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REVIEW ARTICLE

Tularemia of the head and neck in the pediatric population – a review and recommendations for otorhinolaryngological practice

Manifestacje tularemii w obrębie głowy i szyi u dzieci – przegląd piśmiennictwa i rekomendacje dla praktyki otorynolaryngologicznej

Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
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F – Literature Search
G – Funds Collection

Kinga Piksa[1BCDEF], Zuzanna Szewczyk[1BCDEF], Katarzyna Baranowska[1BCDEF], Tomasz Biedulski[1BCDEF], Agata Gierlotka[2AE], Ireneusz Bielecki[2AE]

[1]Students' Research Group at the Department of Pediatric Otolaryngology and Surgery of Head and Neck of the Medical University of Silesia, Katowice, Poland
[2]Department of Pediatric Otolaryngology and Surgery of Head and Neck of the Medical University of Silesia, Katowice, Poland

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ABSTRACT:

Introduction: Tularemia, a zoonosis caused by the Gram-negative bacterium *Francisella tularensis*, is a serious threat to public health. The disorder can take the ulceroglandular, pneumonic, oropharyngeal, oculoglandular, gastrointestinal, or typhoidal forms. Infection occurs through contact with infected animals, tick/insect bites, or inhalation of contaminated aerosols. The clinical presentation of tularemia may vary; the condition is often confused with streptococcal pharyngitis, infectious mononucleosis, or other diseases.

Aim: The aim of this paper is to systematize the knowledge on tularemia in the context of ENT practice, to discuss the recommended treatment, and to present typical clinical presentations.

Material and methods: A review of the literature published in the years 2000–2025 as available through the PubMed database was carried out in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Demographic data and information on the clinical course, source and routes of infection, as well as complications and treatment, were extracted for analysis.

Results: The database query returned a total of 178 papers; of these, 12 articles describing 25 children were finally qualified for the review. The results, as reported for children aged 8 months–17 years, were divided into 3 groups depending on the variant of tularemia, namely oropharyngeal tularemia, ulceroglandular tularemia, or tularemia of the middle ear. Oropharyngeal tularemia and ulceroglandular tularemia were the most predominant variants. The main vectors were rodents and ticks. The most common symptoms included fever, sore throat, enlarged lymph nodes, and skin lesions.

Conclusions: Despite being well described in the literature, tularemia remains rarely diagnosed in most Central European countries. Early diagnosis and prompt management are key to preventing severe complications. The best therapeutic results are obtained using antibiotics from the group of fluoroquinolones, tetracyclines, or aminoglycosides. The recommended duration of antibiotic therapy is 14–21 days.

KEYWORDS: children, *Francisella tularensis*, otolaryngology, tularemia, zoonosis

STRESZCZENIE:

Wstęp: Tularemia stanowi poważne zagrożenie dla zdrowia publicznego. Jest to zoonoza wywoływana przez Gram-ujemne bakterie *Francisella tularensis*. Może mieć postać wrzodziejąco-węzłową, płucną, ustno-gardłową, oczno-węzłową, żołądkowo-jelitową oraz tyfoidalną. Zakażenie następuje poprzez: kontakt z zakażonymi zwierzętami, ukąszenia stawonogów lub inhalację skażonego aerozolu. Obraz kliniczny tularemii jest różnorodny, często bywa mylony z paciorkowcowym zapaleniem gardła, mononukleozą zakaźną lub innymi chorobami.

Cel: Celami niniejszej pracy są usystematyzowanie wiedzy na temat tularemii w kontekście otorynolaryngologicznym, omówienie rekomendowanego leczenia oraz przedstawienie typowych obrazów klinicznych.

Materiał i metody: Przeprowadzono przegląd piśmiennictwa z lat 2000–2025 w bazie PubMed, zgodnie z wytycznymi PRISMA. Analizie poddano: dane demograficzne, przebiegi kliniczne, źródło oraz drogi zakażenia, a także powikłania i leczenie.

