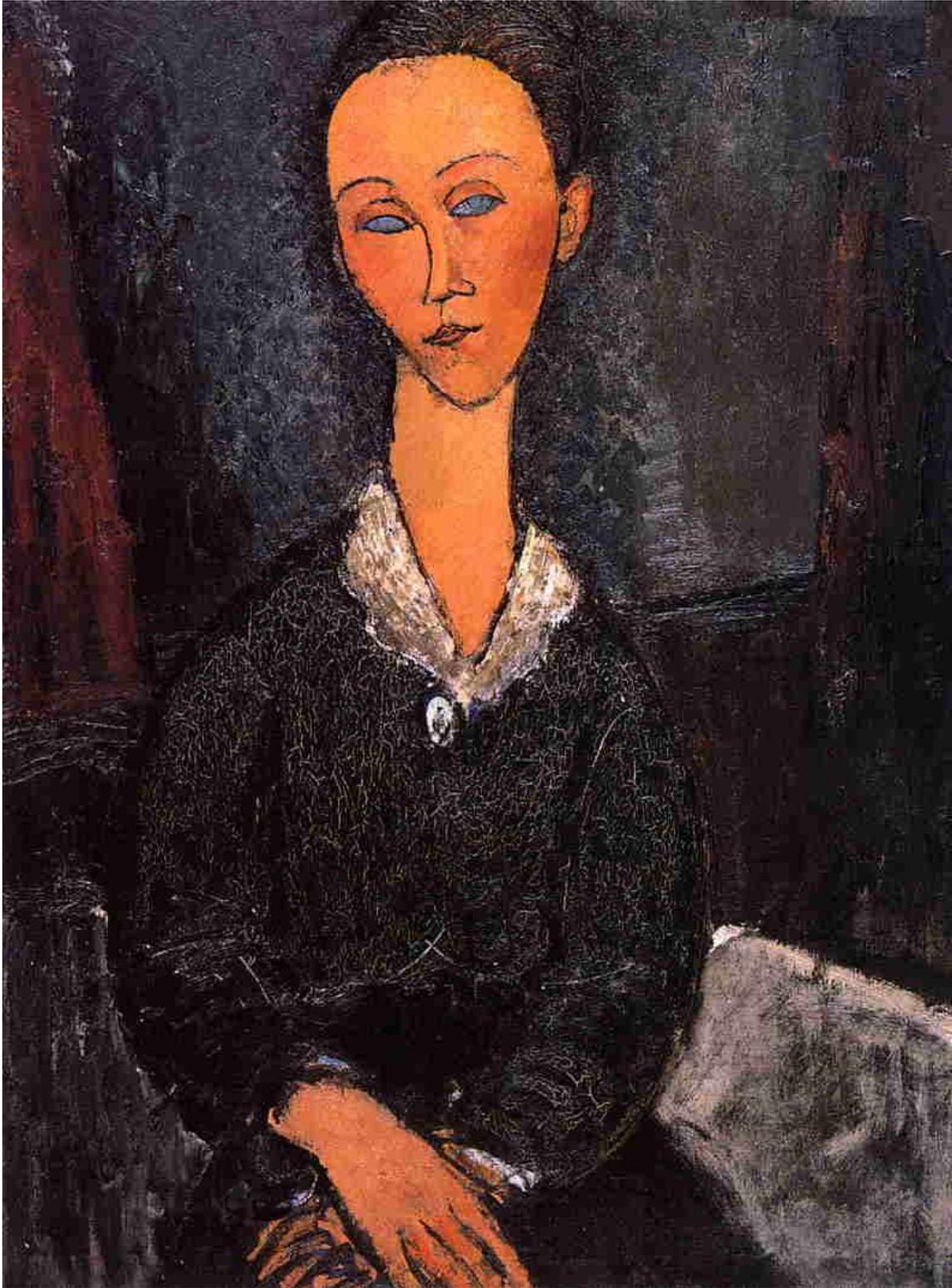


ETHAMBUTOL



"Lunia Czechowska", oil on canvas, 1917, Amedeo Modigliani.

