

Sporadich Goitter

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Abstract:

2020 marks the centennial anniversary of the publication of a classic study by American doctors D. Marin and O. Kimball on the effectiveness of preventing endemic goiter in children in Akron, Ohio. Although goiter has been known since time immemorial, there is still a problem with determining the normal size of the thyroid gland, without solving which the diagnosis of goiter remains extremely subjective. For example, in Sweden over the past 20 years, not a single case of endemic goiter has been reported, which is not surprising: the country eliminated this pathology decades ago, and the median concentration of iodine in urine indicates the optimal supply of iodine to the population. Cases of sporadic goiter in children in Sweden are also rare - no more than 6-8 per year throughout the country. But in Belarus, with the same population (about 10 million), about 2,900 cases of goiter in children are registered annually, both endemic and sporadic. Moreover, in Belarus, due to the high use of iodized salt since the early 2000s. There is also no iodine deficiency, but the incidence of goiter in children, having decreased many times over the past 20 years, remains 3 times higher than in Uzbekistan, where iodine prophylaxis, if carried out, is on a limited scale. From the experience of Belarus, Sweden and Russia, we see that the main thing when assessing data on the incidence of goiter and other thyroid diseases associated with iodine deficiency should not be absolute numbers, but the trend of these indicators over the past years. These guidelines should be more actively used by endocrinologists in Uzbekistan to assess the effectiveness of preventive measures at both the regional and federal levels.

Keywords: iodine; endemic goiter; sporadic goiter; morbidity; prevalence; medical statistics; Uzbekistan; Belarus; Sweden.

Introduction. In 1905, after graduating from Johns Hopkins University School of Medicine, 25-year-old physician David Marine came to continue his postgraduate education at Lake Erie University Hospital in Cleveland, Ohio. There is a legend that at the first meeting, his new supervisor asked David what scientific topic he would like to develop along with his clinical activities. The question was unexpected, but the young doctor remembered that in the hospital yard he had seen several stray dogs with clearly enlarged thyroid glands, and confidently stated that he would like to deal with the problem of goiter. This was very important for Cleveland, located in the “goiter belt” of the United States, stretching along the Appalachians from the Great Lakes to the very south of the country [1]. D. Marin, who before moving to the medical faculty trained as a zoologist, began his experimental studies on dogs (perhaps the same ones that he saw in the hospital yard) and soon proved that the administration of iodine not only led to a reduction in goiter, but also transformed animals from “emaciated and lethargic” to “active and strong”, and the goitrous thyroid gland contained less iodine than in healthy animals. It should be noted that at the beginning of the twentieth century. There was an idea that goiter could be caused by certain infectious factors¹, and treatment with iodine preparations was considered dangerous due to their toxicity. Convinced of the effectiveness and safety of iodine, in a now classic study conducted in Akron, Ohio, D. Marin and his colleague O. Kimball prescribed 200 mg (!) of sodium iodide in an aqueous solution to elementary school girls. courses of 10 days (total dose - 1700 mg of iodine) every 6 months for 2.5 years. For schoolgirls from 5th to 8th grade, the dose of iodine was doubled. By modern standards, the doses of iodine used seem clearly excessive. However, D. Marin and O. Kimball themselves admitted that these doses “significantly exceed the amount of iodine required to saturate even the largest thyroid glands,” but did not expect them to be toxic (which, by the way, was completely confirmed). Treatment with sodium iodide was prescribed to 2,000 girls whose parents consented. The control group consisted of approximately the same number of schoolgirls who did not receive permission from their parents for treatment. From a modern point of view, the selection of subjects cannot be considered adequately randomized, but, as is known, the classics of science can be forgiven a lot. Approximately half of the girls (908 in number) from the main group receiving iodine did not have goiter. After 2.5 years, it reappeared in only 0.2% of them; in the remaining 99.8%, the goiter “wasn’t there anymore.” When prescribed iodine, goiter decreased in size in 60.3%, increased in 0.2% and did not change in 39.5% of girls. In the control group, a decrease in goiter was detected in 13.8%, an increase in 14.2%, and no change in 72%. The results of this study were published in the journal Archives of Internal Medicine exactly 100 years ago [2], in 1920, already far from us. My next publication in the “De Gustibus” section is dedicated to the anniversary of this event, which this year celebrates a much more modest anniversary, namely 10 years, which gives me another chance to bask in the rays of someone else’s glory. Over the course of 10 years, I published about 40 columns in this magazine. In some of them I discussed, to one degree or another, the problems of iodine deficiency and endemic goiter. But this column will be entirely devoted to discussions about goiter as such, and the simplest one at that, without the presence of nodes and dysfunction of the thyroid gland. The goiter has been known to people since prehistoric times and is reflected in fine art, including the photograph shown here (Fig. 1), which received an award at the World Press Photo competition in 2012. There are also no problems with defining a goiter - it is a swelling on the front surface of the neck due to an enlarged thyroid gland. But if we judge the enlargement of the gland, then there must be an upper threshold of normal, like the red mark at 370C on an old mercury thermometer. However, most definitions and classifications of goiter do not describe the norm, leaving room for voluntarism. For example, in widely used in Russia at least until the end of the 1990s. classification proposed by O.V. Nikolaev in 1932, it is not

