A Cooke's Tour of Malaria

Professor Robin A. Cooke

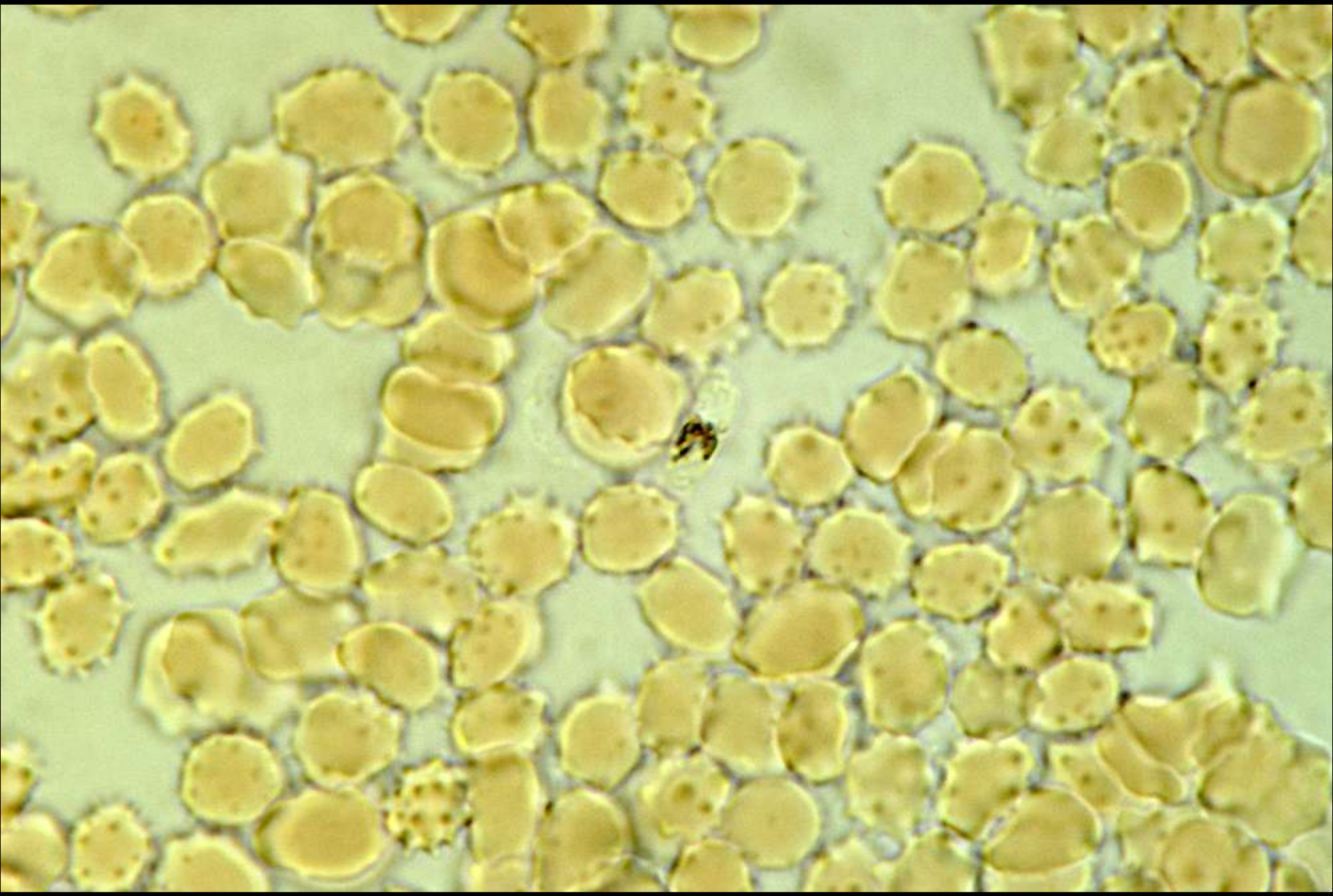
Some names in the elucidation of malaria

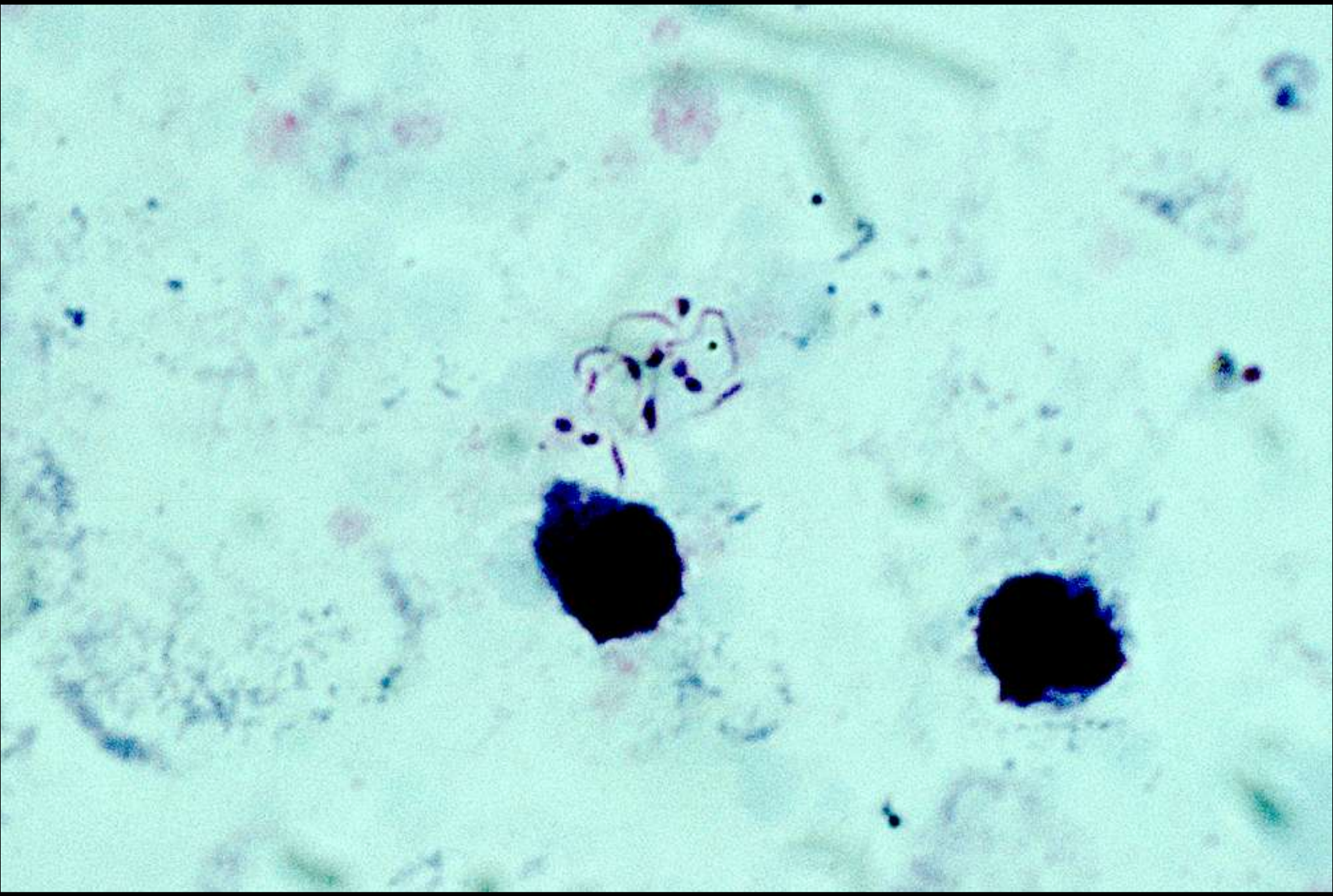
It appears that Hippocrates in the 5th century BC described the clinical features of malaria.

From the earliest times it was known that it occurred particularly in areas of marsh land.

Malaria - bad air

1880





Dimitri Romanowsky (1861-1921) Eosin methylene blue stain 1891


Bât. A. Calmette
Bât. C. Guérin
Bât. Ch. Nicolle, A. Laveran
2e étage Téléphone

PALUDISM.

BY

DR. A. LAVERAN,
PROFESSOR OF MEDICINE IN THE SCHOOL OF VAL DE GRÂCE.

TRANSLATED BY

J. W. MARTIN, M.D., F.R.C.P.E.

LONDON:
THE NEW SYDENHAM SOCIETY.
1893.

1893

Quinine is important in both prophylaxis and treatment

It must be taken under supervision otherwise it is spat out

intermittent fevers. Under the influence of this theory the mortality from paludism was enormous in hot countries. Maillot deserves great credit for showing that this opinion was erroneous, and that quinine should be administered in continued as in intermittent palustral fevers. The therapeutic reform which our illustrious master was the first to describe has had the happiest results, and the opinions of Maillot on continued palustral fever and its treatment are to-day universally admitted.

In serious cases hypodermic injections (1·50 to 2 grammes daily) should be made without regard to the temperature. As soon as the fever has yielded, the treatment for simple fever given above should be followed.

Hydrochlorate of quinine should be prescribed internally in solution or in the form of tabloids. In the military hospitals of Algeria the patients swallow the solution of quinine, which is prescribed and dealt out at the time by an attendant, during the visit of the doctor and in his presence. It is an excellent plan, seeing that it too often happens that when tabloids are prescribed to be taken during the day the medicine is not taken, and a search discovers the packets of quinine thrown into some corner of the ward.

In the grave pulustral fevers accompanied by pernicious symptoms the first thing to attend to, and by far the most important of all, is to get the quinine taken; but in addition to this there is often occasion to prescribe some further aids to the special treatment.

For the patients attacked with algid fever, friction either dry or with evaporating camphor liniment should be used; hot stimulating drinks—alcohol in tea, for example—diffusible stimulants, ether, acetate of ammonia under the form of draught, or, better still, hypodermic injections of ether (2 to 4 grms. of sulphuric ether), must be prescribed. The hypodermic injections of ether also render great service in patients attacked with choleraic complications.

In the case of continued fever with typhoid state and high temperature cold baths are sometimes indicated.

For the comatose symptoms when the individual is strong and plethoric, and when signs of a severe encephalic congestion are noticed, leeches may be applied to the mastoid processes in order to prevent the consecutive congestion. Cold applications to the head, counter-irritants to the extremities, and drastic purgatives are also useful.

