

IMPLEMENTATION OF THE PROGRAM OF MEASLES ELIMINATION IN THE WHO AFRICAN REGION

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Abstract. The review is devoted to the analysis of the available literature on the elimination of measles. The review focuses on the current measles epidemic situation in the African Region (AFR) and the implementation of the WHO strategic plan for the elimination of measles in AFR by 2020. Measles in the AFR is characterized by a severe course with a high risk of death due to malnutrition, vitamin A deficiency, concomitant bacterial and viral infections, and malaria. In 2015, 105,256 cases of measles were reported in the WHO African Region, most of them among children under 5 years old, 79% of whom were not vaccinated or had unknown vaccine status. Initially, the strategy for implementing the measles elimination program in AFRs was based on a combination of immunization campaigns for children under 14 years of age (coverage of more than 90%) and routine vaccination of at least 90% of children aged 9–15 months. It was recommended to repeat the campaign of mass immunization of children aged 9 months up to 4 years every 3–5 years. The use of this strategy has reduced the number of measles cases by 83–97% during the first year of additional immunization programs. The recommended age of routine measles vaccination in AFRs is 9 months — a strategy to reduce infant mortality, including that due to complications of measles. In 2016, measles vaccination was introduced into the national immunization schedule in all AFR countries, and 24 countries introduced revaccination. Currently, the measles elimination program in a number of AFR countries is based on two-dose immunization (MCV1 and MCV2). The measles prevention program in a number of AFR countries was disrupted due to the Ebola epidemic. There are some common problems in the realization of the program in AFR countries. All AFR countries are committed to the measles elimination program. The review provides information on strategies and successes in overcoming challenges to achieve the goals set for the WHO African Region in the implementation of the programme of measles elimination.

Key words: measles, measles elimination program, Africa, vaccination, revaccination.

ОСУЩЕСТВЛЕНИЕ ПРОГРАММЫ ЭЛИМИНАЦИИ КОРИ В АФРИКАНСКОМ РЕГИОНЕ ВОЗ

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Резюме. Обзор посвящен анализу имеющейся литературы по вопросам элиминации кори. Основное внимание в обзоре уделяется текущей ситуации с эпидемией кори в Африканском регионе ВОЗ. Освещаются основные

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события, связанные с выполнением Стратегического плана по элиминации кори Всемирной организации здравоохранения в Африканском регионе к 2020 г. Корь в Африканском регионе ВОЗ характеризуется тяжелым течением с высоким риском смерти из-за недоедания, дефицита витамина А, сопутствующих бактериальных и вирусных инфекций и малярии. В 2015 г. в Африканском регионе ВОЗ было зарегистрировано 105 256 случаев кори, большинство из них среди детей в возрасте до пяти лет, 79% из которых не были вакцинированы или имели неизвестный статус вакцины. Первоначально стратегия реализации программы ликвидации кори в Африканском регионе основывалась на сочетании кампаний иммунизации детей в возрасте до 14 лет с охватом более 90% и плановой вакцинации не менее 90% детей в возрасте 9–15 месяцев. Было рекомендовано повторять кампанию массовой иммунизации детей в возрасте от девяти месяцев до четырех лет каждые 3–5 лет. Использование данной стратегии позволило сократить число случаев кори на 83–97% в течение первого года выполнения дополнительных программ иммунизации. Рекомендуемый возраст плановой вакцинации против кори в Африканском регионе ВОЗ составляет девять месяцев — это стратегия снижения младенческой смертности, в том числе из-за осложнений кори. В 2016 г. вакцинация против кори была включена в Национальный график иммунизации во всех странах Африки, а в 24 странах была введена ревакцинация. В настоящее время программа элиминации кори в ряде стран в Африканском регионе ВОЗ опирается на две дозы иммунизации (MCV1 и MCV2). Программа профилактики кори в ряде стран Африки была сорвана из-за последней эпидемии геморрагической лихорадки Эбола. Существуют некоторые общие для всех регионов ВОЗ проблемы в реализации программы элиминации кори, которые характерны также для стран Африки. В обзоре содержится информация о стратегиях и успехах в преодолении проблем, связанных с достижением целей, поставленных перед Африканским регионом ВОЗ в ходе осуществления программы элиминации кори.

Ключевые слова: корь, программа элиминации кори, Африка, вакцинация, ревакцинация.

