Syphilis in the elderly

Kiła u pacjentów geriatrycznych

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Abstract

Introduction. Syphilis is a sexually transmitted disease (STD) and is caused by the gram-negative bacterium Treponema pallidum. There has been a significant increase in the incidence of syphilis in the elderly, despite effective treatments available. It is associated with an increased risk of severe neurological complications in this group of patients. **Purpose.** Discussion, on the basis of current data, of possible causes of the increasing incidence of syphilis in the geriatric population, diagnostic limitations, treatment methods, various symptoms and possible positive consequences of the increased awareness of the doctors making the diagnosis. **Material and Methods.** Review of scientific articles and current indications available via Google Scholar, ResearchGate and PubMed, using keywords. syphylis, STD, elderly, Treponema pellidum, neurosyphilis. **Results.** The collected data show that insufficient knowledge of seniors combined with atypical symptoms can significantly hinder diagnosis and initiation of appropriate treatment, which is associated with the occurrence of serio-us complications. **Conclusion and relevance.** Education of geriatric patients, taking preventive measures such as contraception and raising the awareness of doctors seems to be necessary to reduce the constantly growing trends in the incidence of syphilis. (Gerontol Pol 2023; 31; 3-10) doi: 10.53139/GP.20233103

Keywords: syphylis, STD, elderly, Treponema pallidum, neurosyphilis

Streszczenie

Wstęp. Kiła jest chorobą przenoszoną drogą płciową (STD) wywoływaną przez Gram-ujemną bakterię Treponema pallidum. Nastąpił znaczny wzrost zachorowań na kiłę u osób starszych, pomimo dostępnych skutecznych metod leczenia. Wiąże się to ze zwiększonym ryzykiem ciężkich powikłań neurologicznych w tej grupie chorych. Cel. Omówienie, na podstawie aktualnych danych, możliwych przyczyn wzrostu zachorowań na kiłę w populacji geriatrycznej, ograniczeń diagnostycznych, metod leczenia, różnorodnych objawów oraz możliwych pozytywnych skutków zwiększonej świadomości lekarzy stawiających diagnozę. Materiał i metody. Przegląd artykułów naukowych i aktualnych wskazań dostępnych w Google Scholar, ResearchGate i PubMed z użyciem słów kluczowych. syphylis, STD, osoby starsze, Treponema pallidum, kiła układu nerwowego. Wyniki. Zebrane dane wskazują, że niedostateczna wiedza seniorów w połączeniu z nietypowymi objawami może znacznie utrudniać rozpoznanie i rozpoczęcie odpowiedniego leczenia, co wiąże się z występowaniem poważnych powikłań. Wnioski. Edukacja pacjentów geriatrycznych, podejmowanie działań profilaktycznych, takich jak antykoncepcja oraz podnoszenie świadomości lekarzy wydaje się być niezbędne do ograniczenia stale narastających tendencji zachorowań na kiłę. (Gerontol Pol 2023; 31; 3-10) doi: 10.53139/GP.20233103

Słowa kluczowe: kiła, STD, osoby starsze, Treponema pallidum, kiła układu nerwowego

Introduction

Syphilis is a sexually transmitted disease (STD). The factor causing systemic symptoms is the gram-negati-

ve bacterium *Treponema pallidum*. The microorganism has little ability to survive outside the human body due to its high sensitivity to drying and high temperatures. It is characterized by limited metabolism and slow repro-

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duction. The infection occurs through unprotected sexual contact, during pregnancy, from mother to child, and through blood [1–4].Research suggests that the substrates necessary for bacteria to initiate infection are laminin and fibronectin [2]. After multiplication of the spirochetes at the site of penetrate, they enter other parts of the body causing systemic symptoms [2,5].

The disease usually presents with primary, secondary, latent and tertiary stages, characterized by various symptoms from the organism [2,3]. In the latent stage, despite the lack of symptoms, sick people may be a source of infection [2]. It has also been shown that the presence of *Treponema pallidum* may increase the probability of HIV infection (human immunodeficiency virus) [6]. Moreover, other sexually transmitted diseases (e.g. AIDS) may occur together with syphilis [1].

