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***Корреспондирующий автор.*** *Аманова Айым, студент 2 курса, Факультета «Общая медицина», НУО «Казахстанско-Российский медицинский университет», Казахстан, Алматы. E-mail: aiym.amanova00@mail.ru.*

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***Corresponding author.*** *Amanova Aiym, 2nd year of student, Faculty of General Medicine, NEI Kazakh-Russian Medical University, Kazakhstan, Almaty. E-mail: aiym.amanova00@mail.ru.*

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# THE EVOLUTION OF TUBERCULOSIS TREATMENT IN INDIA FROM SANATORIUMS TO PERSONALIZED MEDICINE

***Aryan Singh**
NEI «Kazakh-Russian Medical University», Kazakhstan, Almaty

**Summary**

Tuberculosis (TB) is a serious infectious disease that has affected humans for centuries. The treatment of TB has evolved significantly over the years, from the use of sanatoriums as the primary treatment method to the introduction of antibiotics and the emergence of personalized medicine. Sanatoriums were popularized in the late 19th and early 20th centuries but were limited in their accessibility and cost. The discovery and development of antibiotics, such as streptomycin and isoniazid, led to the widespread adoption of antibiotics as the primary treatment for TB. Personalized medicine is a new approach that targets the specific needs of each patient through genotyping and individualized drug regimens. The future of TB treatment may lie in individualized, personalized approaches. This article is a literature review on the mentioned topic based on Case Studies.

***Key word:*** *tuberculosis, sanatoriums, isoniazid, vaccines, NTEP.*

**Aim:** This review will examine the history of tuberculosis treatment with the help of analyzing medical literature, including the development of sanatoriums as a primary treatment method, the introduction of antibiotics, and the emergence of personalized medicine as a new approach to treating the disease.

Tuberculosis (TB) is a chronic infectious disease caused by the bacterium Mycobacterium tuberculosis. It is one of the leading causes of death worldwide, with an estimated 10 million new cases and1.4 million deaths in 2019. India has the highest burden of TB in the world, with an estimated 2.8 million new cases and 480,000 deaths in 2019 [1].

TB is primarily a lung disease but can also affect other parts of the body such as the lymph nodes, bones, and joints. The most common symptoms of TB are a persistent cough, chest pain, and difficulty breathing. Other symptoms may include fever, night sweats, weight loss, and weakness [2].

**Case Study: A Patient with Tuberculosis.**

This is a hypothetical case in which a typical case and treatment plan of tuberculosis is elaborated for the better understanding of the disease.

**Patient Information:**

• Patient is a 35-year-old female who presents with a 2-month history of cough, fever, weight loss, and night sweats.

• Patient has no known underlying medical conditions and is a non-smoker.

• Patient reports no history of recent travel or contact with individuals with TB.

**Medical History:**

• Patient underwent a chest X-ray and sputum culture, which revealed the presence of acid-fast bacilli (AFB) and a positive result for Mycobacterium tuberculosis.

• Patient was diagnosed with pulmonary TB and started on a 6-month regimen of isoniazid, rifampin, pyrazinamide, and ethambutol.

**Clinical Course:**

• Patient's symptoms improved significantly within the first month of treatment, and her sputum culture converted to negative at 2 months.

• Patient completed her 6-month regimen of TB treatment without any significant adverse events.

• Patient underwent repeat chest X-ray and sputum culture at the end of treatment, which both returned negative.

• Patient was considered cured of TB and discharged from TB care.

This case study illustrates a typical presentation and course of treatment for a patient with pulmonary TB. It highlights the importance of early diagnosis and appropriate treatment in achieving a cure and preventing the spread of TB. However, it is important to note that this is a single case and it should not be generalized to all patients with TB [3].

Please note that this is a fictional case study, and it is important to follow all ethical guidelines when conducting any medical research.

**Course of advancement in the treatment of tuberculosis.**

The evolution of tuberculosis (TB) over the decades has been characterized by a number of significant advances in understanding the disease, its causes, and the ways in which it can be treated and prevented. Some key developments include [4]:

**1. Discovery of the causative agent:**

In 1882, Robert Koch, was the first person who discovered the bacterium Mycobacterium tuberculosis which was considered as the cause of TB. This discovery led to the development of diagnostic tests, such as the acid-fast stain, which allowed for the rapid identification of TB bacteria in sputum samples.