Amedeo Modigliani's portraits are strikingly characteristic. At first glance they seem simple, naive even, but this is to miss the genius of the man. With a few seemingly simple lines he could capture the very essence of his subject - an ability that Art experts say make him surprisingly difficult to copy. He made the lines look so deceptively simple and effortless, a trap which has deceived many a would-be forger over the years. Those experts who know his work are quickly able to assess the authenticity of a "Modigliani" original - today worth tens of millions of dollars - should one even come onto the market at all. His portraits, though abstract, were not so much so as to lose all semblance of likeness in the manner of a Picasso. By just a few lines he captured the outward essence his subject. And yet he did not capture the true inner essence of them. Many of them seem quite expressionless, even manikin like. To understand why is to understand his life.

His recent biographer Meryle Secrest argues that Modigliani though outwardly engaging, charming even flamboyant in fact kept a sad distance to most acquaintances. This was due in part to his tuberculosis - as terminal disease in the early Twentieth century. Modigliani's case was advanced when diagnosed. He knew that the doctors could do nothing for him and that his condition was terminal. He would die at the age of just thirty six years. This disease was highly stigmatized and those who contracted it would go to extraordinary lengths to hide it from others. For Modigliani there was the added shame of his desperate poverty, all the more acutely felt in view of his family's once relative wealth, but now disastrously lost in business ventures gone badly wrong. He was also deeply religious. He was terrified of the fate that awaited him in the afterlife, as he believed that his debauched womanizing and drinking would earn him a less than ideal existence in the hereafter. He was well versed in Dante and in drunken diatribes would often quote long passages from the "Inferno". And so he kept his distance from most people, even those supposedly close to him. He disguised his intractable cough with the liberal use of opium and laudanum. He hid his grief and consoled himself with alcohol and viewed the world through the distorted prism of an opium haze and the absinthe glass. And to hide the visible signs of his disease he wore elaborate scarves to conceal the tuberculous nodes in his neck.

His portrait of Lusia Czechowska of 1917 shows all of the hallmarks of his works. It is an abstract work, but by skilful flowing lines still shows a clearly recognizable likeness. In his younger years Modigliani adored sculpture, especially the caryatids of the classical Greek world, and many of his works of women reproduce the classical elongated graceful lines of these ancient structures. One of his bitterest moments was the realization that he could no longer sculpt due to the toll that stone dust was taking on his tuberculous lungs. He turned to painting instead but retained many stylistic features of his sculpture work. During his time as a sculptor he became greatly fascinated by African works - in particular of the mystical elongated face masks with their triangular aspect, long noses and small mouths, that were being produced at the end of the Nineteenth century. One of the striking features of Modigliani's portraits are the Africa mask like appearance of his subjects, the feature that gives them the impenetrable manikin-like appearance. Meryle Secrest has suggested that this symbolism could reflect Modigliani's own emotional mask that he presented to others. With his inability to be close to people perhaps he is seeing the very same detachment in others. He sets up a protective barrier between himself and his subject. This theme is fascinatingly continued in the eyes. Many do not have pupils or defined parts - they merely appear and blank spaces. The eyes being of course the "window to the soul" - he could not bring himself to get that close to anyone, including

his wife Jeanne whose portraits' appear with the same blank eyes. Interestingly also none of his portraits are of people smiling. It was as if his anguish with life seems to have erased his sense of a smile all together. He could paint the aura of serenity or at least peace with an inner hurt - but never an overt outward smile. He once wrote, "Happiness is an angel with a grave face".