It is commonly believed that STDs affect only young people, but in the last decade the number of infected people over 50 has doubled. Diagnosis is a challenge for doctors because syphilis is not typical for the elderly and its symptoms may resemble other diseases [4]. The increased incidence of syphilis among geriatric patients may be due to the widespread availability of erectile dysfunction drugs. Increased vascular blood flow and mucosal sensitivity may additionally promote infection [4,5]. Risk factors include low awareness of seniors in the field of contraception and weakened immunity of the aging organism [4].

Epidemiology

The statistics on the incidence of syphilis are very detailed. There is an obligation to keep records of the disease in many countries around the world. [7] However, most of the statistics come from highly developed countries [8] Detailed data on new cases of primary and secondary syphilis from 2017-2018 in the United States showed an increase in the number of new cases compared to the previous year. The increase was significant because in the 45-54 age group it amounted to 7.2%, while in the 55-64 age group it amounted to 21.1%, but it was the highest in the oldest age group. In people aged 65 and over, it was 28.6%. [9] A cross-sectional study conducted in China (Guangxi) of female sex workers in 2010-2015 showed that older men were the largest group of clients suffering from syphilis. In Africa, and more precisely in South Ethiopia, the highest incidence of syphilis in HIV-infected patients were men over 50 years of age, with primary education, who had not been treated with antiretroviral therapy before but had a blood transfusion in the past. [8] In Poland according to General Statistical Office the latest data fall on a period 2009-2018, the results fall into two categories: age and gender. There are five age groups and the oldest is 45 and over. The incidence in this age group among men remains relatively constant and amounts to an average of 2.31 people per 100,000 population. However, it should be noted that the highest incidence was 3 people per 100,000 people and was in 2018. Among women in the same age group, the highest incidence rate was 0.7 per 100 thousand people, and it was in 2013. In 2018, there were only 0.4 newly registered female cases per 100,000 population [10] In European Economic Area there were available and suitable reports, on age, in 25 countries in 2018. The highest values for new cases were recorded in the 45 years and over, and in the 25-34 years old. In each age group, specific indicators were significantly higher among men than women. [11] The World Health Organization plan to reduce the incidence of syphilis by 90% worldwide.[8]

Symptoms

Clinical manifestations vary depending on the stage of syphilis (primary, secondary, latent and tertiary). Symptoms typical of one stage can be present in the following one [11,12].

The first visible response to Treponema pallidum infection is painless solitary chancre in the site of exposure developing in 10 to 90 days [2]. Chancres mostly involve anogenital region, however, between 2% to 7% can appear in other parts of the body (fingers, nipples, lips, tongue, tonsils) (2,13,14). Changes in cervix or rectum can be easily missed during examination [2]. Atypical multiple chancres in HIV co-infection or painful chancres in HSV co-infection are often [14,15]. In primary stage local lymph nodes are enlarged and painless [14].

Secondary stage is an outcome of untreated or mistreated primary syphilis. This stage develops 1 to 3 months after the infection [2]. Patients may suffer from fatigue, fever, headache, non-itching maculopapular rash, condylomata lata, mucosal lesions. Unusual manifestations are splenomegaly, hepatitis, laryngitis, gastritis, alopecia syphilitica (hair loss can be the only symptom). Affected lymph nodes are enlarged and painless due to generalized lymphadenopathy [2,12–14]. Presence of ocular, auricular, neurologic symptoms (retinitis, iritis, meningitis, cranial nerves disorders) may indicate early neurosyphilis [2,13]. Clinical presentation of secondary syphilis results from bacteriaemia [13].

Latent syphilis is an asymptomatic stage consisting of two periods: early (less than 1 year, serological tests are positive) and late (more than one year with positive serological tests). Patients in early latent stage are believed to be infectious [2,13,15].

Late neurosyphilis, the most common form of tertiary syphilis, involves: meningitis, tabes dorsalis, general paresis and mental health disorders. Strokes are consequence of the meningovascular syphilis. Other types of tertiary stage are cardiovascular syphilis and gummatous syphilis. Cardiovascular syphilis may result in thoracic aortic aneurysm and aortic valve dysfunction. Gummatous syphilis can affect different organs and tissues and damage their structure by perforations and ulcers, it commonly affects skin, mucous membranes, palate [2,14,15].