**2. Introduction of sanatorium treatment:**

In the late 19th and early 20th centuries, sanatoriums were established to treat TB patients. The idea behind sanatorium treatment was to provide patients with a healthy environment, plenty of fresh air and sunshine, and a nutritious diet, with the aim of helping their bodies to fight off the disease [5].

**3. Introduction of drug therapy:**

In the 1940s and 1950s, the first drugs were developed to treat TB, such as streptomycin and isoniazid. These drugs were highly effective in curing TB, but their use was limited by the development of drug-resistant strains of TB.

**4. Introduction of multidrug therapy (MDT) in the 1980s:**

In the 1980s, WHO introduced the concept of multidrug therapy (MDT) for the treatment of TB. MDT consisted of a combination of at least three drugs (isoniazid, rifampin, pyrazinamide, and ethambutol) and was found to be highly effective in curing TB and preventing the development of drug-resistant TB.

**5. Development of new TB drugs:**

In the 1990s and 2000s, new TB drugs were developed, such as fluoroquinolones, and these drugs were added to the treatment regimens for TB.

The development of new drugs to treat tuberculosis (TB) is critical, as the standard TB treatment regimen is long and complicated, and drug-resistant TB is becoming more common. Fluoroquinolones, a class of antibiotics, have been of particular interest in recent years due to their promising activity against TB.

Fluoroquinolones work by inhibiting the bacterial DNA gyrase, which is necessary for DNA replication in the bacteria. By interfering with DNA replication, fluoroquinolones can kill or slow the growth of TB bacteria [5].

One of the most promising fluoroquinolones for TB treatment is moxifloxacin. Studies have shown that adding moxifloxacin to the standard TB treatment regimen can lead to faster sputum conversion (i.e., the time it takes for a patient's sputum to become negative for TB bacteria), as well as better treatment outcomes.

For example, delamanid is a novel fluoroquinolone that has been approved for use in drug-resistant TB, and is being studied for use in combination with other drugs in the standard TB treatment regimen.

**6. Introduction of Directly Observed Treatment, Short-course (DOTS) strategy:**

In the era of 1990s, WHO introduced the DOTS strategy for TB control. DOTS involves the use of a combination of MDT and active case finding, as well as the use of trained health workers to ensure that patients take their medication as prescribed. DOTS has been shown to be highly effective in improving TB treatment outcomes and reducing the spread of TB.

**The DOTS strategy involves five key elements:**

A. Political commitment and sustained financing: Governments are responsible for providing the necessary resources and political commitment to ensure that TB control programs are adequately implemented and sustained over time.

B. Case detection through quality-assured bacteriology: This involves testing suspected TB patients for the presence of TB bacteria using sputum microscopy or other diagnostic tests. Ensuring the accuracy of the diagnosis is critical to the success of the DOTS strategy.

C. Standardized treatment with supervision and patient support: The standard TB treatment regimen consists of a combination of four drugs that must be taken for at least six months. The treatment is supervised by a healthcare worker or trained volunteer, who ensures that the patient takes the medication correctly and consistently.

D. An effective drug supply and management system: This involves ensuring that drugs are available and of high quality, and that the supply chain is well-managed to avoid stock-outs and wastage.

E. Monitoring and evaluation system and impact measurement: This involves monitoring the performance of TB

control programs and evaluating their impact. This information is used to make adjustments to the programs to ensure they are effective and to inform future policy decisions.

In recent years, the DOTS strategy has been expanded to include other interventions, such as the use of rapid diagnostic tests and the treatment of latent TB infection, to further improve TB control efforts.

**7. Development of rapid diagnostic tests:**

In the 2000s, new rapid diagnostic tests for TB were developed, such as GeneXpert and LED-microscopy, which have improved the speed and accuracy of TB diagnosis.