Introduction

In 1989 the World Health Assembly, and in 1990 the Meeting of Heads of State on child health set the goal of reducing measles morbidity and mortality by 90% and 95%, respectively. According to the WHO Advisory group (1996), the presence of only one host (human), a typical clinical manifestation, long-term immunity after the disease, a single antigenic variant and the absence of asymptomatic carriage of the virus makes it possible to eliminate measles worldwide [2, 14].

In 2012, 194 states — members of the World Health Assembly approved the Global plan of vaccine-related activity, whose task was the improvement of health through the dissemination of comprehensive benefits of immunization to all people, regardless of ethnic, social, religious, and other differences [4]. The WHO measles strategy suggested a single vaccination for at least 90% of the target population. In many African countries, seroconversion was only 85% after single vaccination at 9 months of age, i.e. 15% of children remained unprotected. A two-dose immunization scheme (vaccination and revaccination) ensures measles elimination at the national level [2]. A global laboratory network for the diagnosis of measles and rubella has been established to monitor measles and to prove elimination of infection [10].

The Strategic plan for measles elimination by 2020 (WHO, 2012) included a 95% reduction in measles mortality compared to 2000, and elimination of the disease in at least five WHO regions, including Africa [42]. The review is devoted to the

analysis of the available literature on the elimination of measles and focuses on the current measles epidemic situation in the African Region (AFR).

The WHO African region (AFR) comprises 47 countries. The population of Africa is about 1 billion people and, according to the forecast of HSBC Bank (Hong Kong and Shanghai Banking Corporation), will double by 2050 [6].

Clinical characteristics of measles in the AFR

Measles, a systemic disease, is accompanied in Africa by severe malnutrition, lack of vitamin A, as well as co-infection with specific pathogens of bacterial, viral and parasitic nature [22]. In a typical case (moderate form) in nonimmune persons after the incubation period, prodromal symptoms are observed: fever, weakness, cough, runny nose and conjunctivitis. The pathognomonic sign is the presence of typical Belsky–Filatov–Koplik spots on the mucous membrane of the cheeks and lips that can be found in 80% patients 2 days before the rash. Macula-papular rash spreads from the face to the limbs and torso in 3–7 days and is accompanied by high temperature. Then the change in the color of the elements of the rash and their peeling occur (pigmentation period). Patients are contagious throughout the prodromal period and up to 4 days from the onset of rash [5, 41].

In the WHO African region, approximately one third of measles cases are associated with complications. These include ulceration of the oral mucosa, laryngotracheobronchitis (croup), pneumonia, in-

fection of the ears and sinuses, persistent diarrhea. In South Africa, pneumonia and/or diarrhea were reported to be the most common cause of hospitalization of measles-infected children [22]. In Uganda 136 out of 171 children with measles developed bronchopneumonia [15]. Corneal desiccation and ulceration are less common (1–4% of children with measles), although measles causes about half of childhood blindness in Africa [19, 22, 41]. The risk of coinfection with other pathogens or death persists for several months after recovery from acute measles [48]. Among vaccinated people, the number of measles cases with complications is significantly lower compared to unvaccinated ones [18].

Measles on the African continent is one of the main causes of child mortality, especially in children under 5 years of age, which is up to 10% of all child deaths in the region [32, 41]. In Uganda, up to 2000's the mortality rate was 20 to 23%; among the dead 55% were children 6 to 18 months. The cause of death in most cases was lung damage caused by measles virus, but not secondary infections [15]. In 2009–2010, in one of the hospitals in Cape Town, 15 of the 18 children who died of measles (3% of the total number of hospitalized) were younger than one year [22]. Overall, since 2013, measles in AFR results in about 40,000 deaths each year.

Measles incidence in AFR

The largest measles outbreaks were observed in 1992 (South Africa) [22], 1996 (Botswana, Lesotho, Malawi, Namibia, South Africa, Swaziland, Zimbabwe) [49]. After launching the immunization program, the incidence of measles has declined, the number of reported cases decreased from 520,102 cases in 2000 to the historical minimum of 37,012 cases in 2008. In seven South African countries, the number of measles cases reported annually was less than 1 per million population between 2006 and 2008 [35]. However, the level of vaccination coverage achieved could not prevent major measles outbreaks in subsequent years.

