Review Article

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Pneumonia in South-East Asia Region: Public health perspective

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Globally, pneumonia is the leading cause of death in young children and burden of disease is disproportionately high in South-East Asia Region of WHO. This review article presents the current status of pneumonia disease burden, risk factors and the ability of health infrastructure to deal with the situation. Literature survey was done for the last 20 years and data from country offices were also collected. The estimated incidence of pneumonia in under five children is 0.36 episodes per child, per year. Risk factors are malnutrition (40% in India), Indoor air pollution, non-breast feeding, chronic obstructive pulmonary disease, *etc.* Strengthening of health care delivery system for early detection and treatment and as well as minimization of preventable risk factors can avert a large proportion of death due to pneumonia.

Key words Case management - causative organisms - disease burden - pneumonia - preventive interventions - risk factors

Introduction

Pneumonia remains the leading killer of young children despite the availability of simple, safe, effective and inexpensive interventions to reduce its capacity to kill^{1,2}. Childhood pneumonia is mainly a disease of poverty and results from sub-optimal child rearing and care seeking practices compounded by lack of access to healthcare. Pneumonia in adults is no less a public health problem and also requires effective interventions. Active and passive smoking, underlying chronic cardio-pulmonary and neurological illnesses, heavy alcohol intake, major trauma or surgery, long periods of recumbence, indoor air pollution, crowding, poor dental health, old age and institutional habitat or care are recognised risk factors for high incidence and mortality from the disease^{3,4}. Preventive and control interventions can be implemented at all levels

of healthcare but are not available in areas where these are most needed. Ongoing measures have been insufficient. To achieve the Millennium Development Goal on child mortality (MDG-4) in the South-East Asia (SEA) Region of WHO there is urgent need to vigorously renew our efforts against pneumonia.

To assess the status of pneumonia disease burden in SEA Region and associate risk factors, a systematic search of literature, limited to original research articles, systematic review papers/meta-analysis, consensus statements and guidelines in full or abstract form and published in English language between 1990 and 2010 was performed using PubMed, Cochrane Database, Google Search and Medscape. WHO publications from the Headquarters and the Regional Offices were also scanned. Some classic papers from before 1990 were also included.

Regional burden

In young children: The estimated incidence of pneumonia in children under five years of age in the SEA Region is 0.36 episodes per child year while the world average is 0.26 and the average for the developing countries 0.29⁵. For further comparison, incidence in developed countries is 0.05 episodes per child year⁵. Of the 156 million yearly new cases of childhood pneumonia worldwide, 61 million cases occur in the SEA Region. Of the estimated 3.1 million annual deaths among the under-five population in SEAR countries, 19 per cent are attributable to pneumonia and this does not take into account the pneumonia cases among neonatal infections/sepsis⁵.

India needs a special mention in the context of childhood pneumonia. In the numerical term, with 43 million new cases every year, India tops the list of 15 countries across the world with high disease burden⁵. Morbidity rates tend to vary between 0.2 to 0.5 episodes per child-year and approximately 10 to 20 per cent of these episodes tend to be severe⁶⁻¹⁰. Among the high burden countries, India has a mortality rate of 322 per 100 000 under-five population compared to China's 86⁵.

Besides being the leading cause of childhood mortality, lower respiratory infections are also the leading causes of disability-adjusted life years (DALYs) across the world and in the Region. In SEAR countries these account for almost 30 million DALYs and 1.4 million deaths across all age groups every year¹¹. These figures exclude DALYs and deaths caused by such respiratory diseases as TB, measles or whooping cough.

Reliable estimates of incidence or deaths are not available for the adult populations. Various studies including demographic studies and extrapolations from surveillance of "native populations" in developed countries suggest a high burden of pneumococcal disease in the adult populations of developing countries¹². Severe lower respiratory infections were reported to be the cause of deaths in 120 per million men and 76 per million women of 15-59 yr age group, worldwide, in the year 2000^{13} . In the >60 age group, rates of death from such infections increased by more than two-fold for each decade of life¹³. Much higher incidence of pneumonic illnesses among adults with AIDS not on anti-retroviral therapy (ART) is also a matter of serious concern in the Region. Chronic obstructive pulmonary disease (COPD), which is a major host factor to contribute to acute lower respiratory

tract infection or pneumonia in adults, is estimated to be prevalent in about 4 per cent of the Indian population, with male to female ratio of $1.56:1^{14}$.

