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The Treatment of Gonorrhea: Recent Developments in Russia

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Abstract

The recent history of gonorrhea treatment in Russia is discussed here after 2 case histories. Methods of topical treatment and provocation, not used in other countries, are described. Being informed of the lengthy and unpleasant therapy, risk groups avoided dermatovenereological dispensaries (prevention and treatment centers) and practiced self-treatment, which contributed to the spread of sexually transmitted infections. However, it is early to completely discard the topical therapy. The antimicrobial resistance is developing. One of the contributing factors is the use of antibiotics as cattle feed additives and food preservatives

Case 1

A son of a retired general (hereafter patient) awarded himself a next rank every time he contracted gonorrhea (Gn). In this way he became a "generalissimo", illustrating irresponsibility: the patient was proud of his "career". He was one of the informal leaders of a company that, apart from selling to foreigners icons and coins (https://en.wikipedia.org/wiki/Fartsovka), involved adolescents in the binge drinking and young females into sexual contacts e.g. with participants of international exhibitions in Moscow and foreign truck drivers. The risk groups with sexually transmitted infections avoided the dermatovenereological dispensaries (prevention and treatment centers), where the therapy was lengthy and unpleasant, and treated themselves with antibiotics. Intramuscular injections of Hexestrol (known in Russia as Synoestrol) oil solution were used to induce abortions - a well-known method in former Soviet Union (SU) [1]. The patient was exempted from conscription for an unknown reason.

Case 2

A female student residing in a students' dormitory was infected with Gn. It should be mentioned that some female students were manipulated towards sexual contacts by certain administrators and professors [2]. First time she had not noticed any symptoms. Shortly thereafter she met her future husband, and a week later was hospitalized to a gynecology department with the diagnosis of adnexitis. The partner developed acute urethritis with abundant discharge of creamy pus. An acquainted physician prescribed them an overseas antibiotic available at some pharmacies at that time. The patient took it in addition to the hospital medication. The recovery was complete; there were no relapses. Gn was not diagnosed at the hospital, which permitted the couple to evade some of the procedures described below.

The treatment of gonorrhea

Here follow several extracts from instructions by the Ministry of Health, handbooks and manuals containing essentially the same recommendations. If the signs of inflammation persist longer than 5-7 days after a course of antibiotics, a topical therapy was recommended also in the absence of *N. gonorrhoeae* in urethral smears. In acute gonorrhea, a topical treatment was to be started after the completion of a course of antibiotics. In torpid or chronic form of the disease, the topical therapy is performed prior to the antibiotic treatment (at a hospital) or thereafter (in ambulant patients) [3]. Some instructions and monographs [4-11] recommended the topical therapy for acute Gn, including the following: instillations into the urethra of potassium permanganate or 0.25-1 % silver nitrate solution with an additional treatment of focal lesions by 10-20 % silver nitrate via urethroscope. Urethroscopy was recommended prior to the start of topical therapy [12]. The indications for urethroscopy generally included chronic urethritis and the cure control of Gn [13].

The bouginage, urethral massage on the urethroscope, and tamponade of the urethra were recommended both for soft and hard infiltration with subsequent smearing of the urethral mucosa by ichthammol (ichthyol), a tar-like substance produced from oil shale [6,7,9,13,14]. Potential carcinogenicity of ichthammol and Vishnevski liniment containing birch tar and xeroform was discussed previously [15]. Six-seven tamponades were performed per a treatment course [15]. The electrocoagulation of paraurethral glands was applied if periurethritis was diagnosed [5]. In a more recent edition, the following was recommended (from Russian): "In case of a mixed or firm infiltration a tamponade of the urethra should be performed… Colliculitis is treated by bouginage" [16]. Atrophic and catarrhal colliculitis both are treated by curved bougies [9]. Similar recommendations, including instillations of silver nitrate, tamponade and bouginage were given in textbooks [17,18]. The sexual contacts were to be treated in the same way as the patients with chronic Gn, also if no *N. gonorrhoeae* are found in the smears [3]. There was also research on Gn with instillation into the urethra of different substances such as oxygen foam, gastric juice or herbal decoctions [19-21].

The tests of cure, recommended for all treated Gn patients, included different kinds of provocations. Chemical provocations in men included instillations of silver nitrate solution into the urethra, in women - smearing of the urethral mucosa with 1-2 % and cervical canal with 2-5 % silver nitrate solution or Lugol's iodine solution with glycerol. Mechanical provocations included urethroscopy and massage on the urethroscope or bougie [3,18]. If symptoms reappear,

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also in the absence of gonococci in the smears, the treatment and tests of cure were to be repeated. The urethral discharge is examined 24, 48 and 72 hours after the provocation; in the absence of discharge, an examination of secretions from the prostate and seminal vesicles was recommended. If no *N. gonorrhoeae* were found after the first test of cure, the provocation including urethroscopy was to be repeated a month later [3].