One of the most promising rapid diagnostic tests for TB is the Xpert MTB/RIF test, which uses molecular techniques to detect TB bacteria in sputum samples. The test can produce results in as little as two hours and has been shown to be highly accurate in several studies. The Xpert MTB/RIF test also detects resistance to rifampicin, one of the most important drugs used to treat TB, which can help guide treatment decisions for patients with drug-resistant TB [4, 5].

Other rapid diagnostic tests for TB include the line probe assay and loop-mediated isothermal amplification (LAMP) assay, which also use molecular techniques to detect TB bacteria in sputum samples. These tests have shown promising results in several studies and offer the potential for faster and more accurate diagnosis of TB.

Overall, the development of rapid diagnostic tests for TB has the potential to transform TB control efforts by enabling more timely and accurate diagnosis of TB, especially in resource-limited settings where traditional diagnostic methods may not be feasible. These tests can also help guide treatment decisions and improve patient outcomes, which can ultimately lead to a reduction in TB-related morbidity and mortality.

**8. Introduction of new TB treatment regimens:**

In the 2010s, new TB treatment regimens were developed, such as the shorter, all-oral regimen of 6-9 months, which have improved treatment adherence and outcomes for patients with TB.

The introduction of new TB treatment regimens has been an important development in the fight against tuberculosis (TB). Traditional TB treatment consists of a combination of four drugs that must be taken for at least six months. In addition, the emergence of drug-resistant TB has highlighted the need for new, more effective treatment regimens.

One of the most significant advances in new TB treatment regimens has been the introduction of shorter treatment regimens. The Shorter MDR-TB Treatment Regimen is a nine to twelve month regimen for the treatment of multidrug-resistant TB (MDR-TB), which is a form of TB that is resistant to at least two of the most important drugs used to treat TB. The regimen consists of four drugs, including a new drug called bedaquiline, which has been shown to be highly effective against MDR-TB. The regimen has been shown to be highly effective in several clinical trials and has been endorsed by the World Health Organization (WHO) [5].

The introduction of new TB treatment regimens has been a collaborative effort between researchers, industry, and global health organizations. The development of new TB drugs has been supported by initiatives such as the Global TB Drug Pipeline, which aims to accelerate the development of new TB drugs by providing funding and support for research and development.

**9. Development of new TB vaccines:**

In recent years, new TB vaccines have been developed and are currently in clinical trials, such as the MVA85A and the TBVAC, which has shown promising results in preventing TB.

The development of new TB vaccines has been a critical area of research in recent years. TB is a global health problem that affects millions of people each year, and a vaccine is seen as a key tool in controlling the spread of the disease. The current TB vaccine, called the Bacille Calmette-Guérin (BCG) vaccine, has been in use for over 100 years and is only partially effective in preventing TB. Therefore, the development of a new, more effective TB vaccine is a high priority for the global health community.

There are currently several new TB vaccine candidates in various stages of development. These vaccines aim to provide better protection against TB than the BCG vaccine and may be effective against different strains of TB. Some of the most promising vaccine candidates include the M72/AS01E vaccine, the H56:IC31 vaccine, and the ID93/GLA-SE vaccine.

The M72/AS01E vaccine is a protein subunit vaccine that targets two proteins found in the TB bacteria. It has shown promising results in early-stage clinical trials and is currently undergoing larger-scale clinical trials to evaluate its effectiveness.

The H56:IC31 vaccine is another protein subunit vaccine that targets three proteins found in the TB bacteria. It has also shown promising results in early-stage clinical trials and is currently undergoing larger-scale clinical trials [6].

The ID93/GLA-SE vaccine is a subunit vaccine that targets four proteins found in the TB bacteria. It has shown promising results in animal studies and is currently undergoing clinical trials to evaluate its safety and effectiveness.

The development of new TB vaccines has been a collaborative effort between researchers, industry, and global health organizations. The TB Vaccine Initiative (TBVI) is one organization that is working to accelerate the development of new TB vaccines by providing funding and support for research and development.

VPM1002 is a novel tuberculosis (TB) vaccine candidate that is being developed by Serum Institute of India Pvt. Ltd. (SIIPL) in collaboration with the Max Planck Institute for Infection Biology in Berlin, Germany. Here are some key points about the clinical trials of VPM1002:

(A) VPM1002 vaccine: VPM1002 is a genetically modified form of the Bacillus Calmette-Guérin (BCG) vaccine, which is currently the only licensed vaccine for TB. VPM1002 is designed to improve upon the efficacy of the BCG vaccine and provide better protection against TB.