General measures are also necessary

and don't forget leeches

Clinicians and laboratory workers collaborated to correlate the clinical features of the different types of fever

Camillo Golgi in Pavia in Northern Italy in 1885 identified *P. vivax* as the cause of benign tertian malaria

and *P. malariae* as the cause of quartan malaria

Golgi 1885

They worked in Rome in the South of Italy

They were dealing with malaria that often caused death - malignant tertian

Caused by *P.Falciparum*

1889

ON

SUMMER-AUTUMN MALARIAL FEVERS.

BY

E. MARCHIAFAVA, M.D.,
PROFESSOR OF PATHOLOGICAL ANATOMY IN THE UNIVERSITY OF ROME;

AND

A. BIGNAMI, M.D.,
FIRST ASSISTANT IN THE ANATOMICO-PATHOLOGICAL INSTITUTE.

TRANSLATED FROM THE FIRST ITALIAN EDITION

BY

J. HARRY THOMPSON, A.M., M.D.,
LATE PROFESSOR OF PHYSIOLOGY AND OPERATIVE SURGERY,
GEORGETOWN UNIVERSITY;
SURGEON-IN-CHIEF, COLUMBIAN HOSPITAL, WASHINGTON, U.S.A.

WITH NOTES AND APPENDICES BY THE AUTHORS.

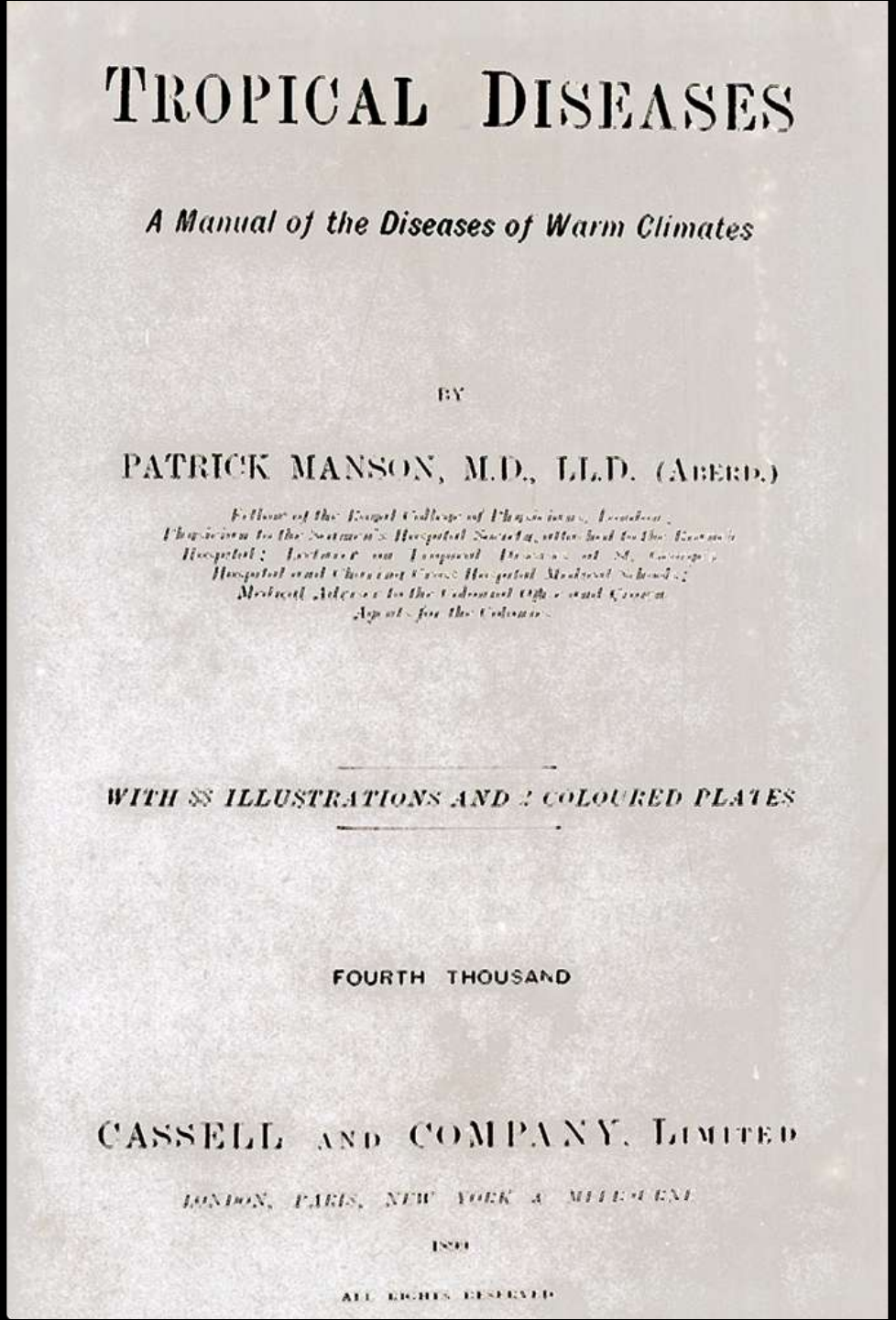
A year after Ross showed that malaria could be transmitted by mosquitoes in birds

he showed mosquito transmission in humans

Giovanni Grassi
1898 in Rome

Manson
'father of
tropical medicine
in England'

Thought that it
was transmitted
by mosquitoes



TROPICAL DISEASES

A Manual of the Diseases of Warm Climates

BY

PATRICK MANSON, M.D., LL.D. (ABERD.)

Fellow of the Royal College of Physicians, London;
Physician to the Seamen's Hospital Society, attached to the Dreadnought
Hospital; Lecturer on Tropical Diseases at St. Thomas's
Hospital and Charing Cross Hospital Medical Schools;
Medical Adviser to the Colonial Office and Crown
Agents for the Colonies.

WITH 88 ILLUSTRATIONS AND 2 COLOURED PLATES

FOURTH THOUSAND

CASSELL AND COMPANY, LIMITED

LONDON, PARIS, NEW YORK & MELBOURNE

1900

The mosquito considered as the extra-corporeal host of the plasmodium.—Further, as the plasmodium whilst in the circulation is always enclosed in a blood corpuscle and is therefore incapable of leaving the body by its own efforts, and as it is never, so far as known, extruded in the excreta, I have suggested that it is removed from the circulation by some blood-eating animal, most probably by some suctorial insect common in the haunts of malaria. This insect, as Laveran has also suggested, I believe to be the mosquito*; an insect whose habits seem well adapted

Ronald Ross Manson's most famous student confirmed his suspicion that transmission was indeed by mosquitoes

At first they thought that transmission was by swallowing drinking water that had mosquitoes in it.

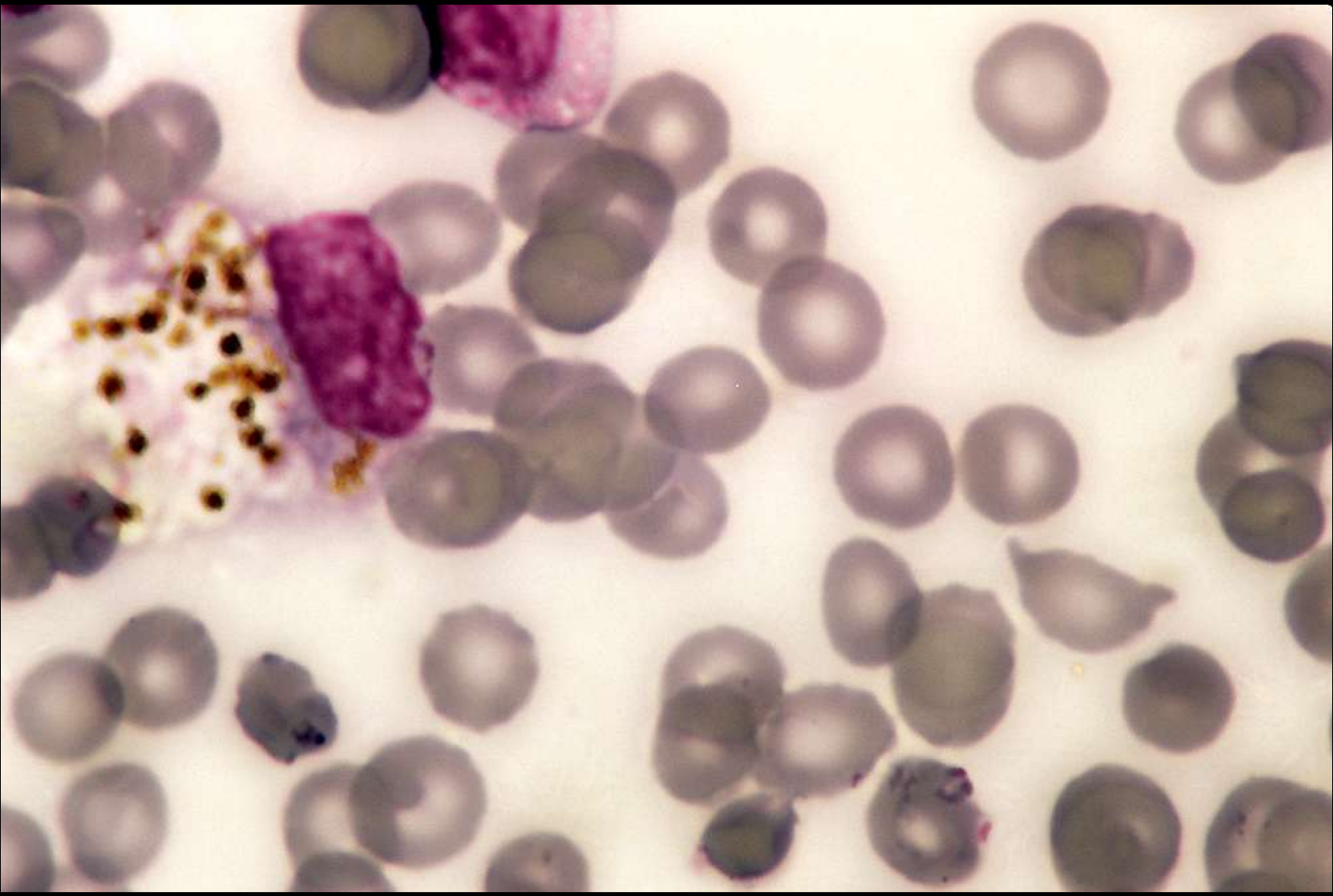
Ross used to joke about this in his lectures after he became Professor of Tropical Medicine in Liverpool.

1897

They knew that malaria parasites in peripheral blood had a number of different forms

But what they had in common was the presence of pigment

Hence the idea was to
‘find the pigment.’