Diagnostics

The diagnosis of syphilis can be problematic because the course of the disease often has subtle or ambiguous symptoms that are easy to overlook [2]. Symptoms may indicate other infectious diseases, for example histoplasmosis [4]. Usually screening is performed in pregnant women, HIV infected, organ donors and blood donors, people with hepatitis A, B and C, patients with other STDs and sudden neurological disorders, so there is little chance of accidental detection of syphilis in an elderly person [16]. The measures taken for the diagnosis depend on the phase of the disease in which the patient is. Only in the case of early syphilis is it possible to find spirochetes in a microscopic specimen made directly from the serous fluid of the ulcer [17].

Most often, serological tests are used to confirm infection. Their disadvantage, however, is the lack of differentiation of spirochete subspecies [2,17].

Nontreponemal antigen tests detecting the reaction of antibodies with cardiolipid antigen include VDRL (Venereal Disease Research Laboratory, USR (unheated serum reagin) and RPR (rapid plasma reagin).

Treponemal reactions detect antibodies whose antigens are strains of *T. pallidum* (Nichols and Reiter strains). These immunofluorescence reactions include FTA (fluorescent treponemal antibody) and FTA-ABS (fluorescent treponemal antibody absorption) and modifications of these tests (Table I.) [17,18].

In traditional screening, the basic test is NTT (nontreponemal test). If there is no response, the patient is considered negative for syphilis. However, obtaining a positive reaction is confirmed by a TT (treponemal test), for example FTA. Only after a positive result infection can be diagnosed.

If the inverse algorithm is used and the first test is TT (eg EIA), obtaining a negative result excludes syphilis. However, in the event of a positive result, a NTT test should be performed. A positive result confirms syphilis, while a negative result obliges you to perform a different TT (eg TPPA).

A negative result is interpreted as no infection, while a positive result confirms past, early or late/ latent syphilis [18,19].

Table I. Treponemal and nontreponemal serological tests	
available in Poland. (Wojas-Pelc A., Pastuszczak M.,	
Serwin A. B., Rudnicka I., Majewski S., Czajkowski R.,	
Flisiak I., Placek W, Maj J., Maleszka R., Rudnicka L.)	

Nontreponemal tests	Treponemal tests
§ RPR	§ TPHA
§ USR	§ TPPA
§ VDRL	§ FTA-ABS
	§ FTA
	§ EIA/lgG
	§ EIA/IgM
	§ IgG and IgM immunoblot

RPR – rapid plasma reagin, USR – unheated serum reagin, VDRL – venereal disease research laboratory, , TPHA – Treponema pallidum haemagglutination, TPPA – Treponema pallidum particle agglutination, FTA--ABS – fluorescent treponemal antibody absorption, FTA – fluorescent treponemal antibody, EIA – enzyme immunoassay

Treatment

Effective treatment requires obtaining treponemicidal concentration of penicillin in serum, or in CSF in the case of neurosyphilis . Concentrations above 0.018 mg / l are considered to be treponemicidal [20].

Studies determined that *T. pallidum* doubles every 30 to 33 h in vivo. Extrapolation of these results to in vitro conditions yields generation time of 30 to 50 h. It is important to maintain the therapeutic concentration of penicillin for the time of several divisions of the *T. pallidum*. It is recommended that this period should not be less than 7-10 days [13].

Shorter treatment leads to an increased relapse rate, especially in the course of late syphilis. Probably due to the auto down-regulation of the *T. pallidum* life cycle and, consequently, its slower divisions during the long-term course of the disease.

The treatment of the first choice is BPG at a dose of 2.4 million units, which provides a treponemicidal penicillin concentration in serum for up to 21-28 days. The long duration of BPG activity allows the treatment to be effective after a single injection. Replacing portion of the solvent solution (0.5–1 cm3) with a 1% epinephrine-free lidocaine solution may reduce BPG injection discomfort [21]. This is impossible with ready-to-inject BPG preparations. After the injection, the patient should be monitored for at least 30 minutes, among others, for anaphylactic reaction, Hoigné syndrome or Jarisch-Herxheimer reaction (up to 90 minutes).

Parenteral administration is the recommended route of administration due to better treatment supervision and higher bioavailability of the antibiotic. The exception is oral amoxicillin and probenecid, it seems to be effective and achieves the therapeutic concentration in the CSF [22,23].

In the case of penicillin allergies, some specialists recommend desensitization due to the poorly proven effectiveness of antibiotics from other groups, especially in the geriatric population.