Risk factors in the Region

In India, poverty, poor immunization status, indoor air pollution, overcrowding and malnutrition/ poor nutritional practices appeared to be the major risk factors. The same factors along with very young age, oxygen saturation (SpO₂) of <90 per cent or abnormal chest X-ray at presentation also determined the outcome¹⁵⁻¹⁹. Poverty and malnutrition underlie both the high incidence and deaths of young children from pneumonia in SEAR countries. But poor access to healthcare services is largely responsible for high mortality.

Malnutrition: Malnutrition contributes to more than one-third of all childhood deaths including that from pneumonia. In the absence of proper imaging, pneumonia in a severely malnourished child can often remain occult and yet be significantly much more lethal^{20,21}. Common bacterial pathogens in such children differ from those reported in children without severe malnutrition with more frequent infections with *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Escherichia coli*²⁰. In India, more than 40 per cent of children aged under-3 yr are underweight and more than half of all children under 6 months are not exclusively breastfed²².

Hygienic practices: Hand and respiratory hygiene are crucial in minimizing the spread of most organisms responsible for acute respiratory infections and pneumonia. Studies have shown that handwashing with soap and water can reduce the incidence of acute respiratory infections and pneumonia by up to 50 per cent²³⁻²⁵. The recommendations to cover the mouth and nose during coughing/ sneezing as a component of respiratory hygiene/cough etiquette have been based on their plausible effectiveness²⁶⁻²⁸.

Indoor air pollution: Air pollution from household use of solid fuels has been identified as one of the strong modifiable risk factors for acute respiratory infections and pneumonia for some time. In the rural and poor urban communities, especially in south Asian countries, traditional open ovens using wood or dried/ dehydrated animal dung as fuels are commonly employed in dwellings for cooking and heating. Children and other family members alike often live and sleep in closed or semi-closed cooking rooms and are thus exposed heavily to particulate matters with carbon monoxide, greenhouse gases, and other pollutants. A semi-quantitative epidemiological study done in Nepal during 1980s showed a direct relation between reported hours per day spent near the stove by infants and children under 2 yr and the episodes of life-threatening acute respiratory infection (ARI)²⁹. A meta-analysis of 24 studies on exposure to indoor air pollution caused by the use of unprocessed solid fuel concluded that the risk of pneumonia increased by a factor of 1.8 among the exposed young children³⁰. Dose-response relationship was also demonstrated for pneumonia deaths with the relative risk varying between 1.47 for some exposure and 5.23 for a high level of exposure³¹. Globally, 50 per cent of all households and 90 per cent of rural households use solid fuels as the main source of energy at homes³². In India and also in other countries of the SEA Region, domestic use of solid fuels for cooking as well as heating rooms is a common practice in the vast majority of the populations³³. In SEAR countries the estimated annual deaths and DALYs attributable to solid fuels are 559 000 and 15.1 million, respectively³⁴.

Mother's lack of education and inexperience as a caregiver is one more risk factor for childhood pneumonia that may be amenable to public health intervention³. Teenage pregnancy and lack of essential support by health services add to the impact from this risk. Fertility rates in South Asia range from 71 to 119 births per 1000 women aged 15-19³⁵. Mothers recognised fast breathing better than chest indrawing, and mothers having prior experience with childhood pneumonia recognised these signs better³⁶. Parental lack of education was shown to be a significant socio-demographic risk factor for both the incidence of childhood pneumonia and as a determinant of the outcome in India^{17,19}.

Active and passive smoking: In one population based case-control study, the risk of community-acquired pneumonia (CAP) attributable to the consumption of any type of tobacco was 32.4 per cent of cases³⁷. In subjects without a history of COPD, the population-attributable risk of tobacco was 23.0 per cent. A positive trend for increased risk of CAP was observed for an increase in the duration of the habit, the average number of cigarettes smoked daily and cumulative cigarette consumption. Former smokers had a 50 per cent reduction in the risk 5 yr after the cessation of smoking³⁷. In a meta-analysis of 38 studies to examine the relationship between parental smoking and acute lower respiratory illness in children, the risk increased

by a factor of 1.57 for smoking by either parent and by 1.72 for maternal smoking³⁸.