In 2010–2011, about 200,000 cases of measles were reported annually in the African region (figure 1) [24]. In 2012, the number of suspected cases of measles in AFR was 106,052, the incidence rate being 118.8 per 1 million population. The number of confirmed cases of measles in the region decreased from 43,800 in 2011 up to 25,905 in 2012; the incidence of confirmed cases being 50.4 and 29.0 per 1 million population, respectively. Large outbreaks of measles were reported in Angola, the Democratic Republic of the Congo (DRC), Nigeria, Ethiopia [11, 24, 26]. In 2013, 71,529 measles cases were confirmed in AFR. In 2015 105,256

cases of measles were detected in the WHO African region, the majority of them among children under 5 years of age. Meanwhile, 79% of these children were not vaccinated or no information about vaccination has been presented. In 2016, 62,293 suspected cases of measles were detected, the highest incidence of measles was in Equatorial Guinea (1938 per 1 million population). However, in 15 AFR countries the incidence rate was less than 1 case per 1 million population [25].

The measles prevention program has been disrupted in some countries of the African region by the humanitarian crisis associated with the Ebola epidemic [37]. The most affected countries in West Africa were Guinea, Liberia and Sierra Leone. According to the national vaccination schedules, vaccination against measles in these countries is carried out once in 9 months. In the Republic of Guinea, vaccination coverage decreased from 90.5% in 2012 to 52% in 2015 [25]. According to our data of serological monitoring, a total of 12.3% of the surveyed persons in the Republic of Guinea were measles-negative. Antibodies to the measles virus have not been revealed or were determined in low titers in 76.2% of patients under the age of 22, probably as a result of violations of vaccination schedule [1, 7, 8, 9]. However, all patients aged 23 years and older were seropositive for measles virus, 60% of them having high antibody titers, indicating a recent history of measles. In 2016, 289 confirmed cases of measles were registered in the Republic of Guinea, in January–March 2017 there was an outbreak of measles (3991 cases); 4 deaths were registered in patients with a diagnosis of measles [47].

In Liberia, vaccine coverage reached 74% in 2013, 58% in 2014 and 64% in 2015. During the Ebola epidemic not a single case of measles was detected; but in 2015 and 2016 433 and 400 confirmed cases were discovered, respectively. The Ministry of Health of the country officially recognized that the measles epidemic was the result of the lack of its vaccine prophylaxis as a result of the Ebola epidemic [12]. In countries where the Ebola epidemic has ended, the World Health Organization recommended that routine vaccination should be resumed and special attention should be paid to children who may have missed immunization.

The Democratic Republic of the Congo (DRC) is one of the poorest countries in the world in terms of measles. Measles vaccine is given once to children 9–11 months old [20, 42]. Additional vaccination of children aged 6 to 59 months old every three years was carried out in 2002–2004 and 2006–2007, while 2010–2013 was marked by political instability in the DRC. The measles outbreak began in the South-East of the country in Katanga province, bordering Zambia. Starting from week 1, 2010

to week 45, 2013, 294,455 cases of measles and 5,045 cases of measles-driven death have been reported. The mortality rate was 1.7% among the reported cases. Between 2011 and 2014, the proportion of cases in the DRC ranged from 45 to 69% of all measles cases reported in the AFR [23, 46]. More than 18.5 million children were vaccinated in response to outbreaks in 2013–2014. Vaccination coverage increased to 79% in 2015 [20, 25, 28, 29, 30], which was not enough to stop the epidemic. In 2016, 13,817 suspected measles cases were reported, 178 of them being fatal. The incidence rate, taking into account only confirmed cases of measles, was 61.7 per 1 million population. In 2017, 2,150 cases of measles were confirmed.

In 2013, 57,892 cases were reported during the outbreak in Nigeria, accounting for 30% of all measles cases in AFR. Nigeria is the largest African country in terms of number of population. In 2013, the Nigerian authorities declared martial law in three northern states in connection with the activities of the terrorist Islamist group Boko Haram. The humanitarian crisis has resulted in the resettlement of people to other states of Nigeria and neighbouring countries, with more than 1.4 million displaced persons living in more than 100 camps. The coverage rate of a single-dose measles vaccine was below 55% over a long period of time. In 2015, 24,421 suspected measles cases were reported, 127 of which were fatal [13, 25, 34]. More than 77% of children under 5 years of age were not vaccinated, and this group had the highest number of cases. To prevent the spread of outbreaks, mass vaccination campaigns for children over 6 months of age have been conducted since 12 January 2017, and 4,766,214 children have been vaccinated, first those living in resettlement camps, and then all children in the conflict-affected states of North-Eastern Nigeria [45].