In his first attempts
Ross dissected
hundreds of
mosquitoes
and did not find
the pigment bodies

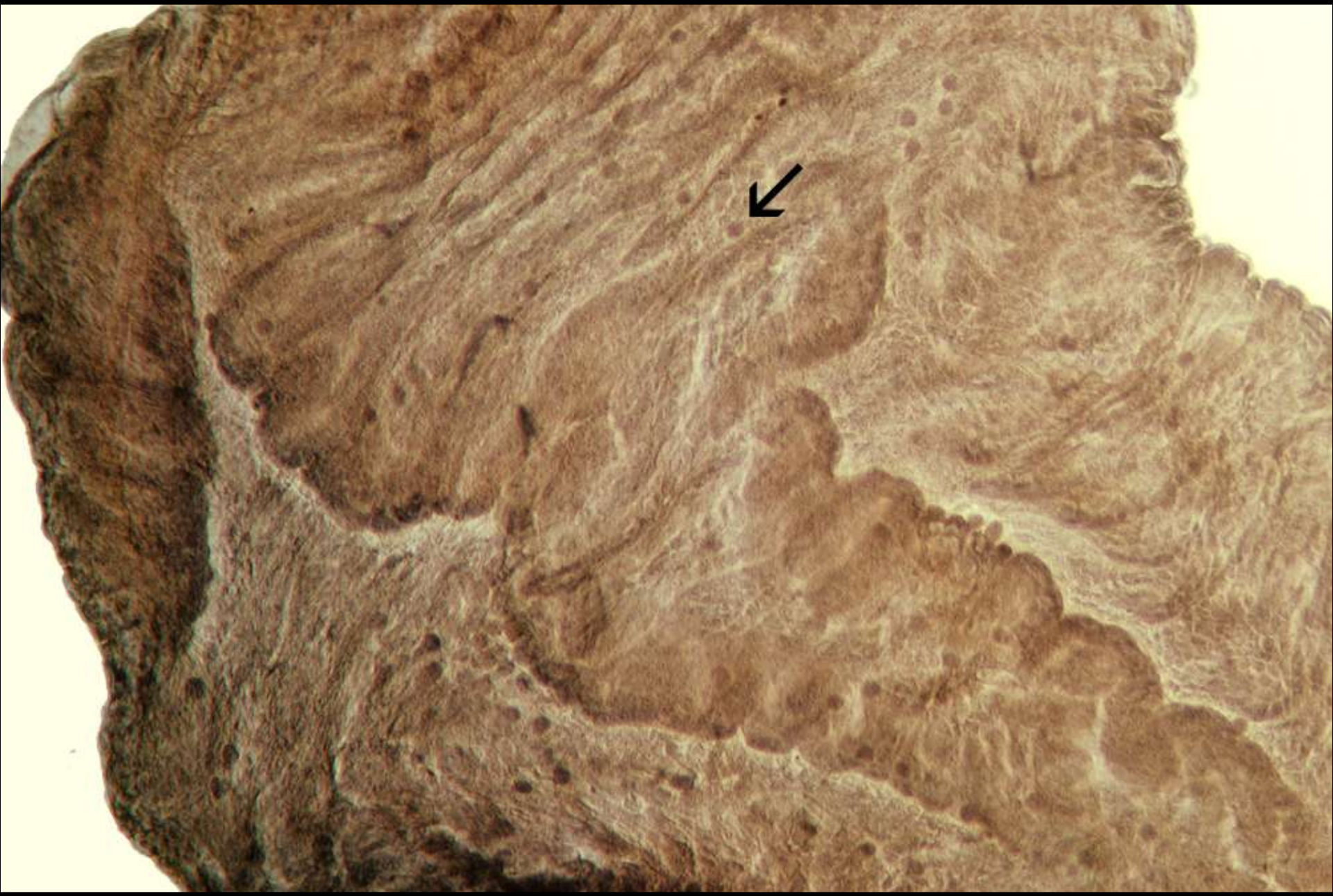
He wanted
to give up

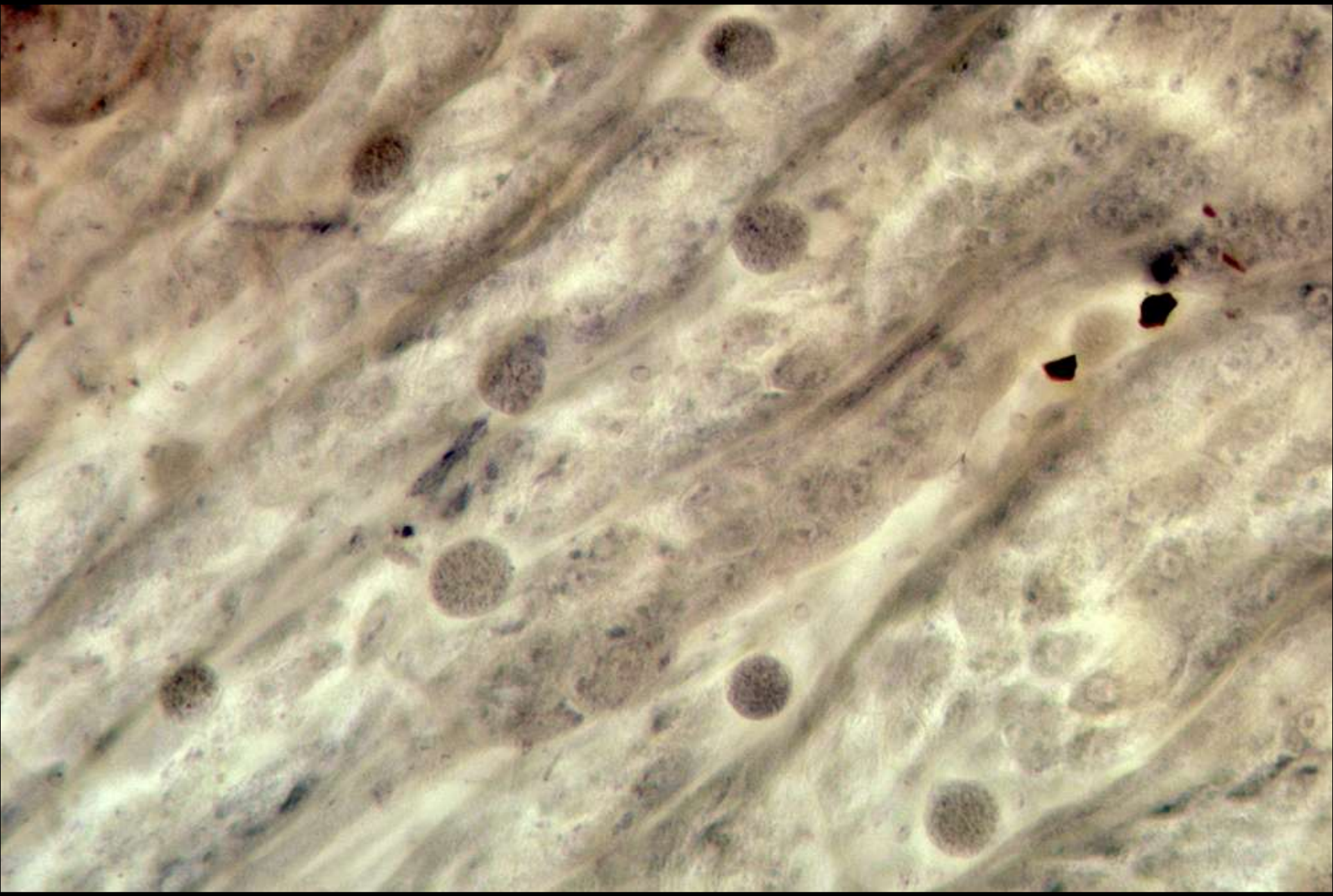
He was transferred
to Secunderabad
on the Deccan
plateau in the South

There he found a
new mosquito.
It had banded legs
and dappled wings

Later identified as
a female anopheline

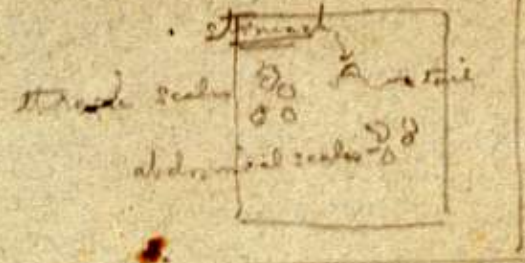
Ole Ole It contained
the pigment bodies
in its stomach.





Here are photographs I obtained with permission from the School of Hygiene and Tropical Medicine in London.

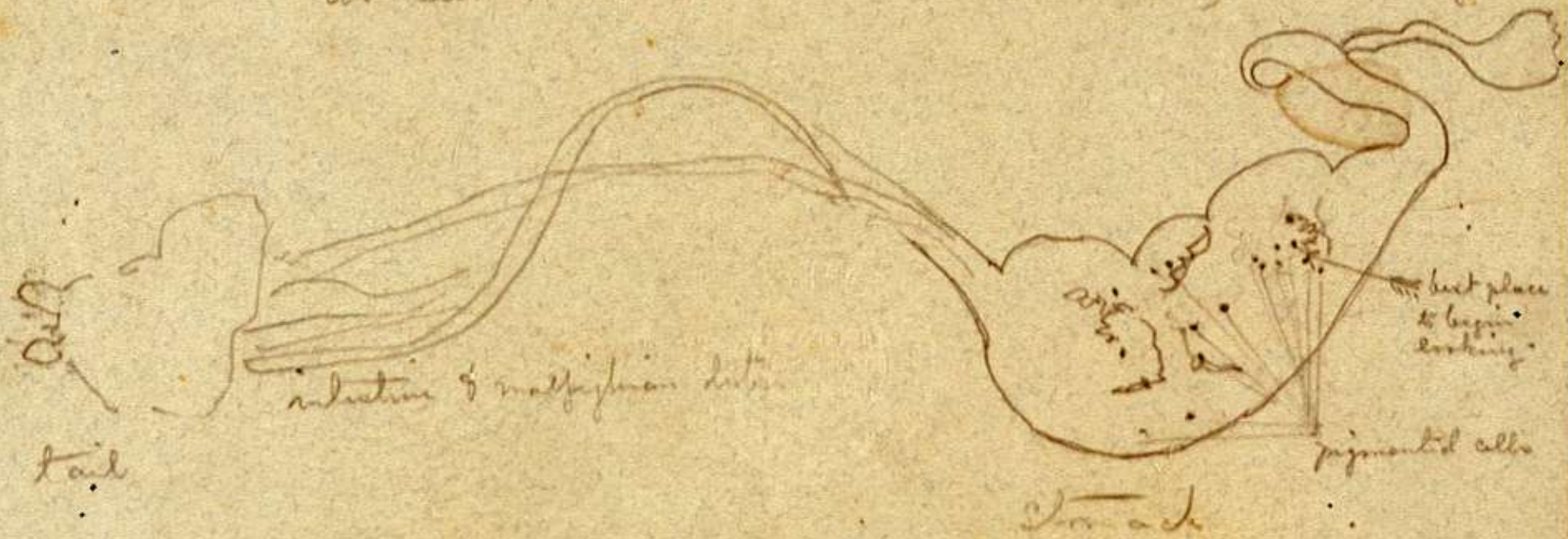
They are the drawings made on sheets of thin brown paper that Ross sent to Manson in London.