(B) Clinical trial phases: The clinical development of VPM1002 is ongoing, with several clinical trials completed or underway. Phase I clinical trials were conducted in Germany in 2009-2010, which showed that VPM1002 was safe and well-tolerated. Phase IIa clinical trials were conducted in South Africa in 2012-2015, which showed that

VPM1002 was safe and induced an immune response [7].

(C) Phase III clinical trials: The phase III clinical trial of VPM1002, known as the VACSEL study, is currently underway in India. The study aims to enroll around 12,000 participants and evaluate the efficacy of VPM1002 in preventing TB in high-risk individuals, such as household contacts of TB patients. The study is expected to be completed by 2024.

(D) VPM1002 availability: If the phase III clinical trial of VPM1002 is successful, it could lead to the licensure and availability of a new and improved TB vaccine in India and other high-burden TB countries. However, it is important to note that the vaccine's efficacy and safety profile will need to be carefully evaluated before it can be widely used [7].

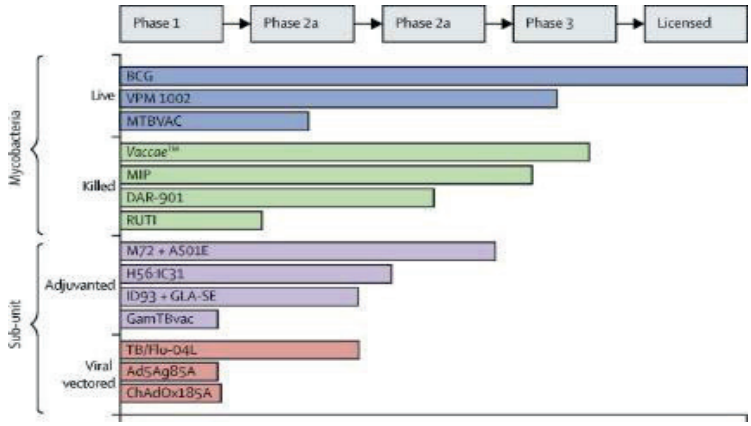


***Figure 1.*** *Clinical trial phases. [Made by Author]*

**10. Introduction of digital tools and mHealth:**

In recent years, digital tools and mHealth have been developed to improve TB control efforts, including the use of mobile phone-based reminders for patients to take their medication and digital platforms for reporting and monitoring TB cases.

In conclusion, tuberculosis is a major public health problem in India and worldwide, and requires a comprehensive, multi-sectoral response. The WHO End TB Strategy and the National TB Elimination Programme in India provide a roadmap for achieving the goal of TB elimination. However, the emergence of drug-resistant strains of TB, including MDR-TB and XDR-TB, highlights the need for continued research and innovation in the development of new drugs, diagnostics, and vaccines [6; 7].

**Indian scenerio of tuberculosis.** India is currently one of the countries most affected by tuberculosis (TB). However, the Indian government has set ambitious goals to combat the disease and improve the health of its citizens.

The National Strategic Plan for TB Elimination (2017-2025) aims to reduce TB deaths by 90% and cut new TB cases by 80% by 2025. To achieve this, the government plans to increase funding for TB control and research, expand access to diagnosis and treatment, and improve the monitoring and evaluation of TB programs.

In addition, the government is working to improve the overall health system by strengthening primary care and increasing access to affordable, quality care. This will help to ensure that people with TB are diagnosed and treated in a timely manner, and that those who are cured do not relapse.

There is a strong focus on community-based approaches such as involving private sector, NGOs, and community-based organizations in identification, referral and follow-up of TB patients. The government is also working to improve the quality of life for people with TB by providing them with social and economic support, such as food, housing, and job training.

The future vision of India in regard of TB is to eliminate the disease as a public health threat by 2025. With the ongoing efforts of the government and the collaboration of various sectors, India is on track to achieving this goal and creating a healthier future for its citizens.