Chronic obstructive pulmonary disease (COPD): This is a common condition in the Region due to the high prevalence of the underlying risk factors, smoking and indoor air pollution^{13,14,39,40}. COPD in the Region tends to occur at an earlier age than in the rest of the world⁴⁰⁻⁴². By using the criteria developed by Anthonisen *et al*, an average patient with COPD suffers 2 or 3 attacks of acute exacerbation each year⁴³. And, more than half of the exacerbations are caused by a bacterial infection and about a third by viral^{44,45}.

Social determinants and access to services by the poor: Pneumonia burden is inversely related to access to healthcare. Healthcare resources in the Region, especially in India, are not seriously inadequate but unequal distribution of resources has been the major determinant of access to healthcare and disease prevention and control. Only about a fifth of the total health expenditure is borne by the State in high burden countries; the rest comes from the individual or family's 'out-of-pocket' expenses⁴⁶. The ratio of hospital beds to population in rural areas in India is 15 times lower than that for urban areas and the ratio of doctors to population in rural areas is almost six times lower than that in the urban population⁴⁷. Only 38 per cent of all Primary Healthcare Centres (PHCs) in India have all the essential manpower and only 31 per cent have all the essential supplies⁴⁸. A child from the low economic group is almost four times more likely to die in childhood than a child from the high economic group⁴⁸. Access to healthcare services suffers further from the deterrence generated by geographical distance and terrain difficulties, psycho-social, socio-economic and also gender distance.

Causative organisms: Pneumonia causing organisms can be viruses, bacteria, fungi or parasites; some of them vaccine preventable and others without a safe and effective vaccine.

Vaccine preventable disease causing organisms

Measles and pertussis: Pneumonia is the most common complication of both pertussis and measles and its frequency among patients with measles is about 2-27 per cent in a community and 16-77 per cent in hospital settings⁴⁹. South-East Asia Region, excluding India, recorded 34,529 and 32,323 cases of measles in 2008 and 2009, respectively. In India, in 2008 alone, 48,181 cases and 188 deaths were reported to the government⁵⁰. Large majority of deaths among the pertussis and measles patients is from pneumonia.

Pneumococcus is a leading cause of pneumonia and is the causative agent in 30-50 per cent of cases^{51,52}. Available data suggest that the disease incidence, including among the adult population, is higher in developing than in industrialized countries. In southern India, 54 per cent of infants were found to be colonised by the bacteria by the age of 2 months and 70 per cent become carriers by 6 months of age⁵³. Approximately 20 serotypes account for over 70 per cent of invasive disease. The global distribution of serotypes varies. Some serotypes commonly responsible for invasive disease in developing countries (particularly types 1 and 5) are no longer common in industrialized countries⁵⁴. The introduction of heptavalent conjugate vaccine in the developed countries and of the nine-valent conjugate vaccine in the Gambia had a substantial impact on the prevention of the disease in children, and indirect benefits to other age groups. Disease caused by antibiotic resistant strains was also reduced along with the reduction in antibiotic use^{55,56}. Newer conjugate vaccines with additional serotypes have the potential to reduce the burden further in developing countries.

Haemophilus influenzae type b is the second most common organism, isolated from 10 to 30 per cent of pneumonia cases, in most bacteriology-based studies of childhood pneumonia. However, the vaccine probe studies with Hib conjugate vaccine in the Region have shown a variable impact on the incidence of pneumonia^{57,58}.

Tuberculosis may also present as acute pneumonic illness. Vaccination with BCG is said to reduce the risks of invasive tuberculosis and death from tuberculosis by about 70 per cent. The degree of protection against pulmonary tuberculosis is uncertain⁵⁹.

Influenza viruses: In Finland, 14 per cent of influenza cases in children developed pneumonia which was mostly mild with mortality of 0.7 per cent⁶⁰. The same cannot be said about the pneumonia cases in developing countries with a greater likelihood of complication. In a recent study in Bangladesh, influenza was the cause in 10 per cent of all childhood pneumonia and 28 per cent of all children with influenza developed pneumonia. Among children with proven influenza, those with pneumonia were younger than those without⁶¹. Among infants hospitalized with pneumonia in rural Thailand, influenza was the responsible organism in 6.4 per cent and the median length of hospital stay was 5.0 days⁶².