Label

Specimen of Pigmented cells in Stomach of mosquito killed 5 days ~~after~~ (120 hours) after being fed on blood containing crescents.

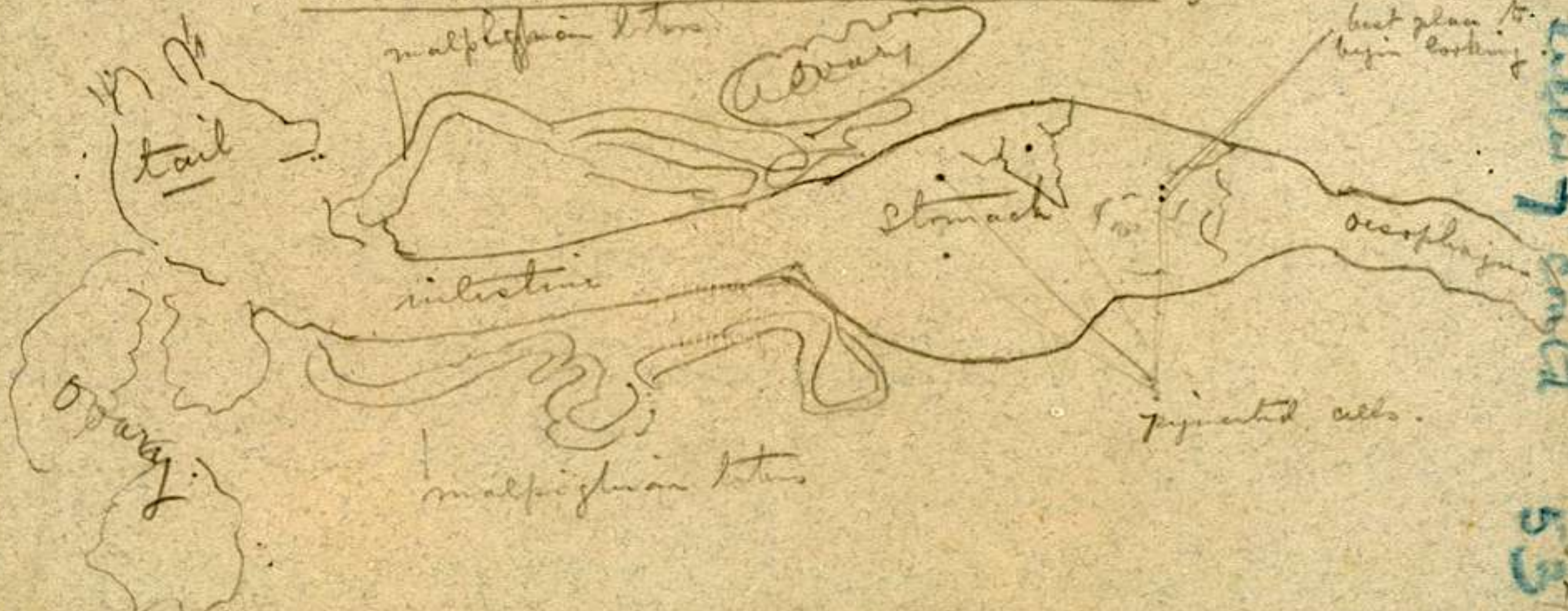
As seen under 1 mm. Leitz (position reversed) oesophagus



54

Specimen of Pigmented Cells
in stomach of malariated mosquito
killed ~~4th~~ 4th days after
being fed on blood containing crescents
Dated 20.8.97 — R Ross.

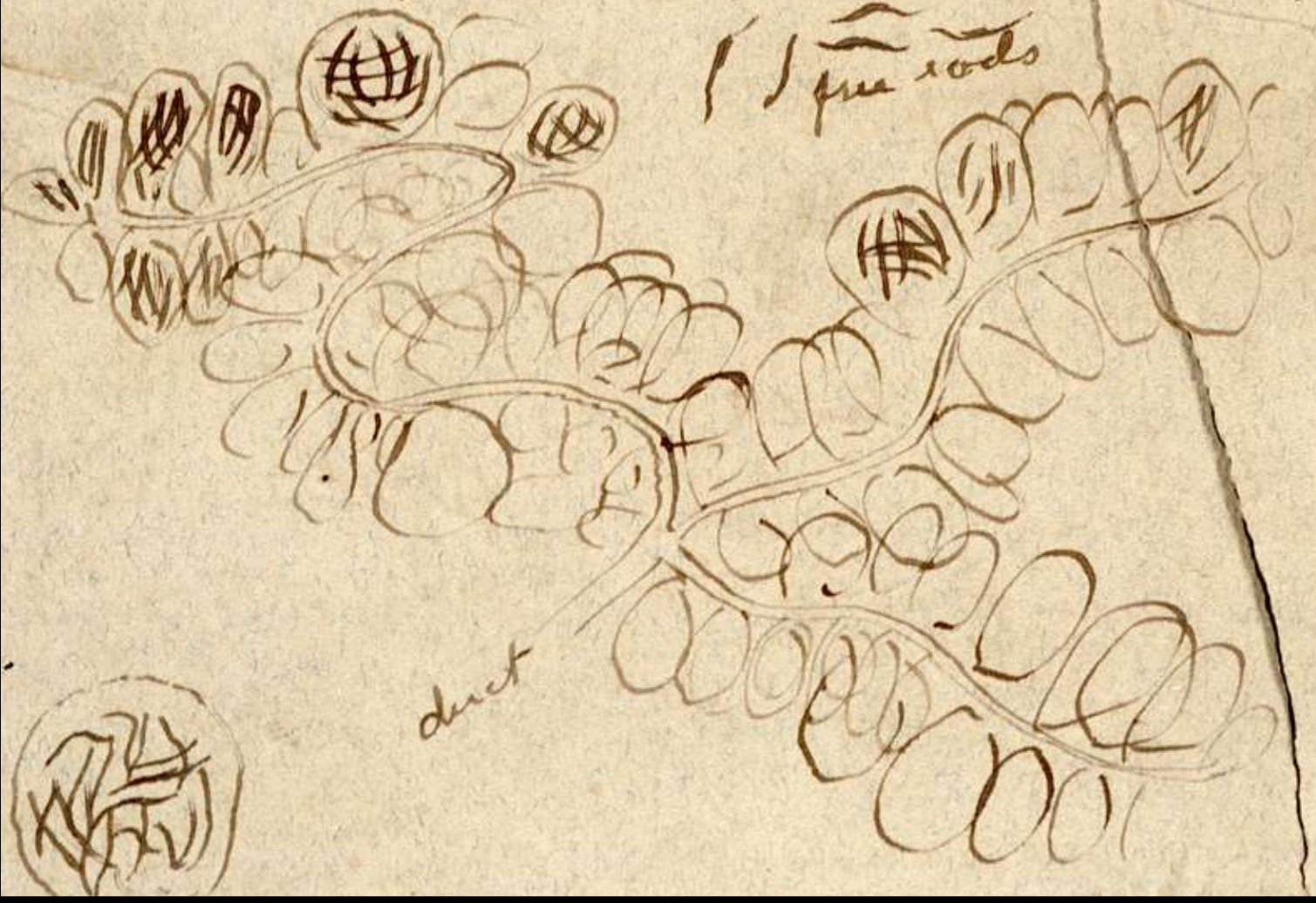
As seen under 1 inch lens (position reversed) —



After demonstrating the pigment bodies in the abdominal wall of mosquitoes he began to pull off the heads of mosquitoes

and there he found structures that he correctly interpreted as being salivary glands.

poured out of them just as they
ions out of the Original Coccidia.



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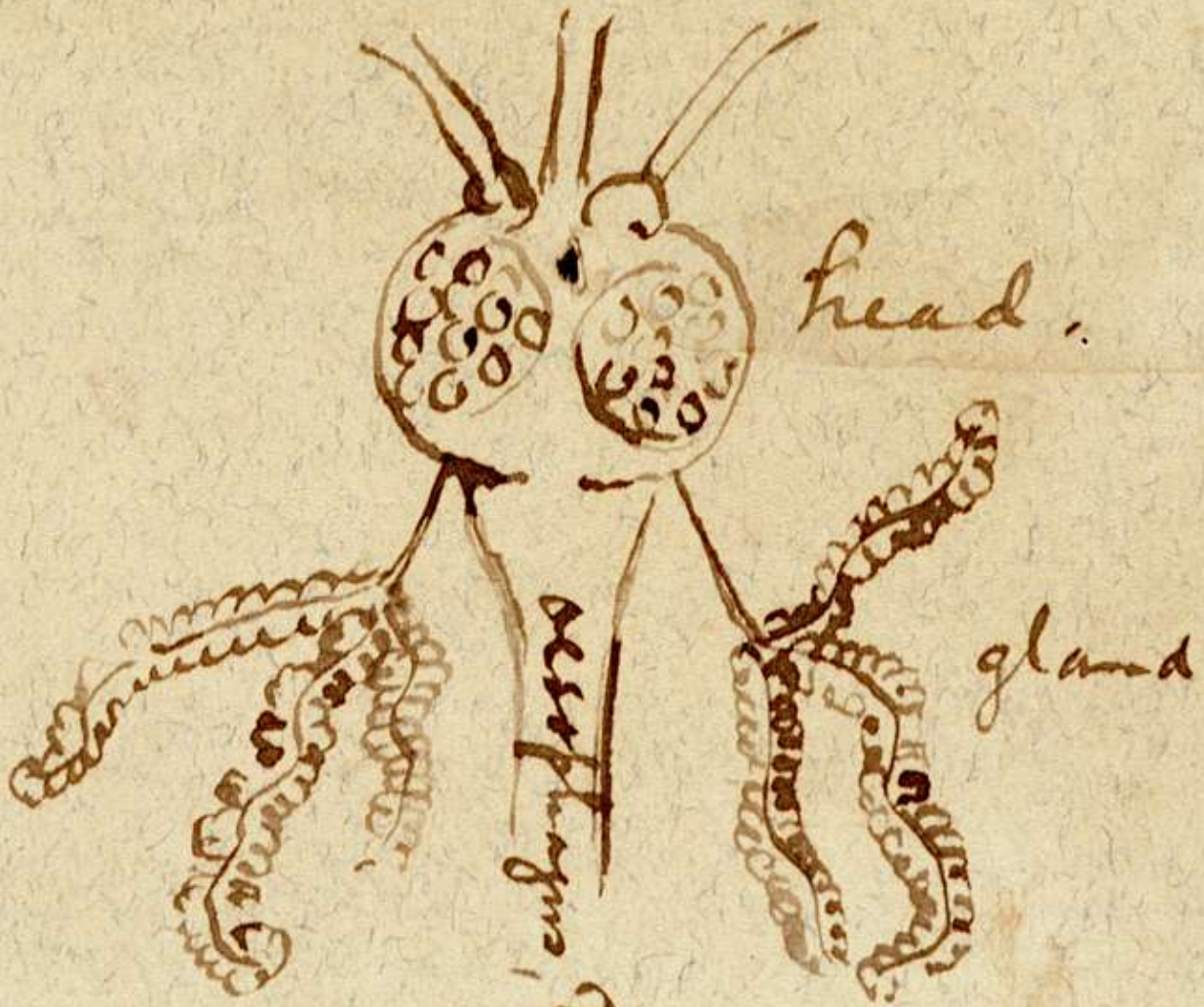
They were full of thin bodies that he recognised as the infective form that was injected into a new host by the bite of the mosquito.