Wyniki: Przegląd pozwolił uzyskać 178 badań, z których ostatecznie do badania zakwalifikowano 12 artykułów opisujących 25 dzieci. Wyniki podzielono na 3 grupy opisujące warianty tularemii: ustno-gardłowy, wrzodziejąco-węzłowy oraz tularemię ucha środkowego, wśród dzieci w wieku 8–17 lat. Dominującymi postaciami klinicznymi tularemii były postacie ustno-gardłowa oraz wrzodziejąco-węzłowa. Głównymi wektorami były gryzonie i kleszcze. Najczęściej obserwowanymi objawami były: gorączka, ból gardła, powiększenie węzłów chłonnych oraz zmiany skórne.

Wnioski: Tularemia, mimo że jest dobrze opisana w literaturze, pozostaje rzadko rozpoznawana w większości krajów Europy Środkowej. Wczesne postawienie diagnozy oraz szybkie wdrożenie leczenia są kluczowe dla zapobiegania ciężkim powikłaniom. Najlepsze wyniki terapeutyczne uzyskuje się poprzez stosowanie antybiotyków z grupy fluorochinolonów, tetracyklin lub aminoglikozydów. Zalecany czas trwania antybiotykoterapii wynosi 14–21 dni.

SŁOWA KLUCZOWE: dzieci, *Francisella tularensis*, otolaryngologia, tularemia, zoonoza

ABBREVIATIONS

CDC – Centers for Disease Control and Prevention
CT – computed tomography
DIC – disseminated intravascular coagulation
EBV – Epstein-Barr virus
ELISA – enzyme-linked immunosorbent assay
ENT – ear, nose, and throat
EPHPP – Effective Public Health Practice Project
PCR – positive molecular test
PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QATAS – Quality Assessment Tool for Quantitative Studies
WHO – World Health Organization

INTRODUCTION

Tularemia is a serious zoonosis caused by the Gram-negative bacterium *Francisella tularensis.* The disease takes on different variant forms depending on the route by which the bacterium enters the body. Manifestations may include pneumonia, pharyngitis, abscesses, and meningitis. Most frequently, infection occurs through contact with infected animals – particularly hares or small rodents, as well as through the bites of arthropod carriers such as ticks or deer flies [1]. Another route of infection may consist of inhalation of contaminated dust or aerosols. Infection also occurs during contact with contaminated environments, e.g., while gardening, bathing in lakes and rivers, or by ingestion of contaminated food or water [2–4]. Tularemia cannot be contracted from another human being [2, 5]. Different strains of bacteria showing varying levels of virulence are prevalent in different geographic areas. A distinction is made between type A and type B strains. The *F. tularensis* (type A) strain is highly virulent and is found only in North America. In contrast, the less virulent *F. tularensis holarctica* (type B) strain is considered endemic throughout the northern hemisphere [6]. Various clinical forms of tularemia can be observed in humans, the symptoms depending on the route by which the bacteria enter the body. The first symptoms usually develop suddenly, 3–5 days after infection, although the incubation period can range 1–21 days [3, 7]. Initially, symptoms are nonspecific and resemble the flu. The most common form of the disease is ulceroglandular tularemia. It is characterized by fever, skin lesions, and enlarged lymph nodes (lymphadenopathy). Some patients develop lymph node abscesses or neck phlegmon. Neck skin ulcerations are also a typical symptom. The glandular form presents with lymph node enlargement alone, without skin lesions. On the other hand, infection of the conjunctiva leads to the development of the oculoglandular form. Pneumonic tularemia develops as a result of inhalatory infection. Consumption of undercooked meat (e.g., rabbits, hares) or contaminated water can result in the envelopment of the oropharyngeal form, which accounts for 1–4% of all cases [3, 5]. In this variant, the predominant symptoms include sore throat and difficulty swallowing, as well as headaches and neck pain. General symptoms such as fever, weakness, lack of appetite, and chills are common. Due to its similar clinical presentation, the oropharyngeal form can be confused with streptococcal tonsillopharyngitis, which often results in ineffective attempts at treatment with penicillin [8]. Tularemia is a notifiable (registrable) infectious disease as per the Polish Act on the Prevention and Control of Infections and Infectious Diseases in Humans of December 5, 2008 [9]. As of the present, no vaccine against *Francisella tularensis* is available [5, 7]. However, deaths from tularemia in Europe are rare [7]. Although the pathogen is well described in the literature, it is not uncommon for tularemia to be overlooked in the differential diagnosis. In the ENT practice, oropharyngeal tularemia is the most commonly diagnosed presentation. This variant of the disease should be taken into account, particularly in patients with tonsillopharyngitis not responding to penicillin treatment. Early and accurate diagnosis can shorten the duration of therapy and reduce the risk of complications, which are not uncommon upon prolonged hospitalization [8].