Syphilis in geriatric patients – what to pay attention to. Long-term care issues

Sometimes a clinical manifestation of syphilis can be confused with a variety of systemic and skin diseases. Sexually transmitted diseases should be taken into account in differentiating with other diseases in elderly age [4,24-26].

Syphilis can be divided into early and late forms with the latter further divided into latent (asymptomatic) and tertiary syphilis. Tertiary syphilis is classified as cardiovascular, neurosyphilis (NS) and gummatous syphilis. Patients with meningovascular NS may present symptoms of TIA or stroke, indistinguishable from atherothrombotic TIA and stroke. Unlike the typical symptoms of a stroke, a stroke caused by meningovascular NS may be preceded by a set of prodromal symptoms. These are usually weeks to months of headaches, malaise, personality changes, and emotional instability [27].

In some examination there were 3270 TIA and stroke reported between 2005-2009. Syphilis serology was requested in 27% of TIA and stroke patients, of whom 4% were seropositive. Syphilis testing should be considered as a part of the diagnostics of TIA and stroke. Many TIA or stroke patients with positive syphilis serology did not receive definitive syphilis treatment during their admission. This is despite a 4-10% conversion of untreated syphilis to NS. It is possible that clinicians did not take account the significance of positive syphilis serology in this cases [24].

A large 2022 study of 7,925 participants in the Taiwanese population showed an approximately 40% higher risk of ischemic stroke (IS) in patients with syphilis compared to those without syphilis [28]. The mechanism consists in inducing inflammation by *T. pallidum* within the vessels with their secondary remodeling. The risk was highest in the over 51 age group. Among the comorbidities, the highest risk was noted in patients with COPD and hypertension [28].

Due to the coincidence of syphilis and the abovementioned diseases, it seems reasonable to implement prophylactic treatment, including anti-inflammatory and antithrombotic drugs. Unfortunately, there are no sufficiently large randomized clinical trials that would enable the standardization of long-term care. Appropriate patient education on modifiable cardiovascular risk factors may be an important element.

Epidemiological studies show that meningeal vascular disease associated with syphilis usually occurs 5–10 years after infection and affects mainly the middle cerebral artery, less often the basilar artery. Parenchymatous neurosyphilis develops the longest, manifesting itself even 20 years after infection, and usually does not appear until the age of 50 [28,29]. Unfortunately, cerebrovascular disease can develop at any time, which is why long-term fallow-up and detailed diagnostic imaging of critical vessels is an important issue [30].

Symptoms of syphilis affecting the large vessels are seen in the late stage of syphilis, therefore they occur mainly in older people. Although it is often considered an unexpected diagnosis, in fact, new cases of cardiova-scular syphilis continue to be reported [31]. The morta-lity rate of a ruptured aortic aneurysm is approximately 85% and is the most serious complication of cardiova-scular syphilis [32]. There is a 2021 report of a fatal rupture of a thoracic aortic aneurysm in a 78-year-old senior with syphilis with mycotic aneurysm and subsequent bacteremia due to *B. fragilis*, which is a normal bacterium of the human flora. This is unique in the context of syphilis because there are only a few reports of mycotic aneurysm associated with *B. fragilis* [33].

A similarly rare form of syphilis in the general population, but whose incidence is primarily in the geriatric population, is papulonodular secondary syphilis. Over the last 30 years, 43 cases have been described, of which only 6 in people under 72 years of age. This form of syphilis is characteristic of people with concomitant HIV infection [34]. The etiopathogenesis of nodular syphilis remains unknown, it may be an expression of hypersensitivity to *T. pallidum* infection, or be an intermediate stage between secondary and tertiary syphilis. Symptoms include purple, grayish-blue various forms of dermatological changes. These include nodules, patches, or plaques. Localized applies to the trunk, face and limbs Table II. Treatment based on 2020 European guideline on the management of syphilis (M. Janier, M. Unemo, N. Dupin, G.S. Tiplica, M. Potočnik, R. Patel)