d ; thus : —

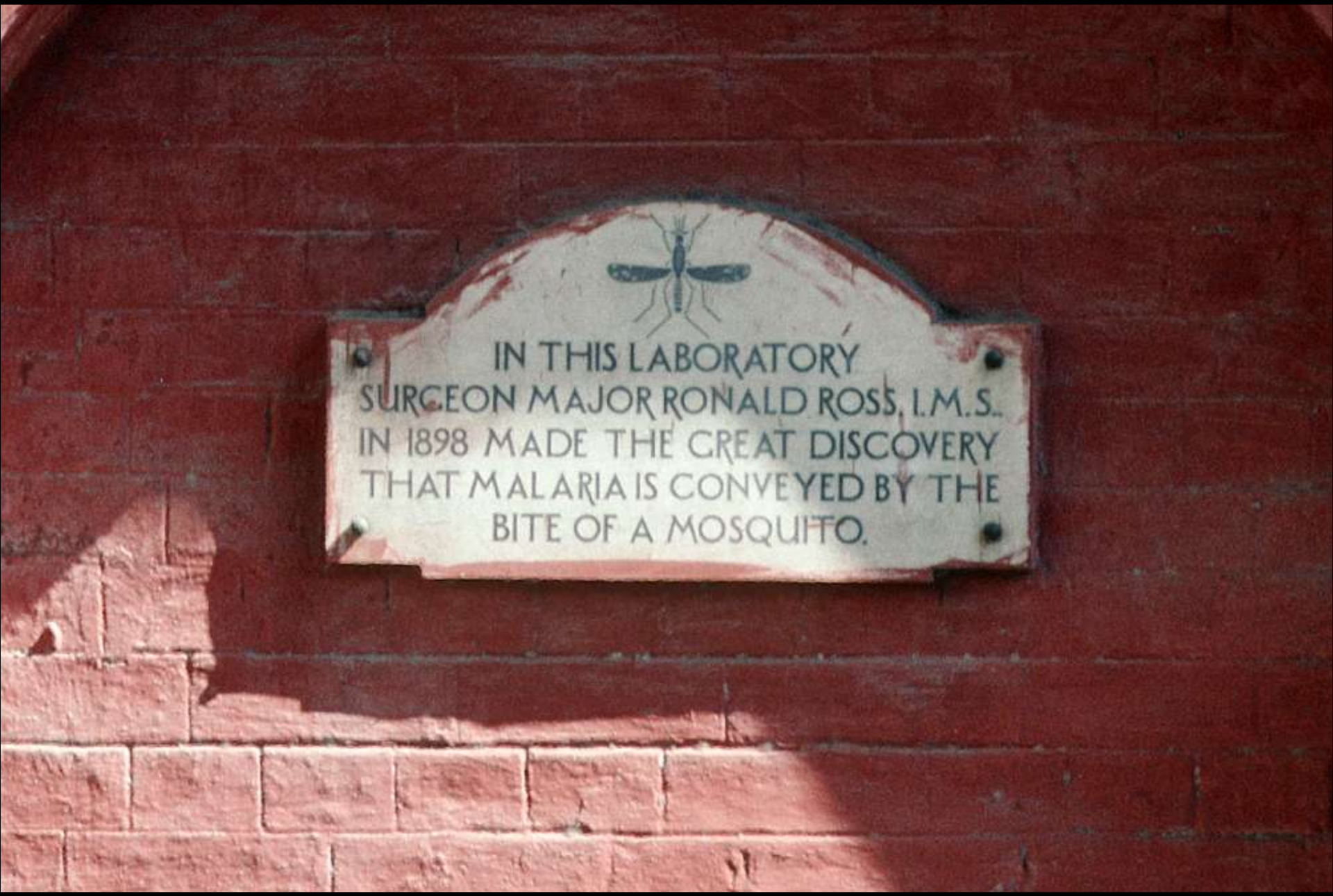


Soon after this he took a period of leave and went to the School of Tropical Medicine that had been established in Calcutta.

There he experimented with bird malaria and showed that it was transmitted by the bite of mosquitoes.


SCHOOL OF TROPICAL MEDICINE

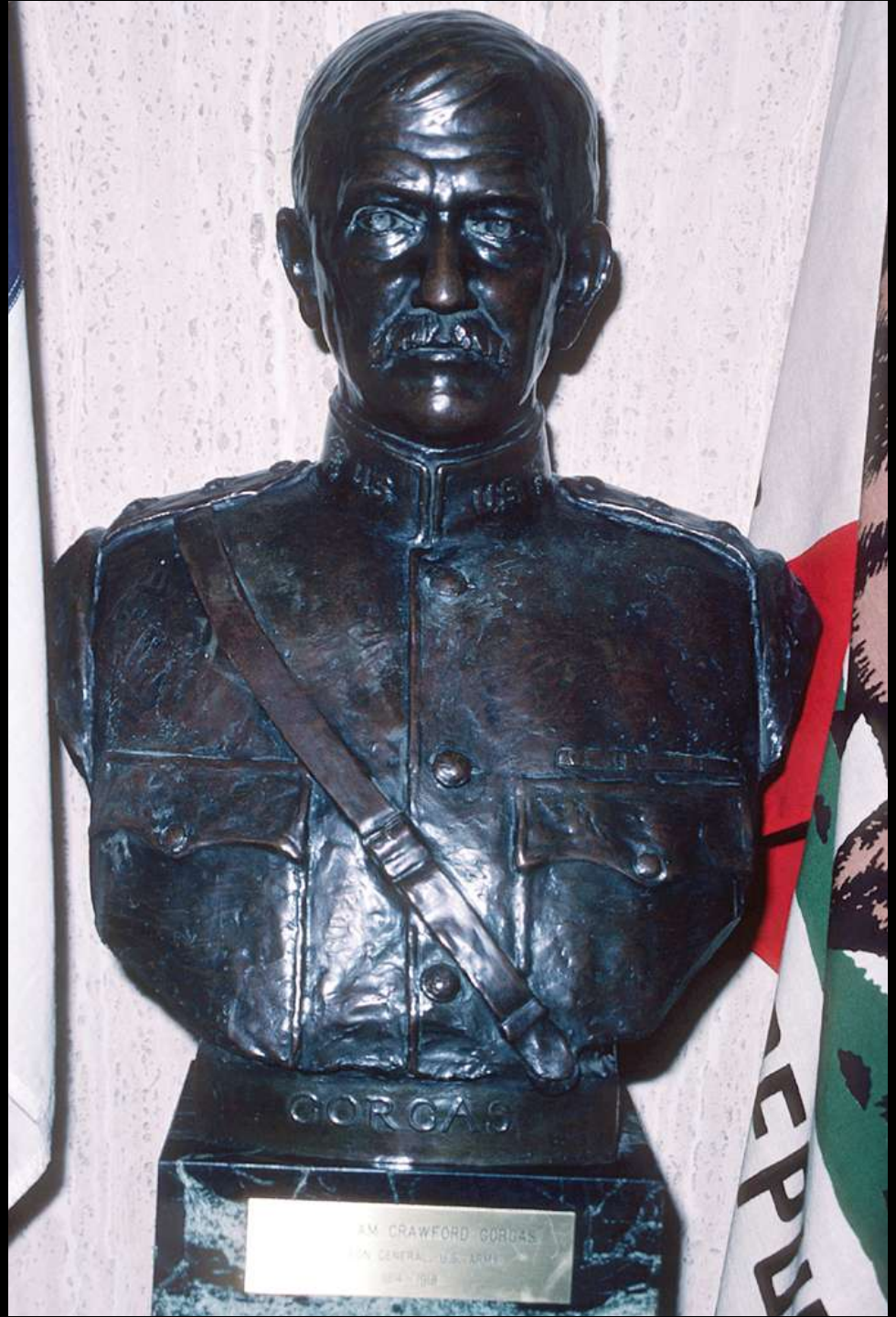

SIR RONALD ROSS K.C.B.


IN THIS LABORATORY
SURGEON MAJOR RONALD ROSS, I.M.S.
IN 1898 MADE THE GREAT DISCOVERY
THAT MALARIA IS CONVEYED BY THE
BITE OF A MOSQUITO.

Ross telegraphed the final report of his entire experiments to Manson a few days before July 28, 1898 when Manson was due to read a paper in Edinburgh at a Soc of Tropical Medicine section of the BMA meeting to be held on that day.

Manson proudly presented the findings of his, by then famous student.

The next big advance came with the control of mosquitoes by the destruction of their breeding grounds



William Gorgas
(1854-1920)
Panama Canal
1904

From 1898-1902 Gorgas worked with Walter Reed and showed that yellow fever is transmitted by mosquitoes and

it could be controlled by draining the swamps where the mosquitoes bred

Roosevlet took over the building of the Panama Canal when the French failed

HOW TO SHRINK THE WORLD

Roosevelt called building the Panama Canal "by far the most important action" he had taken in foreign affairs. Why did he succeed where others had failed? He made his own rules

Manuel Amador Guerrero, first President of Panama

1 CREATE A COUNTRY

Panama was a province of Colombia when Theodore Roosevelt took up the idea of building a canal after a failed attempt by France. When the Colombian government rejected a new treaty allowing the U.S. to build a canal, Roosevelt became enraged. Soon after, a group of Panamanian separatist leaders declared a revolution. That same day, U.S. gunboats appeared off the coast to keep Colombia from reclaiming its territory. Roosevelt vigorously denied that the U.S. had fomented the revolution but defended his actions in characteristic terms: "To have acted otherwise ... would have been betrayal of the interests of the United States."

