

On the Endoscopic Methods Used with Questionable Indications

Keywords: Endoscopy; Bronchoscopy; Bronchial asthma; Bronchitis; Pneumonia; Tuberculosis

Introduction

This letter is a continuation of the series of reports on invasive procedures applied in the former Soviet Union (SU) with questionable clinical indications, also for research [1-4]. The problem is still with us: partial isolation from the international scientific community resulting in persistence of suboptimal practices. In this letter, special attention is given to the bronchoscopy (Bs) in bronchial asthma, used in spite of the widespread opinion that it brings not much benefit [5]. In the international literature, no particular role of Bs in the diagnosis and treatment of asthma has been specified, asthmatics being regarded at enhanced risk for complications from this procedure [5]. Among indications for Bs in asthma are persistent wheeze unresponsive to bronchodilators and other adequate therapy [6,7]. While there are other diagnostic tests, the most common indication for Bs in asthma is a search for alternative causes of the symptoms [6]. Lavage of bronchi can be indicated in severe asthma in certain circumstances [8,9]. More precise formulations are avoided here because this letter is not an instructive publication. The newest Russian-language textbooks are largely based on the international literature. However, earlier textbooks and manuals contained recommendations partly at variance with internationally accepted approaches. In asthmatics, the purpose of Bs was declared to be the search for signs of dependence of the pathological process on the infection and characterization of inflammatory lesions [10,11]. Abundant secretion or mucopurulent sputum in a child was presented as an indication for Bs "for evaluation of the endobronchial inflammation" [12]. It was stated in the instructive monograph [11] that in children Bs is recommended "almost in all subacute and chronic respiratory diseases". Asthma, tuberculosis (Tb), bronchitis, and protracted pulmonary or bronchial conditions in general, were posited as indications for Bs [13-18].

Extension of indications for Bs compared to the more conservative earlier manuals [19,20] is associated with the names of Lev Ioffe and Fedor Uglov [21-26]. Ioffe wrote in an instructive edition that "Bs must be performed in all pulmonary diseases" [21]. In 1976, Uglov reported on 2477 therapeutic and 5000 diagnostic Bs performed in his institution in patients aged 1.5-78 years predominantly with inflammatory diseases such as bronchitis, pneumonia and asthma, aimed at the "assessment of inflammatory changes in the bronchial tree" [25]. The conclusion was that Bs is important for the detailed diagnosis of practically all pulmonary diseases and can be recommended also at an early stage [25]. "After a prolonged course of therapeutic Bs" Uglov applied resections of pulmonary segments or lobes deemed irreversibly changed (bronchitis deformans, bronchiectasis etc.) as a treatment method of asthma [25]; more details are in [1]. Many thousands Bs performed with or without concomitant bronchography in children and adults with non-specific



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Submission: 21 July, 2016

Accepted: 26 July, 2016

Published: 01 August, 2016

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Reviewed & Approved by: Dr. Josef Kainz, Department of General ENT, Medical University of Graz, Austria

respiratory diseases were reported also from peripheral institutions and outpatient facilities [26]. In the same edition, difficulties with the local anesthesia were pointed out, which necessitated general anesthesia in 20-25% of the patients [26]. Apparently, the widespread implementation of endoscopy occurred according to a directive. Interference of authorities with science has been a well-known phenomenon in the former SU [27]. With regard to the medical practice, the so-called administrative factor [28] has played a role: the support of certain methods by the health care authorities, who sometimes favored less individualized approaches applicable to large categories of patients. In consequence of the authoritative management style, some methods, outdated or generally unsupported by the international literature, were applied for long periods of time; overviewed in [1].

Overuse of Bronchoscopy

Bs was applied and recommended in children and adults with bronchial asthma both during remissions and exacerbations, in mild and severe cases [29-37], as well as in the "pre-asthma" i.e. bronchitis with "elements" of bronchospasm and allergy [32,35]. Bs was discussed as a method of "early diagnosis" of all forms of bronchial asthma; it was used repeatedly "for a dynamic observation" [33]. Some experts applied up to 15 bronchoscopies (1-2 weekly) in pediatric asthma [38].

Efficiency of therapeutic Bs in moderate bronchitis was pointed out by Uglov, who applied 5-6 bronchoscopies per treatment course [24]. In particular, the "atrophic type" of chronic bronchitis was regarded as an indication for Bs [15]. Laser therapy was applied in children and adults via bronchoscope in asthma, bronchitis and chronic pneumonia [15,39-43], also in the presence of pronounced atrophy of bronchial mucosa [41], in atrophic bronchitis [44,45] or "primary atrophic bronchopathy" including that supposedly caused by ionizing radiation [46], while histological specimens were thick and difficult to evaluate (Figure 1). Note that, similarly to other forms of electromagnetic radiation, laser at lower power densities causes warming and at higher densities - damage of tissues. From the viewpoint of general pathology, atrophy may advance due to an



Figure 1: Biopsy from a large bronchus. Thick histological section. Translation of the caption: prolonged exposure to coal dust and vibration. Atrophy of bronchial epithelium, sclerosis and hyperelasis of the lamina propria mucosae [46]. Van Gieson stain, X 250.