Other causes

Bacterial: Mycoplasma pneumoniae, Chlamydia species, and Gram-negative bacteria such as *Escherichia coli* and *Pseudomonas* spp. are other less frequent bacterial causes of pneumonia in children. Study of causative organism among Thai adult patients with community-acquired pneumonia showed *C. pneumoniae* in 36.7 per cent, *M. pneumoniae* in 29.6 per cent, and *S. pneumoniae* in 13.3 per cent of outpatients, while *S. pneumoniae* (22.4%) and *C. pneumoniae* (16.3%) were the most common organisms in hospitalized patients⁶³.

Viral: Respiratory viruses account for 15-40 per cent of all admitted cases of pneumonia or acute lower respiratory tract infections in infants and young children in developing countries, and respiratory syncytial virus (RSV) is the leading viral cause in most studies including India^{64,65}. In one recent study from rural India, respiratory syncytial, influenza and parainfluenza virus specific incidence rates of acute lower respiratory tract infection in children under 3 yr of age were 48, 39 and 53 per 1000 child yr, or 0.048, 0.039 and 0.053 episodes per child-year⁶⁶. Human meta-pneumovirus and adenoviruses are other rarer causes that cannot yet be prevented by immunization. Secondary bacterial infection or co-infection with a bacteria or another respiratory virus may be seen in as many as 20 to 30 per cent of pneumonia episodes. RSV infection may leave the sequelae of the reactive airways disease and present as episodes of wheezing.

Fungal pneumonia is caused by any one or a combination of endemic or opportunistic fungi in certain geographic regions. *Pneumocystis jiroveci*, is an important organism among HIV/AIDS patients. During 48 months of follow-up of 1665 participants who were seropositive for human immunodeficiency virus type (HIV-1) but did not have the acquired immunodeficiency syndrome (AIDS) and were not receiving prophylaxis against *P. carinii* pneumonia⁶⁷. As this organism is estimated to cause pneumonia eventually in 75 per cent of AIDS patients and it has much significance from the public health perspective⁶⁸.

Prevention and control

Relatively inexpensive and simple, yet safe and effective measures have been available and are also emerging for both prevention and control of pneumonia or acute lower respiratory infection in all age groups. Reducing risk factors, improving case management at the household, community and facility levels, ensuring regular supervision and reliable logistics, and sound monitoring and evaluation are the most effective ways of reducing morbidity and mortality from pneumonia. Providing effective referral care for cases with severe pneumonia requiring oxygen, second-line antibiotics, and other supportive management will contribute further in reducing mortality. Lack of public health focus and commitment has allowed the burden to remain high. Bringing pneumonia back to the main focus is also crucial to achieve the MDG-4, and national public health programmes can do so by taking the following

Surveillance and disease burden estimation: Reliable estimation of pneumonia burden and region/country/ or locale-specific risk factors is still lacking in the Region especially from the remote areas inhabited by socioeconomically weak and marginalised populations and tribal groups. A focussed active surveillance system at the community level and integrated well with the national integrated disease surveillance system is imperative to determine the true burden, seasonality and trend of this important disease in all age groups. Data thus obtained will assist in ensuring appropriate programmatic focus on the disease.

steps.

Research, monitoring and evaluation: Re-focussing on this forgotten priority in the peripheries of health services means finding ways to scale-up implementation of the available interventions for prevention and case management. Implementation of available interventions for prevention and control has encountered known and unknown barriers in many parts of the Region and therefore there is a need for the researchers to focus on identifying the barriers and the means to remove them for scaling up.

Social mobilization: Spreading awareness about available interventions and educating the community on the ways to implement them locally are important for sustained reduction in pneumonia burden. Healthy and better care seeking practices need to be inculcated. This requires improved and effective communication between health workers and the members of the community. Focussed ethnographic studies at the community level can identify their perceptions about the disease and its causes and thus allow the development of more effective tools for prevention and control at the local level.

Mobilising national and international response: Data generated through reliable surveillance and research studies, especially on the burden size and remediable risk factors and control measures, can be used to mobilise response from the national and international partners and stakeholders through effective advocacy.