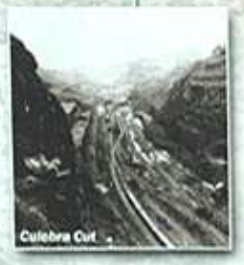
2 GET THE BUGS OUT

The rain forests and squalid towns of Panama were rife with diseases like malaria and yellow fever. As many as 20,000 people died during the French effort to build a canal in the late 1800s. But as a result of his work in Cuba after the Spanish-American War, a tireless American doctor named William Gorgas came to believe strongly in the new discovery that a specific mosquito spread yellow fever. Overcoming doubters, he began a widespread campaign of mosquito eradication and sanitation improvements. The death rate among canal workers plummeted.

Colonel George Goethals

3 CONSOLIDATE POWER

Initially, Congress created a seven-person commission to oversee construction. After the first chief engineer broke down under the stress of the job, Roosevelt sidestepped the panel and gave total power to one man, Army Colonel George Goethals. As absolute ruler of the Canal Zone, Goethals oversaw every detail, from digging and building to resolving personal disputes among workers.

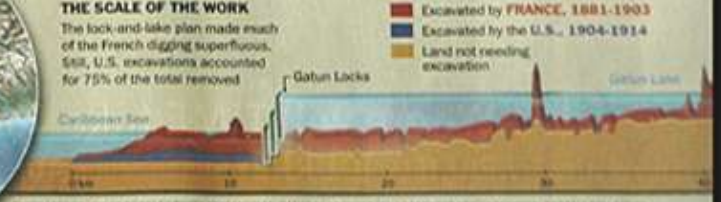


4 MAKE THE DIRT FLY

At first, the Americans pursued the failed French dream: a sea-level passage through the mountains and jungles. In 1906 that plan was overruled in favor of damming the Chagres River to create a vast inland lake that could be entered through flights of locks at either end. That still meant cutting a 13-km trench through the mountains. Every rainy season, mudslides wiped out months of work in a single moment.

THE SCALE OF THE WORK

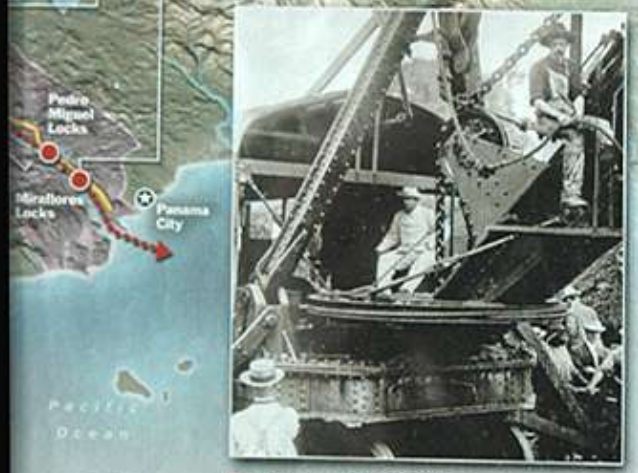
The lock-and-lake plan made much of the French digging superfluous. Still, U.S. excavations accounted for 75% of the total removed



SHIPPING ROUTES

Before the Panama Canal, a trip from New York City to San Francisco was about **22,500 km.** Through the canal, it's only about **9,500 km.**

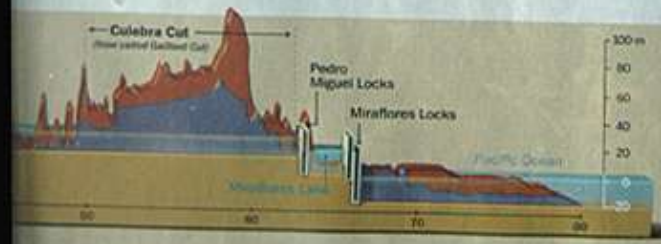
The Panama Railroad, opened in 1855, was the spine along which men, equipment and dirt moved during construction



Sources: *The Path Between the Seas*, by David McCullough; *The Panama Canal*, by Lesley A. Dutenpile; *An Autobiography*, by Theodore Roosevelt; *Letters and Speeches of Theodore Roosevelt*; *Destiny by Design*, by Jeremy Shannan Snapp

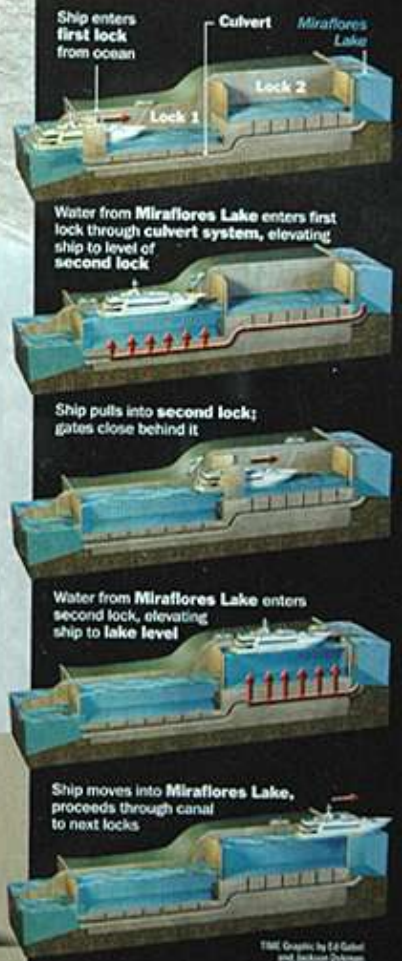
5 RALLY THE TROOPS

In 1906 Roosevelt wanted to see the colossal project for himself. His trip marked the first time a U.S. President left the country while in office. To see conditions at their worst, he went at the height of the rainy season. While touring, he delighted workers by leaping aboard an 86,000 kg Bucyrus steam shovel and grilling the operator about how it worked. The operator seized the moment to ask for overtime pay.