It's also important to note that India is working on the latest technological advancements such as using Artificial Intelligence and Machine Learning in the diagnosis and treatment of TB, which will bring new opportunities in the TB control efforts.

There are several factors that contribute to the high burden of TB in India. The country has a large population, with a high prevalence of poverty and poor living conditions, which increase the risk of TB transmission. Additionally, India has a high burden of HIV infection, which increases the risk of TB among people living with HIV [7].

The Indian government has been implementing the National TB Elimination Programme (NTEP) since 1962, which aims to control and eliminate TB in the country. The program is based on the World Health Organization (WHO) recommended strategy of directly observed therapy, short-course (DOTS) and has been successful in increasing the detection and treatment of TB cases. However, the program has not been able to fully control the TB epidemic in India.

One of the main challenges facing the NTEP is the high proportion of TB cases that are not reported to the program. This is due to a lack of awareness about TB, stigma associated with the disease, and inadequate health infrastructure in many parts of the country.

Another major challenge is the emergence of drug-resistant strains of TB, including multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB). These forms of TB are harder to treat and require more expensive and complex regimens, putting a strain on the already overburdened health system.

In recent years, the Indian government has increased its efforts to control and eliminate TB, including the launch of

the National Strategic Plan for TB Elimination (2017-2025) which aims to achieve the goal of TB elimination by 2025. The plan focuses on increasing case detection, improving treatment outcomes, and reducing TB-related deaths.

It also includes measures to address the needs of vulnerable populations and improve the overall health system.

Under the RNTCP/NTEP, TB services are available at all public health facilities, including primary health centers, district hospitals, and medical colleges. The program also works in collaboration with private healthcare providers to increase the availability of TB diagnosis and treatment services.

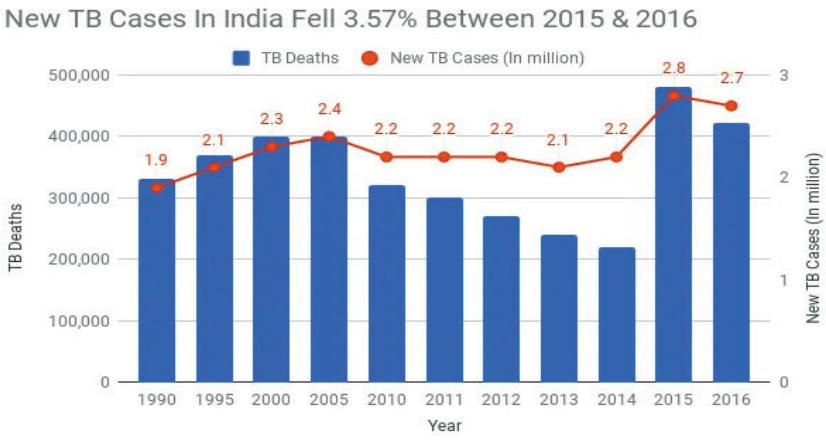


***Figure 2.*** *New TB Cases in India (1190-2016). [Made by Author]*

The RNTCP/NTEP has achieved significant success since its launch in 1997. The program has been successful in reducing the prevalence of TB in India, and has increased the percentage of TB patients who complete their treatment regimen. The program has also made significant progress in detecting and treating drug-resistant TB [6; 7].

However, despite these successes, challenges still remain in the fight against TB in India. These challenges include improving access to TB services in remote areas, strengthening infection control measures, and ensuring that patients complete their treatment regimen.

**References:**

1. World Health Organization (WHO). Global Tuberculosis Report 2021. https://www.who.int/publications/i/item/9789240037021.

2. Migliori G.B., Sotgiu G., Gandhi N.R., et al. Drug resistance in tuberculosis. Cold Spring Harbor perspectives in medicine, 2015, 5(9), a017800. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4556232/.

3. Zumla A., George A., Sharma V., et al. The WHO 2014 Global tuberculosis report—further to go. The Lancet Global Health, 2015, 3(1), e10-e12. https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(14)70361-4/fulltext.

4. World Health Organization (WHO). Treatment of Tuberculosis: Guidelines for Treatment of Drug-Susceptible Tuberculosis and Patient Care, 2017 Update. https://www.who.int/tb/publications/2017/dstb_guidance_2017/en/.