AIM

The aim of this paper is to systematize the knowledge on tularemia in the context of ENT practice, including the recommended treatments and typical clinical presentations.

MATERIAL AND METHODS

The review was carried out in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [10].

Search strategy

The search of the available literature was carried out by 4 independent reviewers. The PubMed database was queried for articles published

between 2000 and 2025. The query phrase used in the search for relevant articles was as follows: children OR pediatrics OR newborn OR infant AND laryngology OR head and neck OR nose OR lymph nodes OR eye OR oral cavity AND "tularemia". The returned records were first submitted for initial screening on the basis of abstracts. Reference lists of articles included in the review were also checked in order to minimize the possibility of skipping relevant reports.

Inclusion and exclusion criteria

Included in the review were articles describing pediatric patients of both genders up to 18 years of age. Publications presenting the clinical course of tularemia and the route or vector of infection were included for analysis. Articles that did not report on the treatment modality or subsequent prognosis were also included in the study as the review focused mainly on the variety of symptoms, disease vectors, and the possibility of differentiating tularemia from other disease entities. Included in the scope of the analysis were full-text English-language papers, including retrospective studies and case reports.

Qualified studies

The query of the PubMed database using the aforementioned phrases returned a total of 178 potentially eligible publications. Eighty-six duplicates were excluded in the preliminary screening of titles and abstracts. Another 71 articles were excluded as they did not meet the inclusion criteria. Of the remaining 21 studies, 9 were excluded due to the lack of valuable results. A total of 12 articles were qualified for the final review. The flow diagram of the process of the analysis and selection of studies eligible for review is shown in Fig. 1.

Data acquisition

The following data were extracted from the included articles: the name of the first author, the age and gender of patients, the variant of tularemia, the vector responsible for the transmission of Francisella tularensis, the main symptoms, and the study quality rating according to the Quality Assessment Tool for Quantitative Studies (QATQS) Global Rating questionnaire [11, 12]. When collecting data from individual papers, special attention was paid to the qualitative analysis thereof.

Data quality

The QATQS, as developed by the Effective Public Health Practice Project (EPHPP), was used to assess the quality of quantitative studies and the potential risk of bias [11, 12]. The tool facilitates a comprehensive evaluation of research conducted according to different research schemes. The QATQS rating consists of 8 separate domains that address the selection bias, study design, confounders, blinding, data collection methods, intervention integrity, and analysis. Each domain is rated on a three-point scale, with the score of 1 corresponding to a strong rating, 2 to a moderate rating, and 3 to a weak rating; the final survey score is based on the number of domains with weak rating. A study receives a strong rating if no domain received a weak rating, a moderate rating if 1 domain received a weak rating, and a weak rating if at least 2 sections received a weak rating. This approach allows for reliable identification of methodological limitations and objective assessment of the quality of the study, which is crucial for the interpretation of the results obtained.

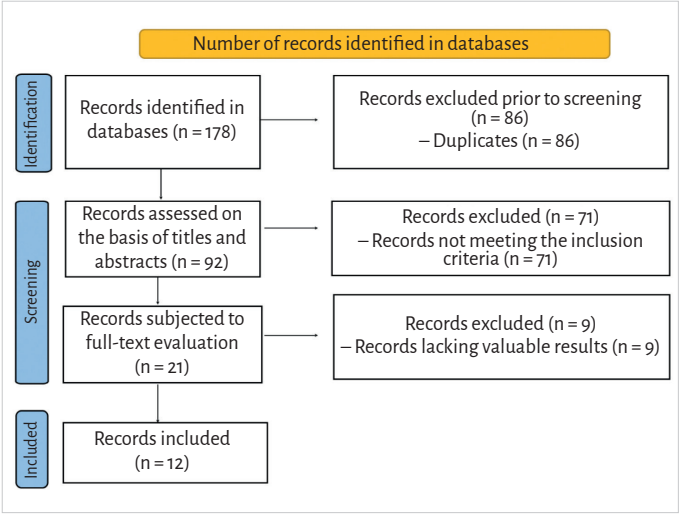


Fig. 1. Flow diagram of the process of the analysis and selection of studies eligible for review.