Preventive interventions

Interventions in the following main areas have been shown to be particularly effective in preventing pneumonia.

Feeding practices: Commencing exclusive breastfeeding early after birth and continuing up to the age of 6 months and continued breastfeeding to the age of 12 months help maintain a good level of nutrition and immunity against most infections in early childhood. These measures on their own have been estimated to prevent 1,301,000 deaths or 13 per cent of all child deaths². Proper attention to complementary feeding can reduce malnutrition by up to 20 per cent, reduce deaths caused by diarrhoea and pneumonia by 10 per cent and reduce the overall child mortality by 6 per cent².

Micronutrient supplement: This is another important aspect of child rearing in developing countries where the average diet of an infant or a young child is commonly deficient in crucial micronutrients such as zinc, vitamin A and iron. Zinc is particularly important in the context of childhood pneumonia and diarrhoea and the outcome of the measles pneumonia is usually poor in vitamin A deficient children. In one meta-analysis of South Asian studies, children who received daily or weekly oral zinc supplement for at least 3 months had the incidence of respiratory tract infections reduced by 8 per cent and that of lower respiratory tract infection or pneumonia by almost 20 per cent compared to those who received placebo⁶⁹. Similar effect was reported by another meta-analytical study of zinc supplementation and the diagnosis of pneumonia by active case-finding and a clinical examination including pulmonary auscultation⁷⁰. Strategy of providing a child with 10 mg twice daily of oral zinc for 10 to 14 days after every episode of acute diarrhoea helps in both the treatment of acute diarrhoea and prevention of pneumonia and diarrhoea for the next 2 to 3 months.

Immunization: Maximum possible coverage by routine immunization with measles vaccines supplemented by second opportunity for immunization with measles can significantly reduce childhood pneumonia and deaths. Increasing coverage with three doses of DPT vaccine during infancy can contribute further by preventing pertussis related pneumonia occurrence. Vaccine can be an important armament in preventing pneumococcal disease burden and an important complement to other available strategies for the prevention and control of pneumonia.

Hygiene practices: As a practical approach, people are advised to cough or sneeze into their arms or elbows to minimize the flight range of the generated droplets. Hand hygiene by washing hands frequently with soap and water or by alcohol based hand-rub should be an integral part of pneumonia prevention strategy.

Reducing indoor air pollution: Interventions to reduce exposure to indoor air pollution include engineering changes to improve household ventilation and domestic stoves, behaviour changes, and use of cleaner fuels. The changes entail personal and community beliefs and attitudes and are also determined by socioeconomic and cultural considerations. Promoting the use of clean burning stoves or ovens (high efficiency/ low emissions) with chimneys to direct the fumes away from homes could be used as a strategy. Research in technology should try to ensure that these can be locally crafted at low-cost. Reductions from 40 to 85 per cent in PM2.5, PM10, and CO concentrations have been described using improved stoves71-73. Alternatively, low cost clean burning fuel that can be used safely in these homes could be developed.

Behaviour change communication: Promotion of healthy practices such as handwashing and cough etiquette can be both difficult and expensive⁷⁴⁻⁷⁶. System change, administrative support with strong leadership, and enhanced motivation and education of caregivers combined with a sound system of public-private partnership have been suggested as helpful tools. Cost-effectiveness of bringing the change and sustainability of the changed behaviour are major issues even though the knowledge of the suggested best practice stays in the community⁷⁷.

Social mobilization and inter-sectoral collaboration/ co-ordination for education of mothers and other caregivers on child-rearing and care-seeking practices, and for promoting better housing, heating and cooking conditions in resource constrained communities will be crucial to enhance mothers' ability to provide appropriate care to their children and to minimize the indoor air pollution. Intensive community mobilization for anti-smoking campaigns is likely to help reduce the incidence of pneumonia in all age groups^{78,79}.