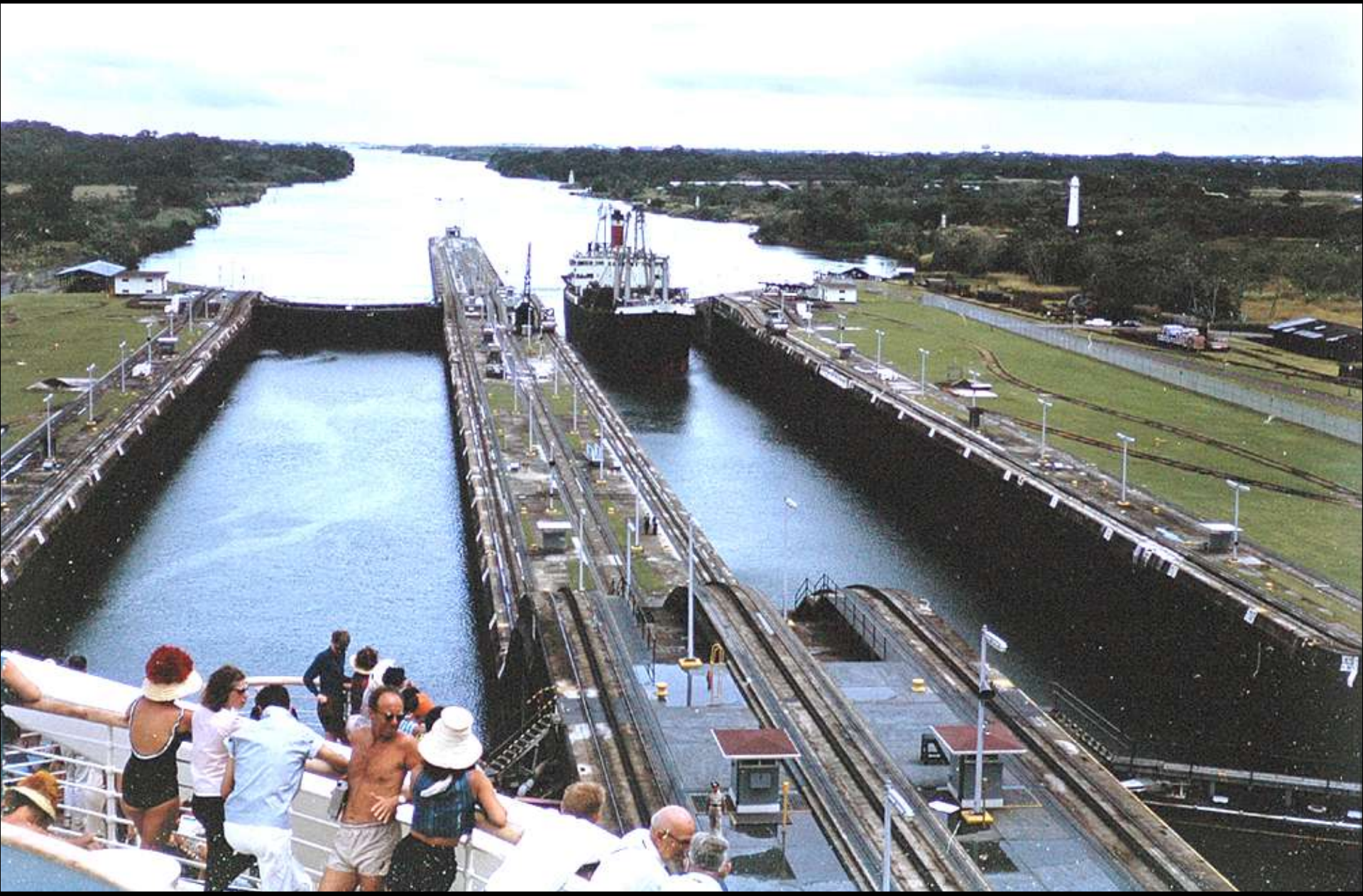


6 LOCK AND LOAD

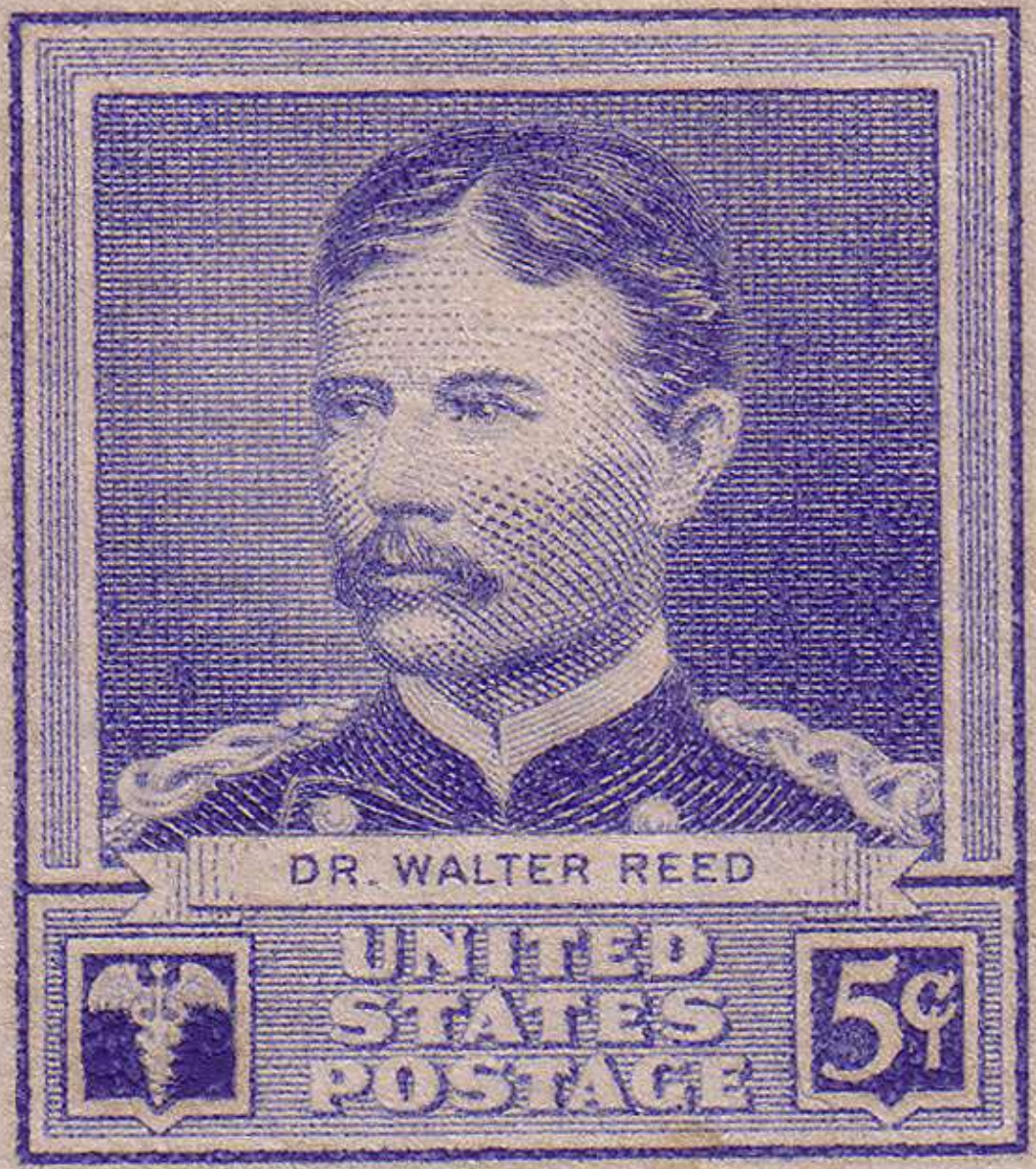
At 300 m long and 33 m wide, the locks were built to handle the largest ships then planned. Even though many modern ships are too big (the *Titanic* would have fit; today's *Queen Mary 2* doesn't), the canal handled more than 14,000 transits in 2005, accounting for about 5% of world trade. How a lock works:



TIME Graphic by Ed Gabel and Jackson Dykman



The highest point in the Panama Canal in 1965


DR. WALTER REED
UNITED
STATES
POSTAGE
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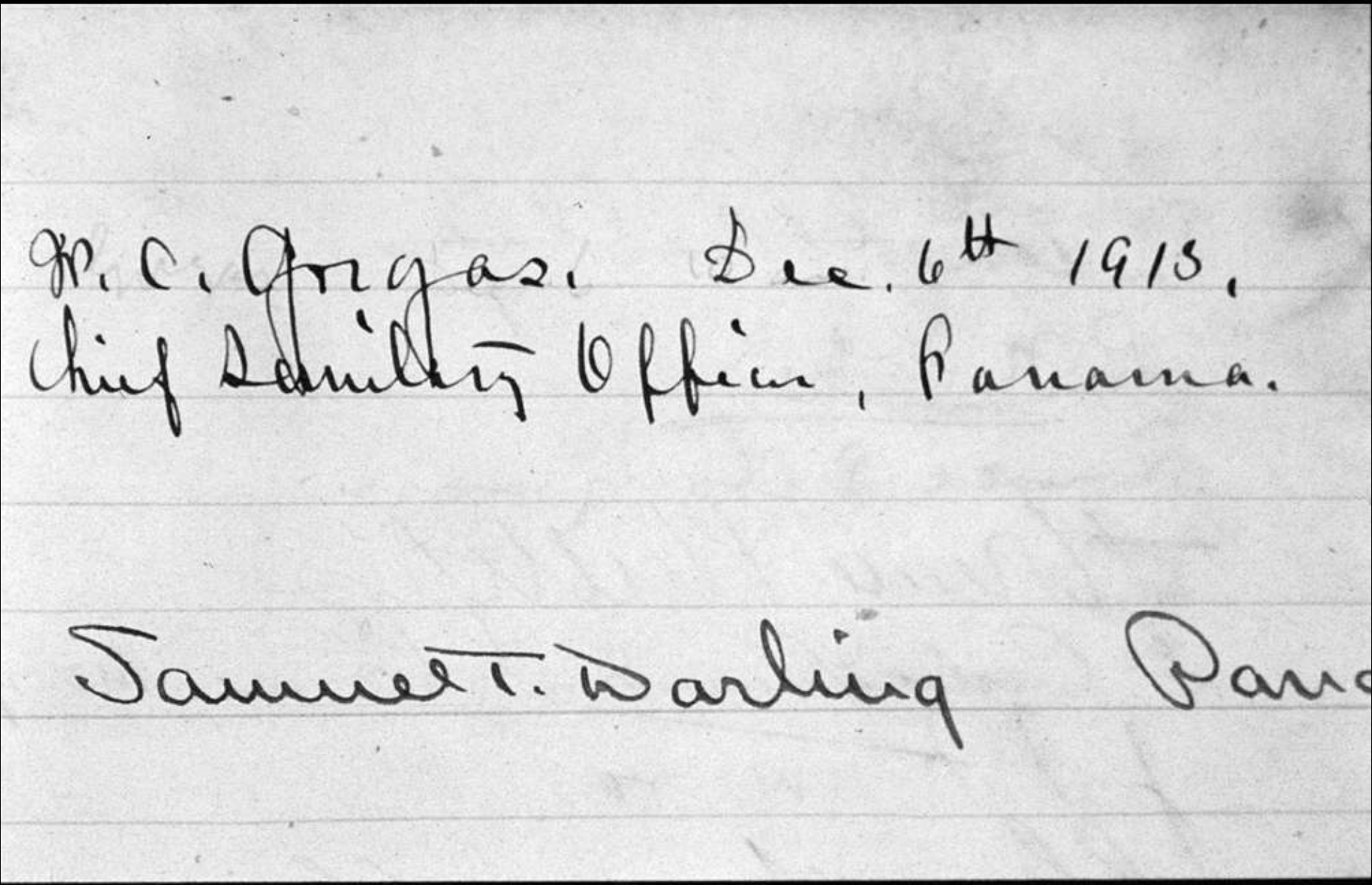

W. C. Gorgas. Dec. 6th 1915.
Chief Sanitary Officer, Panama.

Samuel T. Darling Pana

Signature in the guest book at Institute for Research at Wits Uni Johannesburg in 1915

Cosmos Club Washington

COSMOS CLUB MEMBERS ON CANAL ZONE STAMPS

George W. Davis
1881-1885
1948

William C. Gorgas
1914-1920
1928

John F. Wallace
1904-1921
1948

Sidney B. Williamson
1915-1928
1940

Dr. Gorgas also was on a Panama Stamp, 1939
He is the First Club Member to
Appear on a Stamp, See Above.

Explosive epidemics of malaria that caused many deaths have been recorded since ancient times.

A modern acute epidemic occurred in the 1980s when a group of about 700 people living in a remote part of the Highlands of Papua New Guinea decided that they wanted to become connected to the road system that serviced the rest of the country.

The road was built but it rains heavily almost every night

Up the road came anopheline mosquitoes that bred in all the puddles of water

See the myriads of larvae

Right to the entrance of the houses they came

They bred in the water in the holes made by the pigs that roam freely in the villages

100 villagers died within a few weeks before a medical team could get in to help them.

This woman and her baby died the day after this photo was taken

The old men decided that they did not want to be connected to the rest of the country after all

And the road was allowed to return to the jungle

But the damage had already been done

Historical vingnettes

The story of Cinchona


intact and broken pipe bark

In past centuries it was well known that many people in Rome died every autumn from a fever that seemed to come from the marsh lands in the lower reaches of the Tiber River.

In 1623 when the cardinals of the Catholic Church gathered in Rome to elect a new Pope, almost all of them contracted this fever (called malaria - bad air).

Many of them and many of their attendants died.

Pope Urban 8th (V111) – one of the last survivors - was elected.

In 1630 he appointed the Spanish Archbishop Juan de Lugo, a member of the Jesuit order of priests to the position of Apothecary of Santo Spirito Hospital where he had been treated for his malaria .

Juan de Lugo encouraged members of the Jesuit order to bring back to Rome new medicinal herbs from their missions all over the world.

He got rhubarb from China which was ‘good’ for treating stomach aliments;

bezoar stones from the stomachs of Llamas from South America. (Goodness knows what this was good for, perhaps as an aphrodisiac.)

In 1631 from Lima, Peru, he got a small bundle of dried, bitter tasting bark from a Cinchona tree that was used by the Andean Indians (the Incas) to cure fevers that were associated with shivering.

This became an ingredient in a prescription that was used for treating the Roman ‘malarial’ fever.

It was effective and became known as the Peruvian bark.

It soon spread throughout Europe as a treatment for fevers under the name ‘the Jesuitical bark.’

The export of cinchona bark from Lima, Peru, was made possible by the actions of a Jesuit lay brother, an Italian, Agustino Salumbrino (1580 – 1642).

During a period of 37 years he established a flourishing trade in Cinchona bark.

