitoring infection rates. WHO develops plans against antimicrobial resistance, and recently published their 2015 guidelines to help fight against antimicrobial resistance (WHO, 2015).

Next Steps

The GISP collaboration project is long from complete. This review of past AMR gonorrhea has led to the future of researching AMR incidence geographically and determining the spread pattern in which resistance is spread. Additionally, the population affected when AMR is first reported for each period of resistance, as well as if there are any similarities between populations over time. The hope of this research is to pinpoint whether there is a link between infection, resistance, and spread, based on the population most infected, and whether there is a correlation to the geographical location at the time of resistance.

Continued work will require more time reviewing studies previously published, showing the incidence of AMR by geographical location, as well describe population demographics, to give us an understanding of how these similarities may or may not be present. Funding may be required, however, may not be necessary for the preliminary phases. The past and current treatment policies will be obtained, in order to evaluate best practices and make suggestions to improving prevention and treatment of gonorrhea. Additionally, once research has been conducted, a systematic review will be published, describing the results of the in-depth research.

Conclusion

As we have seen over the last century, gonorrhea has become increasingly difficult to treat, leaving the current population in danger of acquiring untreatable gonorrhea, with risks of developing other serious conditions, and HIV. Over time, resistance to previous first line therapy has increased, leaving health care practitioners scrambling to find new and improved treatments to obtain a cure. Resistance to infection causes our infection rates to increase, despite efforts to prevent gonorrhea.

Moving forward, we need to continue to improve our prevention efforts to aid in minimalizing infection rates, while also improving our treatment efforts, whether it be by changing testing policies or treatment. Currently, there are only two medications that have maintained their effectiveness over time, however, are experiencing their own decreased susceptibility rates. Ceftriaxone and Azithromycin, when used in combination, have both been capable of curing gonococcal infections.

With the future of antimicrobials looking dim, currently, with no hope for new prospects in the future, the last two remaining treatments are all that is left for treating this once easily treated bacterial infection. The looming shadow of untreatable gonorrhea is slowly showing up, and gonorrhea has now become this evolving superbug that threatens the health of every population globally.

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