Case management: This involves resource mobilization, capacity building, finding and diagnosing cases at

various levels of health system and providing effective treatment, referral and follow up advice as appropriate. Bacterial infection seems to account for the vast majority of cases of acute lower respiratory tract infections in both children and adult population and, therefore, antibiotics should remain the cornerstone of initial management once the diagnosis is made. Appropriate follow up by observing for simple clinical parameters is often enough to make a decision about referral and the decision can be further refined by complementing with objective measurements of oxygen saturation and heart rate. Use of handy and inexpensive electronic communication tool is becoming common even in distant rural communities and incorporating the use of such tools into the national prevention and control programme can be expected to improve the referral system as well as the supervision and guidance from higher level facilities and needs to be tested at the field level for cost-effectiveness

In children: This involves identifying a child with cough or difficulty in breathing as having pneumonia, severe or very severe pneumonia or having no pneumonia and then managing them accordingly. In the context of cough or difficulty in breathing, pneumonia is defined as tachypnoea (respiratory rate ≥ 60 breaths per minute for children under 2 months of age, >50 breaths per minute from 2 to 11 months of age, or >40 breaths per minute in children from 1 to 4 yr of age); severe pneumonia is diagnosed if the symptoms are associated with lower chest wall indrawing or subcostal retraction, and very severe pneumonia if there is a danger sign such as central cyanosis, or severe respiratory distress, convulsion, inability to rouse the child or if the child is unable to drink. Correct management of pneumonia requires a staff trained on the standard management protocol for ARI and a steady supply of antibiotics for early treatment based on easily detectable clinical signs of pneumonia. Availability of small and portable pulse oximeter may further simplify the diagnosis of severe and very severe pneumonia both at the facility and community levels. This merits research with randomised field trials

Over the years, interventions at the community level, including the community case management of childhood pneumonia, have been gaining support from both researchers and programme managers but scaling-up of this strategy has been slow in most high burden countries of the SEA Region^{1,4,80}.

In adults: As the disease is also common among the middle-aged and elderly individuals, research on the

feasibility and effectiveness of the community case management strategy in these age groups is probably now overdue. Simplifying diagnosis at the community or household level, based on the presence of cough, volume and purulence of sputum, difficult breathing, increased respiratory rate and activity of the accessory muscles of respiration, pulse oximetry, *etc.* should be possible. This would allow initiating treatment with oral antibiotics such as co-trimoxazole, amoxicillin or a fluoroquinolone.

Way forward

Implementing available interventions and scaling-up: Reducing risk factors by implementing effective interventions, promoting research on more effective ways to implement them, improving case management, having a good system of monitoring, evaluation and supervision, ensuring local availability of essential drugs and supplies, especially the antibiotics, are the most effective ways of reducing morbidity and mortality from pneumonia in the community and first-level facility. Providing effective referral to patients with severe pneumonia who need oxygen, second-line antibiotics and other supportive management will assist further in reducing mortality due to pneumonia.

Integration: Integrating preventive interventions at the community level with effective case management in all age groups is likely to be more effective in reducing the disease burden. Modes of intervention for the prevention and control of pneumonia are not very different from those for acute diarrhoea. Both conditions mostly create the maximum health impact on similar age groups and respond to interventions aimed at health promotion, disease prevention and case management. These interventions require intensive social mobilization, a good system of surveillance at the community level, continuous monitoring and evaluation at regular intervals. Integrating the prevention and control of pneumonia with that of acute diarrhoea therefore becomes a rational and cost-effective approach.

Essential strategic elements: In seeking solution to this important public health problem in the Region, WHO-SEARO established in 2008 Regional Technical Advisory Group (RTAG) for the intensified integrated programme for the prevention and control of acute diarrhoea and respiratory infections which deliberated in April 2009 and made recommendations for a regional strategy comprising five specific points: Preventive interventions, Case management, Community mobilization and empowerment, Surveillance, research, monitoring and evaluation, and Mobilising national and international response.

Taking note of the Regional burden, the 63rd Regional Committee of the South-East Asia Region once again adopted the resolution on the coordinated approach to prevention and control of acute diarrhoea and respiratory infections in September 2010. Improved breastfeeding practices, appropriate complementary feeding, expanded immunization coverage, handwashing and respiratory hygiene, improved air and water quality at homes, improved community sanitation practices, and zinc supplements to children have been identified as the core preventive strategies⁸¹. These interventions have been shown to be effective both at the research and programmatic levels. Research now needs to come up with effective tools for scaling up these interventions and also for further strengthening of case management and referral, monitoring, and supervision system in a cost-effective manner.

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466

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