

Viewpoints

Selected aspects of tuberculosis treatment with special reference to alcoholism

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SURGICAL TREATMENT

Along with the development of medical treatment of tuberculosis (TB), the use of surgery has decreased in many countries. Admittedly, over the last few decades, the spread of drug-resistant strains of *Mycobacterium tuberculosis* (M. tb.) has reduced success rates of treatments with drug therapy alone and increased the number of patients who require surgery. Video-assisted thoracoscopic methods are used increasingly these days. The extensive use of surgery for TB in the former Soviet Union was associated with the name of Mikhail Perelman, who criticised the Directly Observed Treatment, Short Course Programme by the World Health Organization and advocated invasive procedures.^[1] Surgery rates since the 1980s have been analysed elsewhere.^[2] The forms of TB most frequently treated by resections and pneumonectomies have been cavitary disease and tuberculoma (Tm). For example, a series of 578 operations in 502 patients, including those with fibro-cavernous disease (196 cases) and Tm (161 cases), was reported, whereas the most frequent procedures were resection (280 cases) and pneumonectomy (80 cases). The authors concluded that 'indications for surgical management of pulmonary TB should be generally expanded.'^[3] Tm was the form of the disease most often operated by Giller *et al.*: 81 from 179 cases in one series.^[4]

The recommendation to remove Tm stems from Lev Bogush.^[5] Tm larger than 2 cm has been generally regarded as an indication for surgery in adults as well as in children and adolescents.^[6,7] Tm >1 cm was often operated on,^[8-10] which is contradictory to the international practice. Resection was also recommended and applied *in silico* Tm, although the literature indicates the enhanced risk of bleeding associated with the removal of such lesions.^[11] In patients with diabetes mellitus, Tm was removed after 2–5 months of medical therapy and observation.^[12] The same expert also operated on asymptomatic patients, whereas the post-operative complication rate was 15.73%.^[13] The frequency of complications could have been underestimated due to the limited follow-up.

It is widely agreed that the potential instability of Tm does not justify thoracic surgery and that asymptomatic patients with stable solid lesions do not require therapy. Nevertheless, Tm was the most frequent indication for resections in TB patients (44.2%; in children - 40.7%) at the leading institution, Sechenov Medical University in Moscow;^[14,15] while at some hospitals, this percentage reached 50–80%.^[16] Now as before, Tm is amongst the forms of the disease that are most frequently operated on.^[17] Resections for Tm were also recommended for extensive lesions in remaining pulmonary tissues.^[18] Bilateral resections were performed in various forms of the disease including Tm on both sides.^[19-21] Bilateral lobectomies or pneumonectomy and contralateral resection were regarded to be indicated for patients with a specific lesion on one

side and fibrosis in the contralateral lung.^[22] At the time of initial TB diagnosis, surgery is currently considered to be indicated in 15–20% of patients.^[17,23] According to another paper, indications for surgery were found in 20–30% of patients at the time of diagnosis and/or in those with active TB.^[24] In Yekaterinburg and the surrounding province (years 2006–2008), indications for surgery were found in 1784 from 4402 (40.5%) patients with pulmonary TB, while 1079 (24.5%) were operated. Amongst the reasons for the supposedly low surgery rate were the patients' non-compliance and unavailability.^[25] According to the recent monograph, amongst 420 patients operated for Tm, bilateral operations were performed in 130 (31%).^[26] Resections were regarded to be applicable in patients with severe respiratory insufficiency.^[27–30] The treatment was also recommended for patients with inactive healed lesions and fibrosis, including oligosymptomatic cases.^[31] On the other hand, surgeries were performed for florid disseminated disease.^[32]

Resections in TB were performed by some experts with no preceding medical treatment or within 1 month after the diagnosis when the therapy could have been efficient.^[8,33] One of the arguments in favour of the early interventions was the non-compliance increasing with time^[8] as the patients collected knowledge and advice. Lung operations were performed and recommended also for aged patients with comorbidities.^[34–37] Reportedly, Tm was the most common indication and lobectomy - the most frequent operation in elderly patients, whereas potential contagiously was among arguments in favour of the invasive treatment.^[37] Statements of this kind can also be found in recent papers, e.g.: 'Surgery in patients with Tm is recommended to reduce their infectiousness.'^[38] According to Giller *et al.*, a reduction of TB incidence and mortality can be achieved only by means of a 'radical sanitation' of supposedly contagious patients, including those without destructive lesions or cavitation.^[4] Note that Tm is usually not contagious. It seems to be evident that potential contagiosity does not justify intrathoracic interventions. One more citation: 'Active surgical sanitation of infectiously dangerous patients with pulmonary TB contributes to the rapid improvement of epidemiological indicators.'^[39] Informed consent was not mentioned in this connection.

