Letter to the Editor: Treatment of Gonorrhea in Russia: Recent History

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Abstract: The recent history of gonorrhea treatment in Russia is discussed here after three case histories. Some outdated methods of topical treatment and provocation, not used in other countries, are described. Being informed of the lengthy and unpleasant treatment, high-risk groups avoided the prevention and treatment centers (so-called dermato-venerological dispensaries) and practiced self-treatment, which contributed to the spread of sexually transmitted infections (STI). Today there are grounds for optimism: diagnostics and treatment of STI are being adjusted to the international standards. In conclusion, the antimicrobial resistance of *N. gonorrhoeae* is briefly discussed.

Keywords: Gonorrhea, sexually transmitted infections, sexual coercion, medical ethics.

CASE REPORTS

Case 1

A lawyer was infected with gonorrhea (Gn). In accordance with the laws and regulations he went to the dermato-venerological dispensary (prevention and treatment center), was registered and treated according to instructions by the health care authorities. Thereafter the patient said that the treatment was lengthy and unpleasant, and that he would never approach the dispensary again.

Case 2

A son of a higher officer awarded himself a next "rank" every time he was infected with Gn. In this way he became a generalissimo, which illustrates irresponsibility - the patient was in fact proud of his "career". The patient was one of the leaders of a drinking company that involved adolescents into alcohol consumption, teenage girls into sexual contacts, etc. The patient and his companions treated themselves with intramuscular injections of Bicillin (Benzathin-Benzylpenicillin) [1]. Retrospectively it is unclear when it was a fresh infection or an exacerbation: the case was reported to the authorities after many years of the patient's activities. The informer did not conceal the denunciation; later he was battered [2]. This case demonstrates that the society and its institutions factually permitted the spread of STI, particularly, to people from higher social strata. The same company used for induction of abortions intramuscular injections of oil solution of Hexestrol (named Synoestrol in Russia), which was broadly used for that purpose [3].

Case 3

A female student residing in a students' dormitory was infected with Gn. It should be mentioned here that some female students were manipulated towards sexual contacts by certain administrators and professors [4]. First time she had not noticed any symptoms. Shortly thereafter she met her future spouse, and a week later was hospitalized to a gynecology department with the diagnosis of adnexitis. In the meantime, the fiancée developed acute urethritis with abundant discharge of creamy pus. An acquainted physician prescribed them an overseas antibiotic that was unavailable at the hospital. 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 newly married couple to evade some of the procedures described below.

Here follow several extracts from instructions issued by the Ministry of Health [5-7], handbooks and manuals that contained essentially the same recommendations. If the signs of inflammation persist longer than 5-7 days after a course of antibiotics, even in the absence of *N. gonorrhoeae* in the urethral smears, a topical therapy was recommended. In the introduction to a later instruction [5] it was noted that the topical treatment is indicated only in case of intolerance of antibiotics, but further in the text it is pointed out that the topical therapy is indicated also for a torpid or chronic form of the disease. 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 [5]. Earlier instructions [7] and handbooks [8,9] recommended the

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E-ISSN: 2310-998X/16

topical therapy also for acute Gn. The following topical treatments were recommended. 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. Bouginage, urethral massage on the urethroscope, and tamponade of the urethra were recommended both for soft and hard infiltration (beyond the acute phase) with subsequent smearing of the urethral mucosa by ichtyol [8,10]. In a recent edition it is recommended (translated verbatim from Russian): "In case of a mixed or hard infiltration a tamponade of the urethra should be performed… Colliculitis is treated by bouginage" [11]. The same recommendations, including instillations of silver nitrate, tamponade and bouginage can be found in recently edited textbooks [12,13]. There was also research on Gn with instillation into the urethra of different substances such as gastric juice, oxygen foam, plant decoctions etc. [14-16].

The tests of cure, recommended for all 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 of the cervical canal with 2-5 % silver nitrate solution or Lugol's iodine solution with glycerol. Mechanical provocations included urethroscopy and the urethral massage on the urethroscope or bougie [5,12]. If the symptoms reappear, also in the absence of gonococci in the smears, the treatment and the 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 provocation, a combined provocation including urethroscopy was to be performed a month later [5].