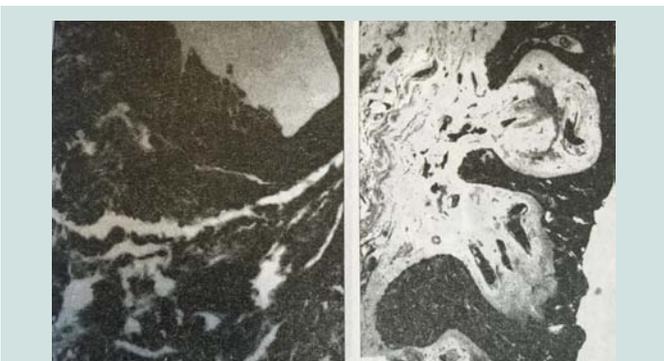


Figure 2: Light-optical examination of biopsies from large bronchi of patients with lung cancer: left - pronounced atrophy of bronchial epithelium (van Gieson stain X 160); right - squamous transformation of bronchial epithelium (semi-thin section, Azure II stain, X 1000) [77].

additional damage. Not only flexible but also rigid bronchoscopes have been used e.g. in chronic bronchitis or asthma also in children [47,48]. For acute pneumonia in children, Bs was recommended to determine the type of inflammation in the bronchi (catarrhal, purulent); in chronic pneumonia Bs was held necessary for the same purpose and also to rule out Tb and congenital conditions [10]. In pediatric chronic pneumonia, Bs was recommended by the Ministry of Health for the diagnosis and therapy as “one of the main methods” [49].

Furthermore, broncho- and gastroduodenoscopy were used as a second step of the screening e.g. in the “chronic non-specific pulmonary diseases” (including asthma and chronic bronchitis) reportedly found in 4.08% of children residing in industrially contaminated areas of Moscow and the suburbs [50]. Bs was used as a screening method in agricultural workers contacting with dust: both in healthy ones and in those with allergic rhinitis or chronic bronchitis [51]; in bronchitis patients professionally contacting with proteolytic enzymes [52]; generally in bronchitis, acute and chronic pneumonia including children [53-57]; in young (mean age 19.5 years) patients diagnosed with community-acquired pneumonia (1478 bronchoscopies in 977 patients) [58].

Bs was applied in all forms of Tb in many institutions and research cohorts [59-65] also when Tb was suspected [66,67]; it was recommended for young patients with “hyperergic” (high degree of hypersensitivity) tuberculin tests [68] or within the diagnostic algorithm for cases of suspected Tb with the sputum negative for *Mycobacteria* [69]. Primary Tb was regarded as an indication for Bs in children [10], although it is reportedly no more sensitive for the culture of *Mycobacteria* than gastric aspiration [6,7]. In destructive Tb, therapeutic Bs (1-2 weekly during 2-4 months) was recommended by the Ministry of Health [70] and applied, while the principle of informed consent was insufficiently known and observed. Bs was used as a screening method for Tb in patients with general malaise, both positive and negative tuberculin tests [71]. Other researchers used Bs as a second step screening method for Tb in children [72]. Endoscopic monitoring of the therapy results has been applied in pulmonary Tb with non-specific bronchial lesions, also recently [62,73].

Research Quality, Indications, and Informed Consent

As mentioned above, bronchial biopsy specimens were used for research, whereas some histological illustrations were suboptimal quality (Figures 1-3), descriptions being stereotype, morphometric and other quantitative indices changing uniformly [46,74] e.g. inflammatory indices (serum immunoglobulins, T- and B-lymphocytes, markers of phagocytosis) influenced both by the medical and surgical asthma treatment in the same direction [75]. Trimming of data was known to occur and proven in some studies; more details and references are in [76]. In some bronchial biopsy studies, scanning electron microscopy was the only morphological method applied [54]. Some histological descriptions were doubtful e.g. “atrophic processes” in bronchi of asthmatic children increasing with time: atrophy or “subatrophy” reportedly found in 79.5% of asthmatic children older than 12 years [47]. Biopsies were taken for research from large bronchi of patients with known lung cancer, whereas quality of histological and ultrastructural images was low (Figures 2 and 3) [77], which means additional discomfort for the cancer patients with no impact on the therapy. Another example: lavage fluid collected by Bs from patients with lung cancer and from those with Tb (including focal forms, tuberculoma etc.) was examined by infrared spectroscopy with no known repercussions for theory and practice [78].