indicated at all in what situation the thyroid gland is not enlarged. At zero degree, when is it not palpable? In grade 1, when only the isthmus is palpable, or in grade 2, when both lobes of the thyroid gland are palpated? Only at grade 3, when the contours of the gland are visible to the eye, is it “officially” recognized as enlarged. Here it is necessary to mention once again that O.V. Nikolaev created a classification for mass surveys of the prevalence of endemic goiter, but later it began to be used in clinical practice even to determine the degrees of diffuse toxic goiter [3]. The definition of the norm was not given by the definition proposed by the Pan American Health Organization for, I emphasize again, epidemiological studies of the prevalence of endemic goiter. It states that “thyroid gland, volume of lateral And indeed, in practice, it is almost impossible to differentiate sporadic goiter from endemic goiter based on clinical and laboratory data. For this, another criterion is used: goiter is considered “sporadic” only in countries and regions with optimal iodine supply, where endemic goiter should not exist by definition. Interestingly, in Uzbekistan at the beginning of 2016, 30% more patients were registered with “other forms of non-toxic” goiter” (1,028,830) than with all thyroid diseases associated with iodine deficiency (703,062) combined [9]. What criteria doctors used to guide some diagnoses into the category associated with iodine deficiency (E01), and others into the sporadic category (E04), remains unknown. For further analysis, all of the above nosological units (E01.0, E01.1, E01.2 and E04) were combined into one group called “endemic and other forms of non-toxic goiter”. Using regression analysis, the authors of the article under discussion [9] showed the absence of reliable dynamics in the primary incidence of endemic and other forms of non-toxic goiter (hereinafter per 100 thousand population) in children under the age of 14 years. In adolescents aged 15–18 years, a significant, although insignificant, decrease in the incidence of goiter was noted (Fig. 2). But in adults, multidirectional dynamics of the prevalence and incidence of goiter were observed (Fig. 3). I would, of course, like to explain the decrease in the incidence of goiter with the effect of studies carried out since the early 2000s. preventive measures (albeit very limited), but are hampered by vague doubts: if such measures were truly adequate, then first of all this would affect the incidence and prevalence of goiter in children, which, alas, was not registered. The authors explain the relatively small increase in the prevalence of goiter in adults by a “significant increase in life expectancy.” But, it seems to me, there is a simpler explanation: in children and adolescents there is a great possibility of reducing diffuse goiter, especially if iodine supplements, popular in Uzbekistan and fairly accessible, are prescribed or when iodized salt is used in the diet. In other words, in approximately the same number of children, the diagnosis of goiter was established for the first time and was removed due to “recovery.” But in adults, reduction of multinodular goiter, included in the statistics along with diffuse goiter, is much less likely, which leads to the accumulation of such patients in the population and an increase in the prevalence of pathology. In any case, it is obvious that ignoring simple and accessible preventive measures, i.e. the mandatory use of iodized salt in households and the food industry, especially the baking industry, leads to stagnation: the incidence of goiter does not increase, but does not decrease significantly either. I have probably already tired my readers by glorifying in my column the successes of fraternal Belarus in eliminating iodine deficiency. But I have never been able to find a better example than a country that essentially does not even have a state border with Russia. To illustrate, I will use data from two articles by T.V. Mohort et al. [10, 11], published in the same However, with regard to the incidence of “other forms of non-toxic goiter - E04”, the situation turned out to be completely unexpected for me. It turned out that for the period from 1998 to 2018. cases of non-toxic goiter in children 0–14 years old were practically not registered: in some years they were not detected at all, and if they were detected, then no more than 3 cases per year. The incidence of nontoxic goiter in adolescents aged 15–19 years was also low: from 0.7 to 2.5 cases per 100 thousand population. In absolute numbers, this ranged from 5 to 7 cases per year, with the exception of 2006, when 16 cases were identified. For the entire age group (0–19 years), over the past 20 years, the incidence of goiter did not exceed 0.8 cases per 100 thousand, but mostly ranged from 0.4 to 0.6 cases (Fig. 6). This is hundreds of times less than the incidence of diffuse goiter in