As noted earlier, measles in Africa is predominantly found in young children [11, 30, 31]. There were no statistically significant differences in the incidence of measles among males and females [18]. The peak of morbidity is usually observed during the dry season [16].

Measles surveillance system in AFR

AFR health care system is based on the regional principle, i.e. medical centers cover certain areas.

The first serious attempt of surveillance for measles in the WHO African region was the adoption of a program with the participation of 20 African countries in 1966. The expanded program of immunization (EPI), initiated by WHO in 1978, included operational research, technical assistance, collaboration with other groups, and the development

of national immunization programs [32]. In 1986, along with EPI, virological surveillance of measles has been introduced. The goal of the EPI for the African region was to make measles immunization available to all children by 1990 and to ensure at least 75% vaccination coverage. In 1991, however, measles vaccination coverage for children aged 12 to 23 months in Africa was only 54% [17].

In 2000, the African regional office of WHO proposed a plan to reduce measles mortality by more than 50% by 2005 [49]. The strategy included global immunization campaigns for children aged 1 to 14 years; routine immunization for at least 90% of children aged 9–15 months and the subsequent campaign of immunization of all children at the age of 9 months to 4 years every 3–5 years in order to involve those children who have not been vaccinated within the calendar period or who have not responded to the previous vaccination. Mass immunization campaigns was supposed to include large populations (whole country or its region) and cover more than 90% of susceptible populations [2]. In 2002, a measles surveillance system was introduced in all countries of the WHO African region based on the investigation of each suspected measles case with laboratory confirmation of the diagnosis [38]. Measles surveillance included the collection of data on cases of exanthema diseases with fever and rash (two or more per 100,000 population), the study of blood samples in one (or more) suspected measles cases in $\geq 80\%$ of the territories, and 100% reporting in all territories [40]. The African region has achieved a 90% reduction in measles mortality compared to estimates in 2000 by the end of 2006 [3].

In 2008, 46 WHO member States of the African region adopted the goal of measles pre-elimination by the end of 2012. This goal, however, was not achieved [39]. In 2009, the Regional Committee for Africa set and in 2011 approved the goal of measles elimination by 2020 [40, 43]. All 47 countries in the WHO African Region joined this plan [42].

Global laboratory network for surveillance for measles and rubella in the WHO in 2012 supported the standardized methods and quality assurance in 44 laboratories of 42 member States in the WHO African region; 43 countries reported data on supervision of measles on the basis of the investigation of each case, and all States have provided annual reports through a single reporting form about the number of measles cases. In 2012, 19 countries were investigating 2 or more cases of illness with fever per 100,000 population and a study of blood samples from 1 or more suspected measles cases in $\geq 80\%$ of [26].

Currently, measles surveillance in the WHO African Region is integrated into global epidemio-

logical surveillance of other vaccine-preventable diseases (acute flaccid paralysis, yellow fever, neonatal tetanus). For AFR, a suspected measles outbreak is defined as 5 or more suspected measles cases reported within one month in a health facility or district with known transmission routes. In this case, an epidemiological investigation should be carried out [41]. Suspected measles is any case of rash, fever, cough, runny nose or conjunctivitis. Suspicious cases are confirmed on the basis of laboratory tests, epidemiological links and clinical criteria. Laboratory confirmation of the diagnosis of measles in all sporadic cases and at least one case in the epidemic chain is a prerequisite for further measures for elimination of the infection [16, 41, 48].

Endemic transmission of the measles virus in AFR

Molecular studies based on the analysis of the variable region of the nucleoprotein gene (450 nt) of the measles virus under a single Protocol (WHO, 1998) are a mandatory part of measles surveillance. According to the principles of nomenclature and names of isolated measles viruses, 22 specific genotypes and 1 possible new one (g3) have been described. Genetically related genotypes are combined into genetic lines (A, B, C, D, E, F, G, H) [44].

In the WHO African region, measles viruses of D2, D4, D8 and D10 genotypes have been detected since the early 2000's. However, the most commonly identified measles viruses are of genetic line B. Genotype B2 is constantly circulating in West Africa. Genotype B3, which includes three sub-genotypes (B3.1, v3.2 and v3.3), is widely distributed in countries of the WHO African region, and was identified in different years in many African States [16, 21, 31, 33, 35, 44].