RESULTS

The query and the selection process returned a total of 12 articles describing 25 children. The cases were divided into 3 groups: oropharyngeal tularemia, ulceroglandular tularemia, and tularemia of the middle ear. The groups differed in vectors, main symptoms, and treatment approaches. The results are shown in Tab. I.

Oropharyngeal tularemia

Oropharyngeal tularemia was described in 3 publications [13, 16, 20] as affecting a total of 15 children between the ages of 5 and 17. In all cases, the vector carrying the *Francisella tularensis* pathogen was a rodent. The most common symptoms included sore and congested throat [20], enlarged and inflamed tonsils [13, 16], headache [16], fever, malaise [13], and enlarged and painful cervical lymph nodes (lymphadenopathy) [13, 16, 20]. In each of the above cases, the initial line of pharmacotherapy proved ineffective. The initial regimens included clindamycin [13], amoxicillin with clavulanic acid [16], and beta-lactam antibiotics or macrolides [12]. After microbiological confirmation of *Francisella tularensis* infection, targeted antibiotic therapy was administered with doxycycline [13, 16] and streptomycin [13, 20]. While gentamicin was also used in some cases as per the World Health Organization (WHO) guidelines [5], no improvement was achieved as a result of this treatment.

Ulceroglandular tularemia

Ulceroglandular tularemia has been described in eight papers [14–18, 21–24] reporting on a total of 9 children between the ages of 8 months and 8 years. In most cases, the infection occurred as a result of a tick/insect bite [14, 15, 18, 21–23]. Less commonly,

Tab. I. Characteristics of the study group, including demographics, clinical presentation, vector, and QATQS scores.

AUTHOR	GENDER	AGE	TULAREMIA VARIANT	VECTOR	MAIN SYMPTOMS	QATQS SCORE
Peker et al. [13]	M M M	9 years 12 years 14 years	oropharyngeal	rodent	fever, sore throat	3
Kukla et al. [14]	M F	2.5 years 6.5 years	ulceroglandular	tick	earlobe ulceration, abscess in the forehead area	3
Kumar et al. [15]	M	8 years	ulceroglandular	tick	fever, painful bilateral enlargement of posterior cervical lymph nodes, sore throat, fatigue	3
Nemmour et al. [16]	M	5 years	oropharyngeal	dead mouse	fever, sore throat, cough, headache	3
Anand et al. [17]	M	7 years	ulceroglandular	cat	fever, sore throat, painful, palpable mass on the right side of the neck	3
Kumar et al. [18]	M	18 months	ulceroglandular	tick	fever, scalp ulceration, enlarged lymph nodes	3
Luotonen et al. [19]	M	10 years	tularemia of the middle ear	mosquito	fever, nausea, otitis externa, and otitis media	3
Kaya et al. [20]	M F	8–17 years	oropharyngeal	rodent	fever, sore throat, and massive swelling of cervical lymph nodes	3
Abdo et al. [21]	F	8 months	ulceroglandular	tick	fever, vomiting, lethargy	3
Hanke et al. [22]	M	16 months	ulceroglandular	mosquito	fever, rash, swelling of the right parotid gland	3
Weiner et al. [23]	M	17 months	ulceroglandular	tick	fever, enlarged lymph node	3
Yanushevych et al. [24]	M	5 years	ulceroglandular	rabbit	fever, non-painful lump on the right side of the neck	3