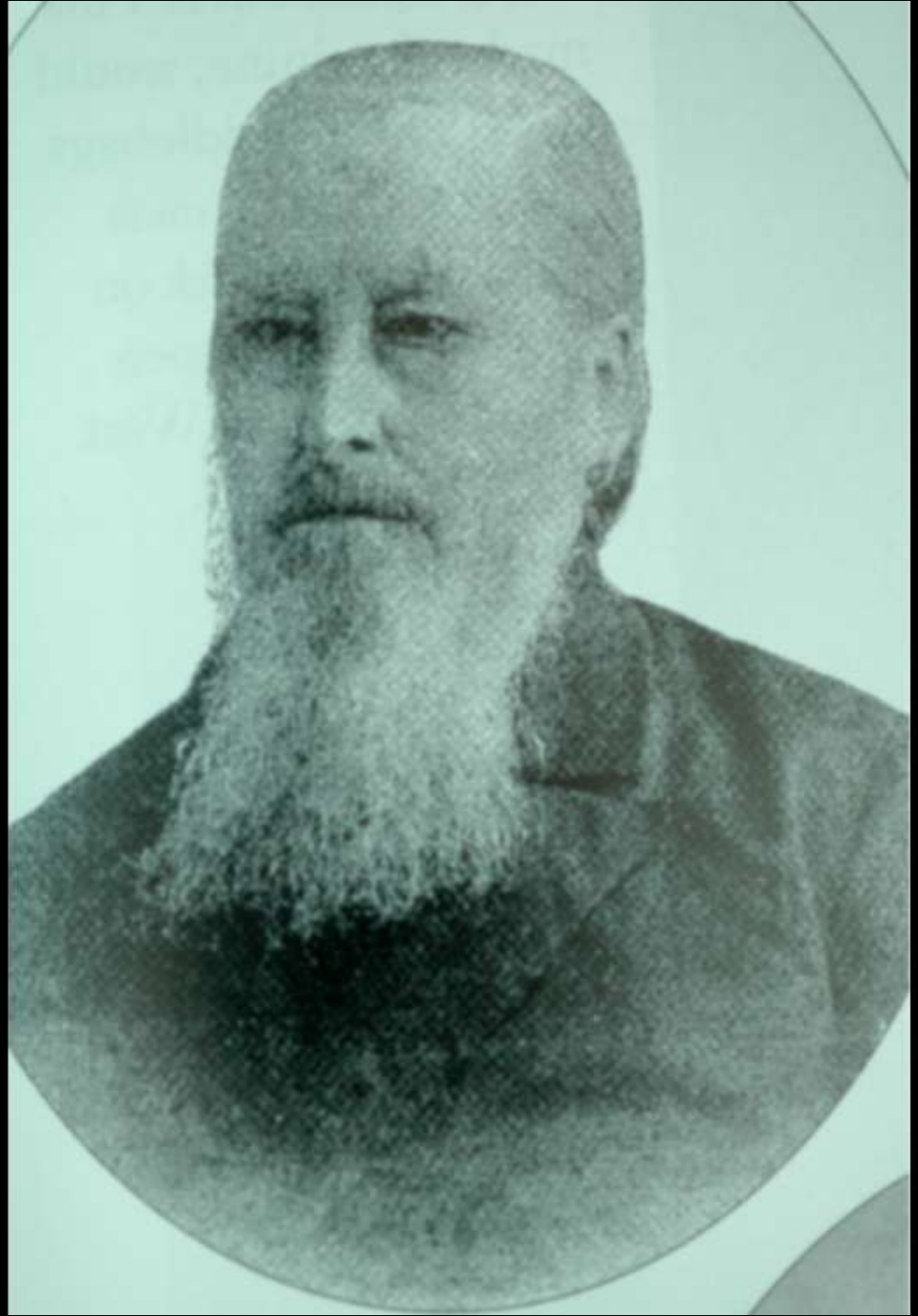
Many attempts were made to get seeds to Europe so that commercial plantations could be established.

Some of these ended in death of the traders and some of the seeds did not produce highly effective bark.

It was not until 1865 that seeds that produced trees with highly effective bark was smuggled out of Peru.

An English trader in Lima,
Charles Ledger befriended a Bolivian,
Manuel Mamani.

Mamani obtained seeds from a special grove of Cinchona trees in the high Andes.



Charles Ledger
1865

Manuel Mamani
1865

Soon afterwards
he was killed by
some of his
countrymen
as being a traitor

C. *ledgeriana*
5 times more
active than
previous types

Some of the seeds were planted in the High Hills in South India, in Sri Lanka and Africa by English planters,
but they did not grow well.

Some seeds were sold to the Dutch and they flourished when planted in Java, Indonesia.

the 'Tjinjiroean government plantation', Java

Right into the mid 1900s most of the world’s supply of cinchona came from the plantations in Java

After 2 years of growth the trees were cut down and the bark was sent to Amsterdam, the Netherlands for refining.

The quinine was used mainly for flavouring in drinks and a lesser amount was used to make medicinal quinine.

In 1820 French Chemists Pierre Pelletier and Joseph Caventou extracted the active alkaloid from the cinchona bark

DECOUVERTE DE LA QUININE

150ème ANNIVERSAIRE DE LA

PAR PELLETIER & CAVENTOU

1820·1970

J. VAN NOTEN 1970

CHINCHONA

20c

REPUBLIQUE RWANDAISE


DECOUVERTE DE LA QUININE
1820 · 1970
J. VAN NOTEN - 1970
150ème ANNIVERSAIRE DE LA
PAR PELLETIER & CAVENTOU
LES PHARMACIENS
J. PELLETIER
J.B. CAVENTOU
70F
REPUBLIQUE RWANDAISE

During WW2 the chief medical officer of the Australian Army realised that Singapore would fall to the Japanese advancing down the Malay peninsula.

So he purchased a large quantity of quinine from Indonesia.

He put half on each of two ships sailing to Australia in case one was lost en route.

Both ships were sunk by Japanese submarines.

Then the Japanese occupied Indonesia.

The Germans had already occupied Holland.

And so the rest of the world had no access to quinine.

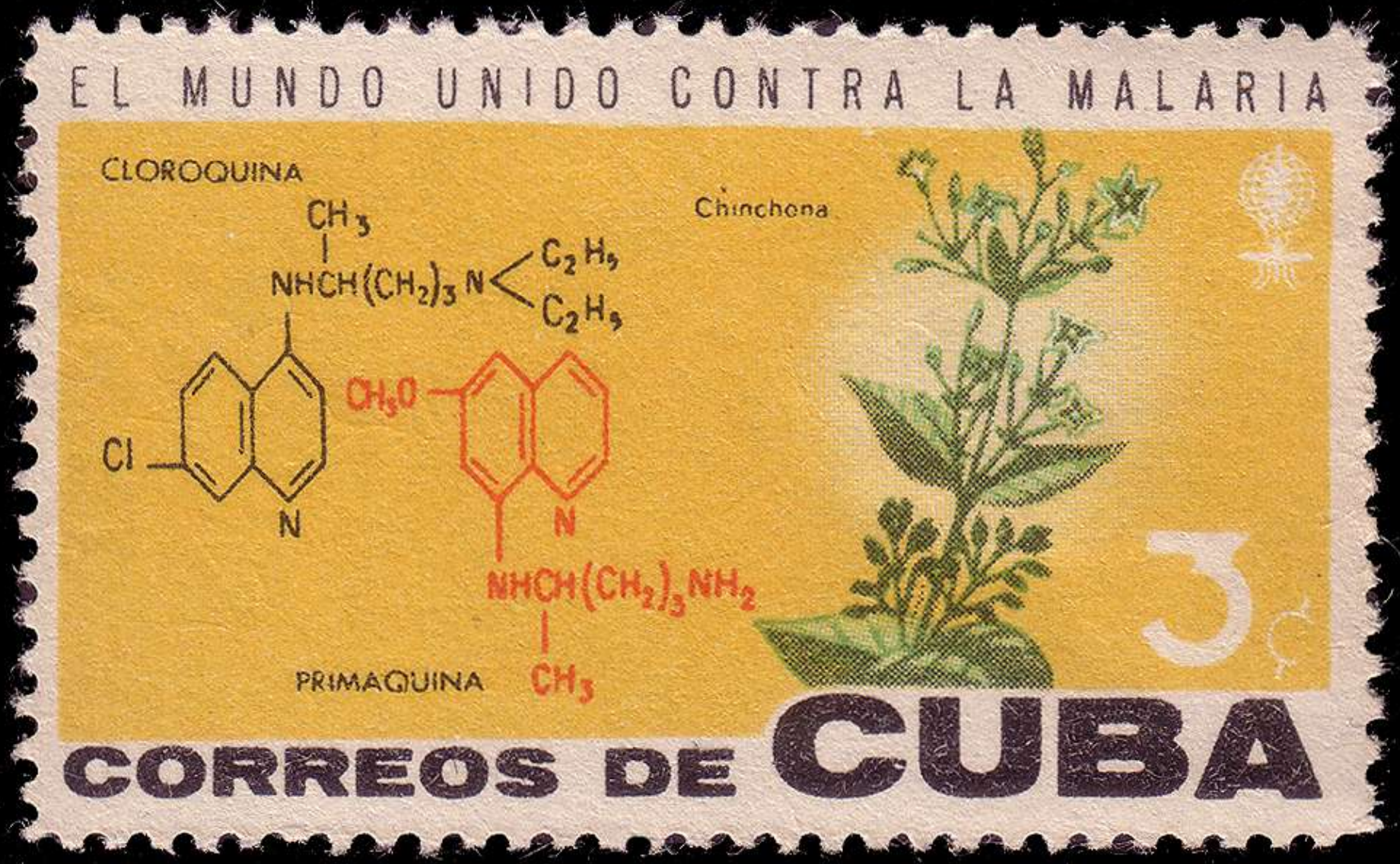
Chemists in the US then made synthetic drugs - Atebrin, Chloroquin, Camoquin and Primaquin from the

Chemists in the US then made synthetic drugs –

Atebrin, Chloroquin, Camoquin and Primaquin

from the quinine molecule.

These drugs played an important part in the subsequent Pacific Campaign.



During WW2 US chemists made synthetic antimalarials from the quinine molecule

The newest antimalarial drug

From about 1990 A drug derived from a plant grown in China has been used effectively against malaria.

The name is artemesenin and the derivative that is currently being used is artemether.

One could say that the ‘wheel has come full circle’ and we are back to treating malaria with herbal medicine which was the universal form of medicine before the introduction of ‘scientific medicine’ in the last half of the 1800s. (nineteenth century).

On the other hand, one could also say that we are now trying to eradicate malaria by using 21st century technology to make an effective vaccine against malaria.