In women, the topical treatment was recommended for "fresh torpid" and chronic Gn [3,17]. The bimanual examination [22] and urethroscopy were recommended in women for diagnostic purposes both in acute and chronic Gn, whereas "technical difficulties" of the urethroscope insertion were pointed out [23]. Considerable discomfort was associated with those "technical difficulties". For chronic urethritis the following was recommended among others: urethral instillations of silver nitrate solution, smearing of the urethral and cervical mucosa with ichthammol [24] or Vishnevski liniment [25], massage on the urethroscope, coagulation of inflamed paraurethral glands [14,22,24], cautery of cervical ectopies (ectropions). It should be commented that diathermocoagulation (electrocautery), cryodestruction or laser treatment of the cervical ectopy in the absence of epithelial dysplasia was performed routinely. Cervical erosions and ectopies were found at mass prophylactic examinations and treated by electro- or thermocautery [26].

If *N. gonorrhoeae* are not found in the urethral smears at a first appointment after the treatment, a provocation by instillation of silver nitrate solution into the urethra and cervical canal was recommended [22]. The test of cure included urethroscopy [6,13]. The provocation in women was performed 7-10 days after the treatment, then repeated after the next menstruation, and then again after 2-3 periods. The combined provocations repeated thrice have been recommended also for Gn in adolescents and children [3,6,27-29]. If the symptoms persisted, but no *N. gonorrhoeae* are found in the smears, the treatment like for chronic Gn was prescribed. In consequence of such approach, non-gonococcal urethritis was sometimes treated by the topical procedures described above. For women with suspected gonorrhea and for those with urogenital inflammatory conditions of unclear etiology, the same treatment as for chronic Gn was recommended [14,22].

The methods of topical treatment and provocation described above have been mentioned neither by internationally used handbooks nor by recommendations by the World Health Organization (WHO); whereas the bougienage is applied only for strictures. The topical treatment was inherited from the pre-antibiotic era. However, in the 1930s, gentler observant tactics were advocated [30]. After the discovery of sulfonamides and especially of penicillin, the local treatment of Gn and the rigorous tests of cure have been largely abandoned. Nevertheless the topical treatment could have been useful in some cases because of the limited availability of modern antibiotics in the former SU. Furthermore it is not entirely clear to a pathologist, what kind of morphological substrate corresponds to the "firm infiltration", where the bouginage was recommended [4,6]. Obviously, inflamed and edematous mucosa can be traumatized, contributing to the scarring and formation of strictures. Excessive instrumentation in conditions of suboptimal procedural quality may contribute to the spread of infections such as viral hepatitis.

Today the situation is changing. At least at central dermatovenereological dispensaries, no mechanical provocations are performed, and urethral instillations are made less frequently than before. The tests for Chlamydia and other pathogens are available. Some recent manuals still recommend topical therapy and instillations for acute and chronic Gn [10,11]; but in many new textbooks and reviews antibiotic therapy is discussed, while the provocations and topical therapy are not mentioned at all. According to recommendations by the Russian Society of Dermatovenerologists and Cosmetologists, the provocations for diagnostic purposes are not indicated. In regard to the topical therapy i.e. instillations of antimicrobial solutions into the urethra, it is written that it is "inefficient" [31,32]. Apparently, it is a "shot over the target" after realization of the fact that such therapy is unnecessary.

After all, it is early to discard the topical therapy. The antimicrobial resistance (AMR) is developing. There are concerns that Gn may become untreatable by antibiotics [33,34], which would bring the topical therapy back to the agenda. One of the factors contributing to AMR is the use of antibiotics in the feeding of cattle and fowl, addition to milk and other perishable foodstuffs e.g. water where frozen fish is stored, which occurs in Russia [35]. The use of antibiotics as cattle feed additives was recommended [36,37]. Antibiotics have been used as food preservatives, being found in various foodstuffs (meat, milk, fish, eggs, fruit) often above permissible concentrations [38]. It has been noticed since the 1990s that non-sterilized (short-life) milk is going rancid rather than sour. Antibiotics in food might cause gastrointestinal dysbiosis and have other adverse effects [39], which is outside the scope of this paper. The use of pharmaceuticals beyond their evidence-based applications might generally accelerate the acquisition of AMR by various microbial populations. The need to update the treatment of the gonococcal infection to respond to the AMR has been pointed out in The Guidelines for the Treatment of *N. gonorrhoeae* issued by the WHO [40].

Conclusion

Factors contributing to the use of invasive procedures with questionable indications included the partial isolation from international scientific community, insufficient consideration of the principles of professional autonomy, informed consent and scientific polemics, as well as paternalistic attitude to patients. In conditions of paternalism, misinformation of patients and persuasion are deemed permissible [41]. Suboptimal practices have been used as per instructions by healthcare authorities and leading experts' publications. Insufficient international coordination of medical research and partial isolation from the scientific community may lead to parallelism in research with repetition of studies on a low quality level, unnecessary experimentation, and application of invasive procedures without sufficient indications.

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