In 2013–2016, according to WHO, all 249 measles virus isolates from 14 countries of the African region were of genotype B3 [25]. Viruses of genetic line B are endemic to the African region, and their transmission continues.

Vaccination against measles

Since 2001, AFR has started programs of supplementary immunization activities (SIAs) for children aged 9 months to 14 years. In Central Africa large immunization campaigns were carried out in 2002 — 2004, then in 2006 and 2007. However, the vaccination coverage was below 95%. In 2008, a total of 7.7 million infants (27% of children born the current year) did not receive a single-dose measles vaccine [24].

Currently, one- and two-dose vaccination strategies are used [38]. Routine one-dose vaccina-

tion in all States is carried out mainly at the age of 9 months. Two-times immunization against measles has been introduced into the national immunization schedule in 25 AFR countries, a second dose of measles — containing vaccine is planned in Cameroon, Comoros, Uganda; a similar option is being considered in Mali and Mauritania [25, 26]. Revaccination is carried out in most countries at the age of 15–18 months. Immunization is also carried out through supplementary immunization programs (campaigns). For some countries, SIAs is the only way to vaccinate the population [24, 32]. The implementation of the SIAs is supported by national budgets and a coalition of partners: the American Red Cross, the United Nations Foundation, UNICEF, WHO and CDC [27].

Overall, by 2010 the coverage of single-dose measles vaccination in the African region had increased to 75%. During 2011–2012, approximately 133 million children have been vaccinated in the course of 35 supplementary vaccination campaigns.

In 2013–2016 52 SIAs have been realized in 42 AFR countries, which have involved about 300 million children. Vaccination coverage during the supplementary immunization campaign was at least 95%. In 2015, the highest vaccination coverage rates were achieved in Mauritania (99%), Tanzania (99%) and Seychelles (98%); the lowest ones were achieved in Southern Sudan (20%), Equatorial Guinea (27%) and the Central African Republic (49%) [25]. In 2016, single-dose vaccine coverage in AFR was 72%, and double-dose — 24%. Scheduled SIAs were planned in 28 countries of the WHO African region, including Côte d'Ivoire, Guinea, Nigeria and Sierra Leone in 2017 and Chad, Equatorial Guinea, Guinea Bissau and South Sudan in 2018 [24].

Thus, the coverage of one dose of measles vaccine in AFR does not exceed 75% over a long period of time, which is not sufficient to prevent the spread of measles in the region.

Conclusion

There are problems with the measles elimination programme that are common to different WHO regions. This is an incomplete list: untimely diagnosis of diseases, untimely beginning and incomplete volume of anti-epidemic measures in the outbreak site, incorrect determination of the number of vaccinations, insufficient explanatory work with the population and others.

All AFR countries are committed to the measles elimination program. According to available literature data the high level of vaccination coverage in the WHO African region is hampered by the inaccessibility of territories and population groups, poor communication, lack of roads, the problem of keeping

temperature regimen in the course of vaccines transportation, lack of medical personnel, active population movement and military conflicts [29, 33].

Health care therefore needs to be improved. Currently, not all measles-infected patients receive necessary medical care, and not all measles cases are reported [29]. Some health centers and laboratories are insufficiently equipped. The population is not sufficiently informed about the benefits of vaccination. In Nigeria alone, more than 4,000 vaccination teams were needed to implement SIAs [45]. Many African countries have begun to train national staff for immunization.

In developing countries, WHO recommended age for the first dose of measles vaccine is 7 to 9 months. Single immunization of children under one year

of age is not sufficient to prevent measles outbreaks. In Nigeria, for instance, as much as 54% of laboratory-confirmed measles patients were vaccinated [18].

WHO notes that errors in classification, reporting of measles cases in large outbreaks, submission of incomplete reports, lack of staff for databases filling, and errors in summarizing consolidated reporting can distort the true level of morbidity.

The purpose of surveillance for measles in countries of AFR with a low incidence of measles — increase coverage of second dose of the vaccine, surveillance for measles by the standards of elimination, broad coverage SIAs. Countries with high morbidity need to address a range of issues, including legal, political, health system strengthening, etc. [26, 36].

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