In women, the topical treatment was recommended for "fresh torpid" and chronic Gn [5,13]. However, some earlier instructions and monographs recommended topical treatment (urethra washings, instillations) in women also for acute Gn [5-7]. Bimanual examination [17] and urethroscopy were recommended in women for diagnostic purposes for both acute and chronic Gn, whereas technical difficulties of urethroscope insertion were pointed out [18]. For chronic urethritis the following was recommended among others: urethral instillations of silver nitrate solution, smearing of the urethral and cervical mucosa with ichthyol (a product of shale oil) [19], Vishnevski liniment containing xeroform and tar [20] (possible carcinogenicity of these substances was discussed previously [21]), urethral massage on the urethroscope, coagulation of inflamed paraurethral glands [10,17,19], coagulation of cervical pseudo-erosions (cervical ectopy, ectropion). It should be commented that diathermocoagulation (electrocautery), cryodestruction or laser treatment [13,22,23] of the cervical ectopy in the absence of epithelial dysplasia (potentially precancerous lesions) was performed routinely because the ectopy *per se* was regarded to be precancerous or "predisposing" to cancer [19,24,25]. Cylindrical endocervical-type epithelium and mucous glands within the ectopy were designated as "pathological tissue" that was to be removed [26]. It occurred in accordance with the Soviet-time concept of prophylaxis priority in the healthcare [25]. It was also speculated that cervical pseudo-erosions contribute to infertility and complications of pregnancy [27]. Routine coagulation of the uterine cervical ectopy without epithelial dysplasia is at variance with the scientific evidence, which does not support the hypothesis that such treatment of ectopies provides protection against cervical cancer [28]. Cervical erosions and pseudo-erosions were found at mass prophylactic checkups and treated by electro- or thermocautery [29,30], whereas complications of such treatment were noticed [23,31,32]. It was recommended to start the treatment of a pseudo-erosion possibly early, while large lesions were to be treated by "diathermoconization" (conization by means of an electrocautery electrode [19]), a procedure associated with complications [33]. It should be noted that according to the international literature, "in most women during the reproductive period, the mucin-secreting columnar epithelium of the endocervix is present on the cervical portio, forming the endocervical ectropion or cervical ectopy" [34] i.e. cervical ectopy and the associated squamous metaplasia are considered to be physiological phenomena [28].

If at the first appointment *N. gonorrhoeae* are not found in the urethral smears, a provocation by means of an instillation of silver nitrate solution into the urethra and cervical canal was recommended [17]. The test of cure included urethroscopy [6]. The combined provocation in women was performed 7-10 days after the treatment, then repeated after the next menstruation, and then again after 2-3 menstrual periods. The combined provocations repeated thrice have been recommended also for Gn in female adolescents and children [35-37]. If the symptoms persisted, but no gonococci are found in the smears,

the treatment as for chronic Gn was prescribed. In consequence of such approach, non-gonococcal urethritis was sometimes treated by means of the topical procedures described above. For women with urogenital inflammatory conditions of unclear etiology some handbooks recommended the same treatment as for chronic Gn [17].

The methods of local treatment and provocation described above were not mentioned by internationally used handbooks, reviews and recommendations by the World Health Organization (WHO) of that time [38-46], while the bouginage was recommended only for strictures [41]. These methods were inherited from the pre-antibiotic era [47]; after the discovery of sulfonamides and especially of penicillin, the topical treatment of Gn and the rigorous tests of cure have largely lost their significance. Nevertheless the topical treatment could have been meaningful in some cases because of the limited availability of modern antibiotics in the former Soviet Union (SU). Furthermore it is not entirely clear to a pathologist, what kind of morphological substrate corresponds to the "hard infiltration", where the bouginage was recommended [6,7]. Obviously, an inflamed and edematous mucosa can be traumatized, possibly contributing to the scarring and formation of strictures. Moreover, excessive instrumentation in conditions of suboptimal procedural quality assurance might have contributed to the spread of infections such as viral hepatitis.

Many physicians realized the obsoleteness of instructions and made exceptions. Vaguely formulated recommendations in some manuals [10,11,48,49] left space for personal judgment. Under these circumstances, ideation of punishment coupled with irresponsibility has apparently played a role in some medical personnel and health care functionaries [1]. There are witnesses that abortions and gynecological manipulations were sometimes performed in a harsh manner and were painful, especially in women deemed socially unprotected or "immoral". At the same time, pap-smears for early detection of cervical cancer and precancerous lesions have been performed infrequently and not up to the international standards [50], cervical cancer being therefore diagnosed relatively late [51].

Today the situation is changing. At least at central dermato-venerological dispensaries no mechanical provocations are performed, and instillations are made less frequently than before. The tests for Chlamydia and other pathogens are available today. Modern diagnostics and therapy are offered by private institutions. In some newly edited Russian-language textbooks and reviews [52-55], antibiotic therapy of Gn is discussed, while the provocations and topical therapy are not mentioned at all. According to the last recommendations by the Russian Society of Dermatovenerologists and Cosmetologists [56], provocations for diagnostic purposes are not indicated. About topical therapy i.e. instillations of antimicrobial solutions into the urethra it is written that it is "inefficient" [56,57]. Apparently, it is a "shot over the target" after the realization of the fact that such therapy is outdated. The topical treatment had been the main therapeutic modality of Gn prior to the discovery of antibiotics [47]. It seems to be too early to completely discard the topical therapy of Gn. The antimicrobial resistance (AMR) of *N. gonorrhoeae* is developing [58]. There are concerns that Gn might become "untreatable" [59] by antibiotics, which would bring the topical therapy back to the agenda. One of the factors contributing to the AMR might be the broad use of antibiotics e.g. in the cattle feeding, addition of antibiotics to milk and other perishable foodstuff, e.g., water where frozen fish is stored, which is known to occur in Russia [60,61]. It has been noticed in this country 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 [62], which is outside the scope of this letter. Irresponsible use of antibiotics beyond their evidence-based medical applications might generally accelerate the acquisition of AMR in diverse microbial populations [63]. The need to update the treatment recommendations for gonococcal infections to respond to the AMR has been pointed out in the last instruction on the management of Gn issued by the WHO [64].

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Received on 20-09-2016 Accepted on 01-11-2016 Published on 09-11-2016

DOI: http://dx.doi.org/10.12970/2310-998X.2016.04.01.1