Though he could not easily get emotionally close to women, even though he was a "hot blooded" Italian, he loved women dearly - almost all his works are of women rather than men. Besides the graceful lines, the masklike faces and the blank eyes, another striking feature we see is the long elongated swan-like necks of his women. A feature much less pronounced, or otherwise entirely missing in his few portraits of men that we see. In this regard he was following an ideal Pre-Raphaelite aesthetic. He was well familiar with their works of the mid Nineteenth century. This aesthetic had its roots in the saintly ethereal idyll of the beautiful and sometimes heroically tragic muse, drifting around with loose flowing robes and plunging necklines that revealed the perfect Victorian alabaster swan neck. Indeed a perfect neck was a sign of good health - no evidence of tuberculous nodes. We see this time and again in particular with Rossetti's depictions of Jane Morris, his mistress (and wife of his good friend, William Morris). For Modigliani also, a perfect neck was an essential feature of a perfect woman.

One afternoon Modigliani had distressed his lover Lusia Czechowska. She had been increasingly concerned by his manic behaviour, which frequently alternated with his bouts of severe depression. He had been singing at the top of his voice whilst sitting on a windowsill high above the street level and she had become afraid that in his elevated state (literally as well as figuratively) he would fall. She invited him for dinner in order to try and calm him. She sat him down and lit a small candle in the fading light, and spoke to him softly while she cooked, until he calmed, then went quite. He suddenly asked to her look up and by the light of the candle he produced a beautiful portrait of her, and finished it off by embellishing it with his favourite aphorism of the final few months of his life... "Life is a gift".

The first antibiotics effective against tuberculosis were developed in the 1950s, tragically too late for Amedeo, and countless other young people of his generation who died of the disease in the 1920s. Modern anti-tuberculosis drugs if used early could have saved Modigliani - a young person who understood that "life was a gift". These agents could have also improved his quality of life, enabling him to discard his neck scarf. His sense of life was heightened by the unnatural limit that dread fate had put on it. A fate that engendered an idealism as well as and a sad fatalism, dealt with by alcohol, opioids and his Art. Out of great sadness and tragedy however is frequently born great Art.

ETHAMBUTOL

Introduction

Ethambutol is a specific **anti-tuberculosis** drug.

It is used in combination with other **anti - tuberculosis drugs** to treat infections caused by **mycobacteria**.

History

Ethambutol was developed in 1961.

Classification

The anti-mycobacterial drugs are those that have specific anti-mycobacteria activity and include:

1. Anti- tuberculosis agents

Examples include:

- Streptomycin
- Isoniazid
- Rifampicin
- **Ethambutol**
- Pyrazinamide

2. Anti-leprosy agents:

Examples include:

- Dapsone
- Rifampicin
- Clofazimine

Preparation

Ethambutol hydrochloride as:

Tablets:

- 100 mg

- 400 mg

Mechanism of Action

Ethambutol is thought to inhibit the incorporation of mycolic acid into the mycobacterial cell wall.

It is slowly bacteriostatic against M. tuberculosis.

Pharmacodynamics

Ethambutol is effective against strains of M. Tuberculosis.

It is not active against fungi, or other bacteria or viruses.

When used alone for treatment of tuberculosis resistance can develop, however there is reduced incidence of emergence when used in combination with other anti-tuberculosis drugs.

No cross resistance between ethambutol and other antituberculosis drugs

Pharmacokinetics

Absorption:

- Ethambutol is administered orally.

Distribution:

- Protein binding is moderate and variable at around 10 - 30 %
- Ethambutol can cross the human placenta.
- Ethambutol is excreted into human breast milk in small amounts.

Metabolism and excretion:

- The main pathway of metabolism is conversion to a dicarboxylic acid
- Approximately 50% is excreted unchanged in the urine
- Half life is around 2 - 4 hours.

Indications

Indications include

1. Treatment of tuberculosis in combination with other anti-tuberculosis drugs.

2. Mycobacterium avium complex (MAC)

Note that, as for all antibiotics, the prevalence of bacterial resistance may vary geographically and over time for selected species and local information on resistance is also important, particularly when treating severe infections.