5. Johnson J.L., Neumann G., MacKenzie T., et al. Optimizing treatment for drug-resistant tuberculosis. PLoS medicine, 2006, 3 (3), e120. https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0030120.

6. Centers for Disease Control and Prevention (CDC). Treatment of Tuberculosis. CDC, 2022. https://www.cdc.gov/tb/topic/treatment/default.htm.

7. World Health Organization (WHO). The End TB Strategy. WHO, 2015. https://www.who.int/tb/post2015_strategy/en/.

## ЭВОЛЮЦИЯ ЛЕЧЕНИЯ ТУБЕРКУЛЕЗА В ИНДИИ ОТ САНАТОРНО КУРОРТНОГО ЛЕЧЕНИЯ К ПЕРСОНАЛИЗИРОВАННОЙ МЕДИЦИНЕ

***Aryan Singh**

НУО «Казахстанско-Российский медицинский университет», Казахстан, Алматы

**Аннотация**

Туберкулез (ТБ) – тяжелое инфекционное заболевание, поражающее людей на протяжении веков. Лечение туберкулеза значительно эволюционировало с годами: от использования санаториев в качестве основного метода лечения до внедрения антибиотиков и появления персонализированной медицины. Санатории были популярны в конце 19 - начале 20 веков, но их доступность и стоимость были ограничены. Открытие и разработка антибиотиков, таких как стрептомицин и изониазид, привели к широкому внедрению антибиотиков в качестве основного средства лечения туберкулеза. Персонализированная медицина — это новый подход, ориентированный на конкретные потребности каждого пациента посредством генотипирования и индивидуальных схем лечения. Будущее лечения туберкулеза может заключаться в индивидуальных подходах. Данная статья представляет собой обзор литературы по указанной теме на основе тематических исследований.

***Ключевые слова:*** *туберкулез (ТБ), санатории, изониазид, вакцина, НИСТ.*

# ҮНДІСТАНДАҒЫ ТУБЕРКУЛЕЗДІ ЕМДЕУДЕ КУРОРТТЫҚ ЕМДЕУДЕН ЖЕКЕ МЕДИЦИНАҒА ДЕЙІНГІ ЭВОЛЮЦИЯСЫ

***Aryan Singh**
«Қазақстан-Ресей медициналық университеті» МЕББМ, Қазақстан, Алматы

**Түйінді**

Туберкулез (ТА) ғасырлар бойы адамдарды ауыртып келген ауыр жұқпалы ауру. Туберкулезді емдеу жылдар бойы шипажайда емдеудің негізі ретінде пайдаланудан антибиотиктерді енгізуге және жеке медицинаның пайда болуына дейін айтарлықтай дамыды. Шипажайлар 19 - ғасырдың аяғы мен 20 - ғасырдың басында танымал болды, бірақ олардың қолжетімділігі мен құны шектеулі болды. Стрептомицин және изониазид сияқты антибиотиктердің ашылуы және дамуы антибиотиктерді туберкулездің негізгі емі ретінде кеңінен енгізуге әкелді. Жекелендірілген медицина – генотиптеу және жеке емдеу режимдері арқылы әрбір пациенттің нақты қажеттіліктеріне бағытталған жаңа көзқарас. Туберкулезді емдеудің болашағы жеке тәсілдерге байланысты болуы мүмкін. Бұл мақалада осы тақырып бойынша мысалдар негізіндегі әдебиеттерге шолу жасалады.

***Кілт сөздер:*** *туберкулез (ТА), шипажайлар, изониазид, вакцина, ҰСЖТИ.*

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***Корреспондирующий автор.*** *Aryan Singh, студент 2 курса, Факультета «Общая медицина», НУО «Казахстанско-Российский медицинский университет», Казахстан, г. Алматы. E-mail: nauka@medkrmu.kz; https://orcid.org/0000-0003-2724-2328.*

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***Corresponding author.*** *Aryan Singh, 2nd year of student, Faculty of General Medicine, NEI «Kazakh-Russian Medical University», Kazakhstan, Almaty. E-mail: nauka@medkrmu.kz; https://orcid.org/0000-0003-2724-2328.*

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