BRONCHOSCOPY (Bs)

Bs has been applied in all forms of TB in many institutions and research cohorts, also when the disease was suspected, and within a diagnostic algorithm for the cases with sputum negative for *M. tb.*^[40] Primary TB was regarded as an indication of Bs in children.^[41] Bs was used as a screening tool in patients with general malaise, having both negative and 'hyperergic' (high degree of hypersensitivity) tuberculin tests^[42,43] or as a second step of screening in children.^[44] In the recent handbook of paediatric pulmonology, suspicion

of TB is listed amongst indications for Bs.^[45] Therapeutic Bs and bronchoscopic monitoring have been applied in TB with non-specific bronchial lesions.^[46,47] For 'destructive tuberculosis', therapeutic Bs (1–2 weekly during 2–4 months) was recommended by the Health Ministry.^[48] An example: 22,469 Bs were performed in 5195 patients from 1994 to 2013 (1123 Bs yearly on average), including 1766 (34%) patients older than 65 years, at a physiological hospital in Moscow (705–1225 beds at different times; 368 surgeries performed in 2013).^[49,50] Of note, viruses can be transmitted by endoscopy. The incidence of hepatitis B was found to be five times higher amongst TB patients than in the general population of Russia.^[51]

SURFACTANT (Sf) THERAPY

The Sf therapy for pulmonary diseases, including TB, acute respiratory distress syndrome (ARDS), pneumonia and other conditions (except newborn respiratory distress syndrome - [NRDS]) and Bs as the delivery method has been discussed previously.^[2] Sf-BL from bovine lungs was developed in Russia. The manufacturing method is described in the patent^[52], where it is stated that Sf-BL contains ~2% of protein. Endobronchial instillations of xenogeneic proteins may cause immune reactions. A more pronounced immune response can be expected in adults and children than in premature infants with NRDS. Apparently, exogenous Sf is useless if alveoli are filled with exudation or destroyed; the instillations would just add protein-containing substance to the bronchial contents. Reportedly, endobronchial instillations of porcine Sf enhanced eosinophilic inflammation in asthmatics.^[53] Nonetheless, St-BL was used in asthma, bronchitis, pneumonia, chronic obstructive pulmonary diseases and TB; more details are in the review and patent.^[52,54] St-BL was also used in patients with COVID-19,^[55] where immune reactions might contribute to the 'cytokine storm.' Bs was used as the delivery method of Sf preparations (references are in the preceding article^[2]); and bronchial biopsies were collected.^[56] Sf-BL was recommended by the Health Ministry^[57] for viral pneumonia, referring to the manufacturer's Instruction, where the following is stated: Sf-BL can be used preventively in threatening ARDS in patients with chronic (including obstructive) lung disease. The optimal method of the Sf delivery is instillation into individual segmental bronchi.^[58] The following information is provided in regard to TB: in patients with no favourable effect from chemotherapy during 2–6 months, an additional 2-month course of Sf-BL inhalations resulted in the disappearance of *M. tb.* from sputum in 80% of cases, reduction or disappearance of infiltrative and focal lesions in 100% and closure of caverns in 70% of patients.^[58] Physiologically, these effects are hardly understandable. The treatment method,

including endobronchial instillations of Sf every other day for 3–8 weeks has been patented.^[59] No similar reports were found in the international literature.