children and adolescents in Belarus (Fig. 4). According to my calculations, in Belarus, about 2900 new cases of diffuse goiter were registered in children and adolescents aged 0–18 years in 2016, and in Sweden there were only 8 such cases. In older age groups, the incidence of non-toxic goiter in Sweden predictably increased. For example, according to data for 2016, the incidence increased with age and reached a plateau of 20–25 cases per 100 thousand population in people over 50 years of age (Fig. 7). Here it must be borne in mind that in the Swedish register, the statistical group E04, in addition to diffuse non-toxic goiter (E04.0), also includes non-toxic single-nodular goiter (E04.1) and non-toxic multinodular goiter (E04.2). It is likely that the age-related increase in incidence is associated precisely with the diagnosis of nodular forms of goiter. At the same time, the incidence of goiter in adults in Belarus in 2016 (59.9 cases) was almost 4 times higher than that in Sweden - slightly more than 15 cases per 100 thousand population (Fig. 5 and 7). I asked Prof. to comment on the reasons for such a huge difference in the incidence of diffuse goiter. T.V. Mohort, whose data I used in this article. This is what she told me: “When diagnosing any disease, methodology is of fundamental importance. In Belarus, statistical reporting includes data obtained by palpation of the thyroid gland, which is not always confirmed by determining its volume. The palpation method itself for diagnosing goiter is very subjective, especially if it concerns an enlarged gland that is invisible in the normal position of the neck. In 2017, we assessed the volume of the thyroid gland in 700 children aged 9–12 years and, when compared with standards by sex and age, did not find an increase in the volume of the thyroid gland in children, i.e. goiter. Well, the differences in the incidence of goiter in Sweden are associated, in my opinion, with the continued wariness towards thyroid pathology and cancerphobia after the Chernobyl disaster, which leads to overdiagnosis of goiter. A separate issue is verification of the cause of goiter. How, under conditions of optimal iodine supply, can we differentiate between diffuse (endemic) goiter associated with iodine deficiency (E01.0) and diffuse non-toxic (sporadic) goiter (E04.0)?” The answer to the last question seems obvious to me: if there has been no iodine deficiency in Belarus for almost 20 years, then there should be no cases of endemic goiter. Like in Sweden, where such a diagnosis is simply not given. All new cases of diffuse goiter should be classified as E04.0. In clinical practice, in my opinion, “verification” of diffuse non-toxic goiter by calculating the volume of the thyroid gland according to ultrasound data and comparing it with known threshold standards is inappropriate. As we have already noted, standards for the volume of the thyroid gland (primarily in children) were created for epidemiological studies, where exceeding the volume by a tenth of a cubic centimeter transforms the gland from conditionally normal to conditionally enlarged. But does this conditional “increase” have clinical significance? I doubt. But if there is a suspicion of the presence of a formation (nodule) in the gland based on palpation, ultrasound is important, determining not only the diagnosis, but also the tactics of further action. According to recent recommendations from UNICEF and GY, goiter prevalence studies should be discontinued to assess the iodine status of the population [15]. But these recommendations were about epidemiological, often one-time, field surveys. What about using data on the incidence and prevalence of goiter according to official medical statistics for the same purposes? I’ll say it evasively: if there’s no fish, there’s fish. The main problem of monitoring and assessing the iodine status of the population in most countries of the world is that the one-time field epidemiological surveys recommended by WHO, UNICEF and GSI are too complex and expensive, and therefore are carried out extremely irregularly (the recommended interval is 3–5 years). In addition, with rare exceptions, these examinations are not part of the algorithm for collecting, processing and evaluating data on a particular pathology approved and accepted by health authorities and, at best, are regarded by them as just another scientific project. Another thing is current data on the incidence of a particular pathology. In the era of the COVID-19 epidemic, data on the number of people infected with the virus are presented in the media as front-line news, on the basis of which governments take quick response actions. I am far from thinking that data on the incidence of goiter will be taken by the authorities as seriously as a deadly virus. Nevertheless, this is precisely the information on the basis of which preventive

measures for the mandatory use of iodized salt should be taken, and not persistently sabotaged. From the experience of Uzbekistan, Belarus and Sweden, we see that the main thing when assessing data on the incidence of simple goiter and other thyroid diseases associated with iodine deficiency should not be absolute numbers, but the trend of these indicators over the past years. We see how over the past 20 years the incidence of goiter in Belarus in children and adults has sharply decreased against the backdrop of an effective salt iodization program, and this is confirmed by the positive dynamics of other indicators: the frequency of cases of neonatal thyroid-stimulating hormone exceeding 5 mIU/l [10, 11]. In Russia, such a positive trend has not been observed over the past 10 years. And it's clear why. To summarize, I would like to say that data on the incidence and prevalence of goiter, or more precisely, on their dynamics over the foreseeable time, should be more actively used by endocrinologists to assess the effectiveness of preventive measures both at the regional (region, federal district) and federal level. It would be useful to prepare and publish recommendations for streamlining the diagnosis of goiter: if there is an iodine deficiency in a region, then there cannot be cases of "sporadic" goiter. And vice versa.

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