Early syphilis (Primary, Secondary and Early latent, i.e. acquired <1 year previously)
first line treatment: BPG at a dose of 2.4 MU (IM) - one injection of 2.4 MU or two injections of 1.2 MU in each buttock [Ib; A
second line treatment:
Procaine penicillin 600,000 units IM daily for 10-14 days, i.e. if BPG is not available (1, C)
Late latent (i.e. acquired ≥1 year previously or of unknown duration), cardiovascular and gummatous syphilis
first line treatment:
BPG 2.4 million units IM, given as one injection of 2.4 million units or two separate injections of 1.2 million units in each buttock, on day 1, 8 and 15 (1, C)
second line treatment:
Procaine penicillin 600,000 units IM daily for 17-21 days, i.e. if BPG is not available (1, C)
Bleeding disorders
Ceftriaxone 1g intravenously (IV) in a single daily dose for 10 days (1, C)
Doxycycline 200 mg daily (either 100 mg twice daily or as a single 200 mg dose) orally for 14 days (1, C) Azithromycin a a dose of 2 g orally once [I; B].
Penicillin allergy or refusal of parenteral treatment
Desensitization to penicillin followed by the first line regimen (1, C)
Doxycycline 200 mg daily (either 100 mg twice daily or as a single 200 mg dose) orally for 14 days (1, C) Azithromycin a a dose of 2 g orally once [I; B].
Neurosyphilis, ocular and auricular syphilis
first line treatment: Benzyl penicillin 18-24 million units IV daily, as 3-4 million units every 4 hours for 10-14 days (1, C)
second line treatment: If hospitalization and IV benzyl penicillin is impossible Ceftriaxone 1-2 g IV in a single daily dose for 10-14 days (1, C) Procaine penicillin 1.2-2.4 million units IM daily AND probenecid 500 mg four times daily, both for 10-1 days (1, C)
HIV infected patients
Treatment should be the same as for HIV-negative patients
Syphilis induced by solid organ transplant
first line therapyBPG 2.4 million units IM (one injection 2.4 million units single dose or 1.2 million units in each buttock) weekly on day 1, 8 and 15 (1, B)
second line therapyProcaine penicillin 600,000 units IM daily for 10-14 days, i.e. if BPG is not available (1, C)

- more often the upper ones, sparing the palmar surface [34].

Oral manifestations are observed in 30% of patients with secondary syphilis and it could be the only one sign of the infection. Clinically, the oral manifestation of syphilis may resemble other diseases, which hampers the correct diagnosis. One case presents a 79-year-old male with weight loss and feeding difficulties. He had an ulcerative lesions in the oral cavity. Positive serological tests confirmed the diagnosis of syphilis. The patient was treated with Benzathine penicillin G. After two weeks of treatment the oral lesion disappeared and the patient returned to normal feeding and weight. This case report highlights the need to remind physicians and dentists of sexually transmitted infections in the differential diagnosis of oral ulcerative lesions in elderly sexually active patients [4].

The tertiary syphilis can involve mental health disorders. Older patients have a high prevalence of neurological and psychiatric disorders [25]. The treponemal serological status was analyzed in 800 patients over 65 years old. Twenty-one were found to be positive and the venereologists did not implement treatment in all cases. The question is posed whether syphilis serology screening in the elderly mentally ill should be confined to those patients with obvious clinical manifestation of syphilis or with unclear psychiatric presentations [26].

Disscusion

The world's human population is steadily growing, the comfort of life is increasing and more and more people are leading healthy, long lives. So it's not surprising that more older people report an active sex life, since sexuality is strongly related to quality of life. A survey of mid-dle-aged and older women shows that the sexual zone is an important part of life for them [35]. Recent evidence suggests that sexual activity among the elderly is increasing, possibly due to the effects of cGMP-specific phosphodiesterase-5 inhibitors on erectile dysfunction in older men. Also, changing societal views, higher divorce rates and even the development of aviation and various travel opportunities, or older people's access to the Internet and dating sites, are influencing them to engage in risky sexual behavior [35–37].