the vectors included a cat [17] or a rabbit [24]. The most common symptoms included fever [14, 15, 17, 18, 21–24], earlobe (auricle) ulceration [14, 23], bluish induration and swelling at the bite site [14] sore throat [15, 17], fatigue [15, 21, 23], lymphadenopathy [14, 15, 18, 22–24], scalp rash [14, 18, 22], cough [18], vomiting [21, 23], neck abscess [14, 22, 24], and diarrhea [23]. Just like in case of oropharyngeal tularemia, the initial pharmacotherapy proved ineffective. The initial treatments included penicillin, azithromycin, amoxicillin [15, 21, 23], doxycycline [21], clindamycin [15, 17, 18, 22], cefuroxime [14], clarithromycin [14, 24], linezolid, cefotiam [22], ceftriaxone [23], vancomycin, and metronidazole. In 1 case, anti-tuberculosis treatment including isoniazid, rifampicin, and pyrazinamide was initiated due to a positive molecular test (PCR) for *Mycobacterium tuberculosis* complex [24]. One child died despite the implemented treatment due to the advanced stage of the disease and ineffective treatment [23].

Tularemia of the middle ear

Tularemia of the middle ear was described in 1 article reporting on a 10-year-old boy who had been bitten by an infected mosquito. The patient presented at the hospital with symptoms of purulent otitis externa with visible granulation tissue, swelling, and purulent discharge in the external ear canal, as well as fever and malaise, which had persisted for 2 weeks. A computed tomography (CT) scan revealed inflammatory changes in the ear canal, tympanic cavity, and the mastoid process. Azithromycin and cephalexin were administered in first-line antibiotic therapy and subsequently switched to cefuroxime, with no improvement being achieved. The positive result of the microbiological test for *Francisella tularensis* was followed by the treatment with ciprofloxacin and topical treatment with ear drops containing dexamethasone, framycetin, and gramicidin. The treatment had a positive effect and resulted in recovery [19].

DISCUSSION

The diagnosis of tularemia is based on detailed history, clinical presentation, and laboratory findings. In the past, the gold standard was to obtain cell culture from biological material such as lymph node contents, sputum, blood, or pleural fluid. Recently, however, this method has been superseded by more advanced diagnostic techniques [25]. The disadvantages of isolating the bacteria in cell cultures included the significant risk of infection by inhalation for laboratory diagnosticians and the long waiting times before the result could be obtained due to the slow growth of bacteria [26]. Modern recommendations are based on a two-step approach to serological diagnosis [1, 4], involving a combination of an ELISA screening assay and a confirmatory immunoblot assay [25]. Serological testing involves the determination of specific IgM and IgG antibodies by ELISA or the detection of specific IgG antibodies by microagglutination. However, the objective, positive serological results are not typical for patients in the early stages of the disease, as adequate levels of antibodies usually do not appear until 10–20 days after infection. A fourfold increase in antibody titers over a two-week interval confirms the diagnosis. Infection is also confirmed by the detection of the genetic material of *Francisella tularensis* within the lymph node contents, sputum, or scrapings from skin lesions. On the