COMPULSORY HOSPITALISATION AND TREATMENT

According to the governmental Regulation No. 378 of June 16, 2006, patients with contagious TB are not permitted to reside in one apartment with other people. The outpatient treatment is supposed to be hardly applicable.^[60] As per the Federal Law 77-FZ ‘Prevention of tuberculosis spread’ of June 18, 2001 (amended 2013), ‘patients with contagious TB, repeatedly violating the anti-epidemic regimen, and those evading examinations *or* therapy, are hospitalised for obligatory examination and treatment.’ It is specified by the same law that the principle of informed consent is not applicable under these circumstances and that the patients must undergo prescribed examination and therapy. The non-observance of this law may lead to a criminal procedure. The police are obliged to help at hospitalisations and to search evading individuals. The implementation of compulsory examinations and treatments is increasingly efficient these days. Reportedly, 100% of M. tb. excretory in the Moscow region have been hospitalised since 2019.^[61] Compulsory treatments are generally at variance with the international regulations and ethical standpoints. The consent for invasive procedures and chemotherapy is of particular importance in conditions where an overtreatment may occur.

THE COMORBIDITY OF TB AND ALCOHOL-RELATED CONDITIONS

A particular ethical problem has been the overuse of surgery in patients concomitantly diagnosed with an alcohol use disorder. According to official instructions, indications for surgery were broader in alcohol-dependent than in other TB patients.^[62] Interventions were recommended to be performed earlier, after a shorter period of medical therapy.^[9] Perelman insisted on early surgery in patients with alcohol dependence and operated them also in the absence of demonstrable M. tb.^[63] The same expert noticed that alcoholics have more frequent post-surgery complications.^[63] Bs was applied in cases with bronchitis,^[64] the latter being frequent amongst alcoholics in Russia due to smoking and the risk of sleeping down in a cold place. It was reported that about 60% patients of a ‘phthisio-narcological’ institution for compulsory treatment broke out; over 50% of them were returned by the police.^[65] The duration of stay in such institutions was a year or longer.^[64] The compulsory treatment has been endorsed by laws and regulations. Enforced therapy of socially dangerous alcoholics is stipulated by Articles 97 and 98 of the Criminal Code of RF; besides, there is a legal

mechanism enabling compulsory treatment of inmates with alcohol use disorders in prisons.

DISCUSSION

The mentioning of informed consent has started in Russian publications not long ago. It has been recommended in the recent monograph titled ‘Pulmonary tuberculoma’ to ‘explain to the patients in a popular form that surgery is necessary’^[26] instead of objective depiction of pros and cons. Justifications of hyper-radicalism could be heard in private conversations amongst medics, for example: ‘The hopelessly ill are dangerous’, i.e., may commit reckless acts undesirable by the state. For example, glioblastoma patients were routinely operated on, while it was believed by some staff that the treatment was generally useless, just forcing many patients to spend the rest of their lives in bed.^[66] The training of medical personnel under the imperative of readiness for war has been another motive.

Invasive procedures with questionable indications were advocated by some military surgeons. Amongst others, hyper-radicalism originated from Sergei Iudin (the spelling is like in PubMed; in earlier papers spelt Sergey Yudin). During World War II, he was one of the leading surgeons of the Soviet army. Iudin advocated a radical approach to wounds and fractures: ‘Wide excision of tissues’;^[67] ‘Total and wide resection of devitalised tissue... resection rather than drainage and removal of bone fragments in joint wounds (including knee and hip joints)’;^[68] ‘Unhesitatingly excise muscular tissue to access the fractured bone’.^[69] The former health minister Boris Petrovsky wrote that Iudin’s radicalism in military surgery, followed by colleagues, led to haemorrhages and extensive defects of osseous and soft tissues.^[70,71] Iudin’s articles advocating gastrectomy for peptic ulcers were republished later with approving editorial commentaries.^[72] References to Iudin continued until recently, mentioning the fact that he performed primary resections in 75% of perforated gastroduodenal ulcers.^[73] The term ‘deontology’ is often used for medical ethics in this country. Textbooks and monographs on deontology explained the matter somewhat vaguely, with truisms and generalities but not much practical guidance.

CONCLUSION

In conclusion, the role of surgery in TB remains controversial. The message of this article is that patients should not undergo operations to comply with doctrines. Evidence-based clinical indications must be determined individually, the patients being objectively informed on potential benefits and risks.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Use of artificial intelligence (AI)-assisted technology for manuscript preparation

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