Contraindications/ Precautions

These include:

1. Known hypersensitivity to ethambutol.
2. Optic neuritis:
 - Further deterioration in vision may occur where there are visual defects, e.g. diabetic retinopathy, cataract.

However this risk must be balanced against the potential benefit. Seek specialist advice
3. Renal impairment:
 - Reduce dose if Cr Cl < 25 mL/minute.

Seek specialist advice as concentration monitoring may be advisable due to the risk of optic neuritis.

Although it is more likely to occur with daily doses > 15 mg / kg, it is unlikely if renal function is normal and the course is < 2 months.
4. Children:

Avoid ethambutol in children < 6 years old unless it is necessary to ensure cure as tests used to monitor for optic neuritis are difficult to carry out (young children may also be unable to report changes in vision).

Pregnancy

Ethambutol is classified as a category A drug with respect to pregnancy.

Category A drugs are those drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

Ethambutol use during pregnancy has not been associated with an increased risk of congenital malformations.

Ethambutol has been used as part of a multi-drug regimen in the treatment of tuberculosis, and is recommended for use during pregnancy where indicated.

Breast feeding

Small amounts of ethambutol are excreted into breast milk, but these amounts are unlikely to pose harmful effects to the breastfed infant.

Ethambutol is safe to use during breastfeeding, but observe the breastfed infant for potential adverse effects such as diarrhoea, vomiting, skin rash or thrush.

Adverse Effects

These include:

1. Allergic reactions
2. Mild GIT upset.
3. Lethargy / malaise
4. Hypersensitivity skin reactions (e.g. Stevens-Johnson syndrome)
5. Optic neuritis (the most serious adverse effect):
 - This is dose-related
 - It is usually reversible
 - It is characterized by decreased visual acuity, scotoma or colour blindness.
 - It can involve only one eye or can be bilateral
6. Hyperuricaemia / acute gout.

Dosing

Use doses below for the first 2 months of the 6 month multidrug regimen.

Tuberculosis:

Adults:

- Daily regimen, oral 15 - 20 mg/kg once daily.
- Three times a week regimen, oral 25 - 30 mg/kg 3 times each week.

Children (> 1 month):

- Daily regimen, oral 20 mg/kg once daily.
- Three times a week regimen, oral 30 mg/kg 3 times each week.

Prevention and treatment of MAC

Adult, oral 15 mg/kg once daily in multidrug regimen.

Child, HIV-positive, oral 15 - 25 mg/kg once daily in multidrug regimen.

Renal impairment:

Adult, CrCl 10 - 25 mL/minute:

- Oral 15 mg/kg every 24 - 36 hours.

Adult, CrCl <10 mL/minute:

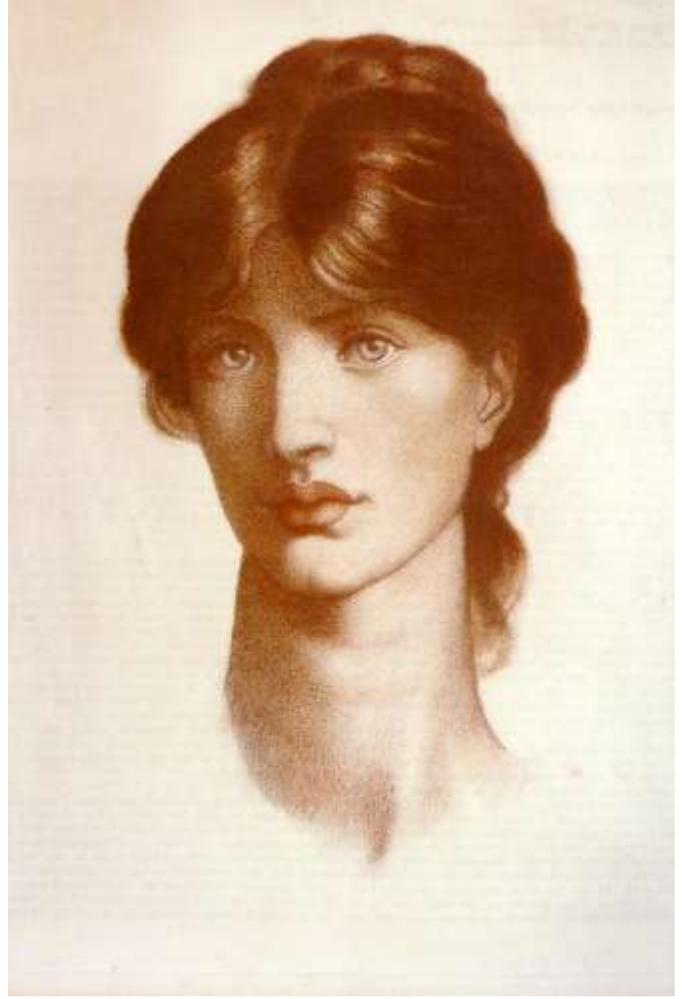
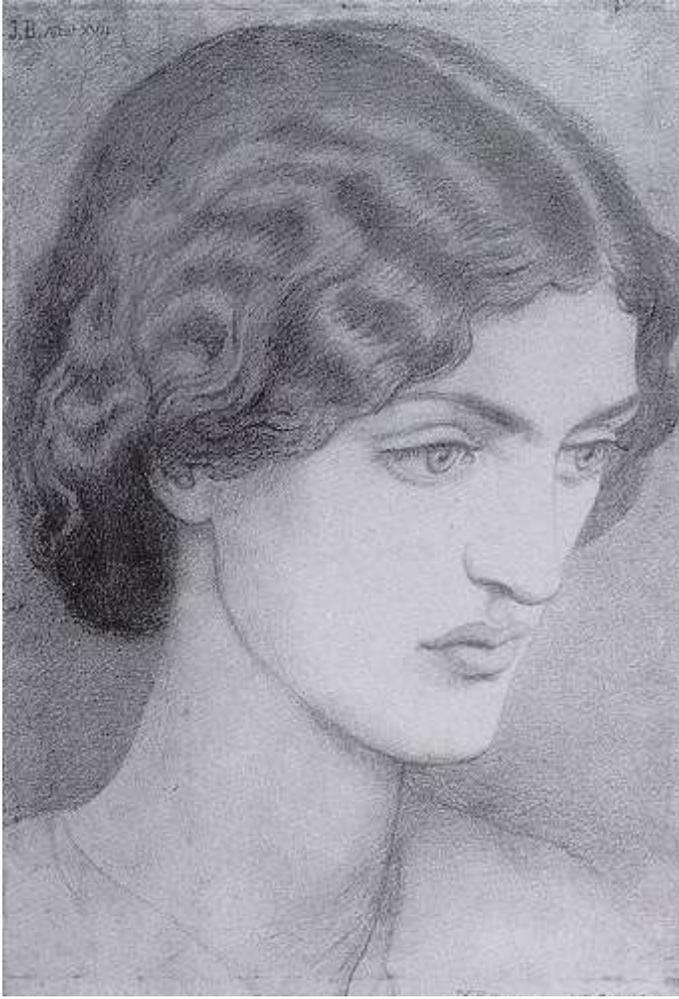
- Oral 15 mg/kg every 48 hours.

Monitoring:

Measure CrCl at baseline and regularly during treatment, especially if treatment is to continue for > 2 months.

Monitor visual acuity and colour vision at start of treatment and each month if:

- The dose is >15 mg/kg
- Treating for > 2 months
- There is renal impairment.



Left: Jane Morris, Muse of Dante Gabriel Rossetti. Right: Rossetti's Study for "A Vision of Fiametta", colored chalks on paper, c.1878. Both works are quintessential examples of the Re-Raphaelite feminine idyll of the unblemished long swan-like neck.

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