other hand, histopathological examination is not sufficient for an unambiguous diagnosis; the predominant presentation is that of non-specific inflammatory granulation tissue with the presence of tuberculosis-like lesions, necrotic foci, and multinucleated giant cells [24, 27]. Due to its rarity and non-specific symptoms, tularemia poses a diagnostic challenge. It is not uncommon for it to be confused with other conditions presenting with fever and lymph node enlargement [26, 27]. The differential diagnosis of tularemia should include *streptococcal* infections, *staphylococcal* infections, cat scratch disease, toxoplasmosis, mycobacteriosis, sporotrichosis, anthrax, plague, AIDS, lymphoproliferative diseases, sarcoidosis, adenoviral infections, cytomegalovirus, and Epstein-Barr virus (EBV) infection [25]. In the case of pneumonic tularemia, it is important that the disease be differentiated from pneumonia caused by other community pathogens, such as *Mycoplasma pneumoniae, Chlamydophila pneumoniae, Legionella pneumophila, Chlamydia psittaci, Coxiella burnetii, Mycobacterium tuberculosis*, or non-tuberculous mycobacteria. The differential diagnosis of the typhoid (gastrointestinal) variant should include Q fever, malaria, rickettsioses, as well as *Salmonella typhi*, *Brucella* spp., *Legionella* spp., and *Plasmodium* spp. infections [5, 27]. Cases of co-infections with *Francisella tularensis* and other pathogens were also described; these can result from a single bite by a tick infected with several microorganisms or from multiple bites by different arachnids, each carrying a different pathogen. Serological studies conducted in Poland have shown the possibility of *Rickettsia* spp./*Francisella tularensis* and *Borrelia* spp./*Francisella tularensis* co-infections, which can lead to the manifestations of symptoms characteristic of both diseases [7, 25]. The treatment of tularemia involves antibiotic therapy with drugs from the group of fluoroquinolones (ciprofloxacin), tetracyclines (doxycycline), and aminoglycosides (gentamicin) [26]. Antibiotic therapy should last 14–21 days. For mild infections, it is recommended that ciprofloxacin be administered intravenously 3 times a day at 10 mg/kg, with a maximum of 400 mg 3 times a day; in children, doxycycline should be administered at a dose of 2 mg/kg/day in patients weighing < 50 kg and 100 mg administered twice a day in patients weighing 100 mg for 14–21 days. In severe or complicated infections, gentamicin remains the standard treatment, administered intravenously at a dose of 5 mg/kg/day in 2–3 divided doses over 10 days. It is imperative that the potential adverse effects of this antibiotic, such as ototoxicity, nephrotoxicity, and neurotoxicity, be taken into account, particularly in the pediatric population [28]. Individuals exposed to the pathogen should take post-exposure prophylaxis. It is recommended that treatment with ciprofloxacin (oral or intravenous) or doxycycline be started within 24 hours of exposure [5, 29]. For neck abscesses and phlegmon, surgical intervention with abscess/phlegmon drainage is necessary [26]. Improperly diagnosed and inadequately treated tularemia is associated with the risk of complications, which depend on the clinical variant of the disease. The most common complications include meningitis and encephalitis, exudative peritonitis, arthritis, endocarditis and pericarditis, thrombophlebitis, liver failure, renal failure, disseminated intravascular coagulation (DIC), and sepsis [5, 25]. These complications are more common in immunocompromised patients. The rare prevalence of tularemia, the ambiguous clinical presentation, the similarity to other more common conditions, and the bacteria's natural resistance to beta-lactam and macrolide antibiotics make this disease a major clinical challenge [1]. Tularemia should be taken into account as a potential diagnosis, particularly in patients with lymphadenitis, skin lesions, and soft tissue inflammation, especially when necrosis or abscesses are present and previous empirical treatment is unsuccessful. Making a diagnosis can be difficult as tularemia has a varied and variable clinical presentation. Prompt implementation of appropriate antibiotic therapy increases the chances of successful treatment, especially in the pediatric population. For this reason, it is crucial that specialists have comprehensive knowledge of the diagnostics of tularemia and take a thorough medical history of the patient. Arrival from endemic areas, contact with wild animals, or a history of tick bites, as well as the exclusion of more common causes of symptoms, should prompt consideration of tularemia [25, 30]. Although the disease is rare in Poland, it is important that the knowledge of its course and treatment be promoted among family physicians, pediatricians, internal medicine specialists, and otolaryngologists. The clinical course of tularemia can range from asymptomatic to severe, life-threatening disease. The greatest threat is posed by pneumonic tularemia. The potential use of *F. tularensis* as a biological weapon may lead to numerous cases of pneumonia and a mass, life-threatening hazard. As shown by the studies conducted in the 1960s, illness in a healthy individual can be induced by as few as several microorganisms per 10 liters of air, which illustrates the high bioterrorism risk associated with *F. tularensis* [2, 30]. The U.S. Centers for Disease Control and Prevention (CDC) have classified *F. tularensis* within Category A of biological agents, a group of highly infectious and highly lethal pathogens with the potential to be used in bioterrorism activities [31].

CONCLUSIONS

Despite being well described in the literature, tularemia remains rarely diagnosed in most Central European countries. Early diagnosis and prompt management are key to preventing severe complications. The best therapeutic results are obtained using antibiotics from the group of fluoroquinolones, tetracyclines, or aminoglycosides. The recommended duration of antibiotic therapy is 14–21 days.

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Corresponding author: Agata Gierlotka (ORCID: 0009-0008-0436-1766); Department of Paediatric Otolaryngology and Surgery of Head and Neck of the Medical University of Silesia; Medyków street 16, 40-752 Katowice, Poland; Phone: +48 322071973;
E-mail: agierlotka@gczd.katowice.pl

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