Interestingly, in a study conducted in sub-Saharan Africa, reported sexual intercourse with two or more partners in a year was more common among men over the age of 50 than among younger participants [35]. In Malawi, meanwhile, nearly half of the women aged 50-64 participating in the study reported having had sexual intercourse in the recent past, and among women over 64, one in four confirmed this. 46% of men participating in a cross-sectional survey in China confirmed intercourse with prostitutes, 24% had multiple sexual partners, and less than 4% of them used condoms. Among a study group of women over the age of 46 attending British GUM, 59% of the sexually active group reported no condom use during sexual intercourse [35]. It has been proven that elderly people have a significantly higher risk of STDs than young people aged 15-24 [38]. Prejudice and lack of information about contraception can make older people vulnerable to sexually transmitted diseases (STDs), including AIDS and syphilis [4]. The scope of one Portuguese study was to assess older people's knowledge of STDs. Fifty-five people over the age of 60 were surveyed. Only 30.9% of respondents said they had an active sex life, but when asked about condom use, 90.9% said they did not use condoms, 67.3% said they did not know about syphilis, and 70.9% did not know the form of transmission [39]. STDs prevention campaigns tend to target younger audiences, and neglecting the elderly can make this age group a potentially vulnerable group.

The risk of STDs in the elderly also increases due to a depleted immune system. The elderly are found to have impaired T-lymphocyte activity, as well as decreased immunoglobulin production. Reduced estrogen production in menopausal and post-menopausal women leads to vaginal dryness and thus greater exposure to micro-trauma during sexual intercourse, which is exploited by pathogens to enter the organism. The issue of sexuality in the elderly is still considered a taboo subject, even by health professionals [35,39]. The elderly face an information barrier due to the omission of their age group as being in the risk group for STDs, and the fear of stigma and embarrassment to themselves or doctors. This results in limited access to health care and treatment options [36]. A U.S. study has shown that among those in the 40-80 age range experiencing sexual health problems, as many as 75% have not received health care [36]. The National Institute for Health and Care Excellence (NICE) suggests that health care professionals ask about the sexual history of older patients and provide education to inform them of the risks involved [36]. The occurrence of syphilis in the elderly can be correlated with concomitant HIV infection, which significantly complicates the treatment process in these individuals and significantly reduces quality of life. A recently published study showed an increase in the cost of HIV care, in England, between 2014 and 2019, with people over the age of 50 responsible for the increase in rates. At the same time, younger age groups saw a decrease in costs [36,38].

As shown in a study conducted by Azevedo Junior W., et al. in 2022 in the Brazilian Amazon, one of the reasons for the higher incidence of STDs in older people is educational level and socioeconomic status. The study was conducted on 213 participants, aged 50 and older. It showed a positive correlation between the presence of markers of syphilis infection and low education of the participants. Among the people studied, the prevalence of syphilis was 15.5%, and in 3.03% of these people the infection coexisted with the presence of HIV [38]. Higher results were obtained by researchers conducting a study in Shenzhen, China, involving homosexual men over the age of 50, between 2009 and 2017. The prevalence of syphilis in this group of subjects was 27.71% and HIV co-infection was estimated at 9.24% [38]. In the same country, a study was conducted in Guangxi province on a group of 944 people aged 50 and older. Syphilis was confirmed in 12.7% of patients [35]. Analysis of the data revealed gaps in this group's knowledge about syphilis. Education about STDs should also be carried out among the elderly. Health care professionals compiling anamnesis of their patients should include questions about sexual history and be prepared to recognize oral and systemic manifestations of STDs, especially syphilis. [4,25,26,36]. It seems not insignificant to increase access to screening tests, increasing the number of diagnosed cases and thus speeding up the treatment process [38].

Conclusions

Despite the effective treatment available in recent years, there has been an increase in the incidence of syphilis with a disturbingly large proportion of the geriatric population. Depending on the research, every third patient diagnosed with syphilis is over 60 years of age [40]. It is related to the widespread phenomenon of aging societies, low awareness of seniors in the field of contraception and weakened immunity of the aging organism [4]. Another important reason is ignoring the issue of the sexuality of the elderly, even by Healthcare Professionals [39]. When interviewing patients, questions about the patient's recent sexual history should be considered and being prepared to recognize and diagnose sexually transmitted diseases is imperative. It is important that the issue of sexual health, including aspects related to the risk of sexually transmitted diseases, is an element of education at all stages of life, also among seniors. Often subtle and ambiguous symptoms that may affect multiple organs require interdisciplinary diagnostic care. Consideration should be given to extending the diagnosis of patients with neurological deficits in the geriatric population due to the risk of meningovascular NS in the form of stroke, TIA, and dementia syndromes [24]. The above measures will contribute not only to reducing the incidence of syphilis but also to strengthening the health policy of seniors and reducing the spread of sexually transmitted diseases in general.

Conflict of interest None

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