Figure 3: Bronchoscopic biopsy from a large bronchus. Translation of the caption [75]: left - destruction of cilia and formation of microvilli on the apical surface, alteration of cytoplasmatic organelles; right - endothelium-like bronchial epithelial cell, X 8000.

In the pediatric clinic of the Moscow Medical Academy (a leading institution where textbooks have been prepared [10]), endoscopic methods started to be broadly applied for the diagnostic, therapeutic and research purposes since the 1960s by Eva Klimanskaia and co-workers [11,12,14,39,50,79-86]. Bs was used in children with pneumonia, bronchitis and asthma [80-82], while complications were noticed [80] and “extreme carefulness” [11] recommended. Besides, gastrodoudenoscopy with biopsy used for research was applied in children with rheumatoid arthritis, dermatomyositis, scleroderma, systemic lupus erythematosus, respiratory and hepatobiliary diseases [50,83-88]. Gastroscopy was used for the screening of children born to mothers with bronchial asthma [89]. Ioffe and co-workers repeatedly applied gastrodoudenoscopy in patients with end stage kidney disease [23]. Finally, a series of studies with the overuse of cystoscopy with biopsy in connection with the overdiagnosis of malignant and premalignant urinary bladder lesions [90] has been commented previously [91].

As mentioned above, the principle of informed consent was not sufficiently known and observed [92], being mentioned only in some recent Bs studies [93-95]. Paternalistic and authoritative attitude to patients often prevailed. For example, coercive methods and compulsory treatments were applied to alcoholics: lengthy intravenous infusions (commented in [96]), sorbent hemoperfusion, endolymphatic and endobronchial delivery of antituberculosis drugs etc. [97-100]. There has been a stereotype: post-graduate students and doctoral candidates came to Moscow and other centers from different parts of the country, some of them prepared to pay for literature reviews, preparation of specimens, etc. Some researchers planning emigration completed their dissertations under the time pressure. Among others, invasive methods were applied without sufficient clinical indications sometimes in conditions of suboptimal procedural quality assurance; overviewed in [1-3]. Admittedly, as far as it can be perceived from the literature, endoscopy is less frequently used for research today. However, Bs as a screening method has been applied in the settings of military medicine [54,58]; more examples were discussed in [1]. In the recent study [93], Bs was performed in children 5-15 years of age with moderate to severe asthma, while informed consent was obtained from the children’s parents.

Some bronchoscopic methods applied for diagnostics and therapy have been patented; several examples follow. Therapy monitoring of chronic catarrhal bronchitis by means of repeated examinations of bronchial washings obtained by Bs performed every other day during the whole period of treatment [101]; laser therapy via bronchoscope of “atrophic bronchitis deformans” [102-104]; bronchitis diagnostics in children and adults [105-107], treatment of pulmonary Tb by endobronchial instillations of surfactant preparations produced from bovine lung or human amniotic fluid every other day during 3-8 weeks [108]; discussed in [109].

Conclusion

The purpose of this letter was to overview some endoscopic methods, applied with questionable indications, and to remind that the risk-to-benefit ratio should be kept as low as possible. Invasive procedures including endoscopy and biopsy used for research without sufficient clinical indications fall under the jurisdiction of the Declaration of Helsinki [110]. In any case, such research presupposes

integrity and informed consent. When a child is able to give assent to decisions about participation in the research, the investigator must obtain it in addition to the consent by parents or legally authorized representatives [111]. Adolescents are in a sense between children, who are to be treated according to their best interests represented by parents or legally authorized persons, and independent adults, who are to be treated according to their wishes [112]. Consent of human subjects for participation in research requires that they fully understand their role and risks, and can withdraw at any time without being disadvantaged. Children require additional protection [113,114]. In the author’s opinion, endoscopy for research, Bs in particular, should not exist as such; it must always be performed according to clinical indications. Research can be performed on biopsy specimens obtained for diagnostic purposes (discussed in [115]). However, if suboptimal for the diagnosis methods, consuming the tissue, are applied, enough tissue must remain for the diagnostics. Note that tissue in a paraffin block may become necessary for future diagnostic examinations. In any case, the research involving humans should yield fruitful results for the good of society, being unprocurable by other methods [116]. Furthermore, medical research involving human subjects must be conducted only by experts with appropriate ethics, scientific education and training [110]. Finally, significance of the procedural quality assurance in endoscopy should be stressed. Scheduled procedures should not be performed under the time pressure. The training methods not involving patients e.g. using anatomic models and video technologies must be applied as extensively as possible [6]. Objective selection of capable trainees, prepared to dedicate most of their time for their profession, is of great importance. Nepotism [42,43,80], potentially interfering with objective selection of candidates, should be discouraged. Lack of experience and skills reduces diagnostic and therapeutic yield of endoscopy while increasing risks [117]. In conclusion, practical recommendations must be based on reliable and reproducible research. Only such research should be included into reviews and meta-analyses.

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