Neuromuscular Block

Produced by the Wellcome Film Unit, 1956.
In collaboration with Dr B G B Lucas, Surgical Unit, University College Hospital Medical School.

Directed by Ronald Goodliffe & Douglas Fisher.
Script by Florence Anthony.
Animation: Ronald Goodliffe.
Photography & Editing: Douglas Fisher.
Artist: Joan Goodliffe.
Voice: Peter Hawkins.
Recordist: Maurice Askew.

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Colour
Duration: 00:11:16:06

00:00:00:00

<Opening titles>

<Opening scene shows re-enactment of hospital theatre staff preparing to operate on a patient >

<Surgeon to anaesthetist>

I think you'd better use a relaxant.

<Close-up of anaesthetist with sweat breaking out on his forehead>

<Animation of man narrating in rhyming form to camera>

Why all this panic, friend?
It's not so difficult to comprehend
but since you find it such a tussle, come.
Let's have a diagram.

<Animated man draws diagram>
Here's a muscle and over here a nerve,
down which an impulse travels. And observe,
a chemical is formed, acetylcholine, whose action
is to produce a muscular contraction.
This role played is rapidly destroyed
by an enzyme, cholinesterase.
And, as you see, the cycle just completed
with each succeeding impulse is repeated.
Now for a relaxant. There are, as you see, a host,
but tubocurarine is better known than most.
This blocks the acetylcholine's tracks
and the muscle stays relaxed.

A small dose of neostigmine, note,
is quite an effective antidote.
It combines with cholinesterase
and some of the acetylcholine stays,
accumulates, overcomes the barrier
and the muscle can contract again.
But be careful, there's a danger here:
give too much neostigmine
and all the cholinesterase may disappear.
The acetylcholine will thus remain
and you see the muscle's paralysed again.

Let us now proceed to another relaxant,
succinylcholine. Akin to acetylcholine in action,
it even produces an initial contraction,
but the effect of cholinesterase on this is slow
and paralysis lasts a few minutes or so.

And now the decamethonium.
Similar to the last one and, in fact,
it too can cause a muscle to contract.
But, unaffected by cholinesterase, it will stay
until the bloodstream carries it away.
Its effect is protracted therefore.
The paralysis may last half an hour or more.

Well, and now that we've seen
the simple but abstract scheme,
let's see how well all this makes sense
when tested on the laboratory bench.
At some stage in your education
you must have seen this preparation: *<narrates over live film>*
a rat diaphragm in Ringer solution
stimulated into regular contractions.
Tubocurarine is added.
And here we trace its action.
And in a short time, we're not surprised
to see the muscle fully paralysed.
The bath is emptied, the tubocurarine removed
and upon refilling muscular conditions much improve.
After a second wash to make all sweet,
muscular recovery is complete.

Another dose of tubocurarine is given.

The tracing follows its expected path.
Then neostigmine is added to the bath.
As we anticipate from what has gone before,
the muscle is recovering once more.
But if a second larger dose of antidote we add,
conditions quickly go from good to bad.
Quite soon the muscle's paralysed again.
And, note carefully, excess acetylcholine is to blame.

Now succinylcholine: first a paralysis,
then the bath washed twice,
succinylcholine added once more
and the muscle's paralysed.
Give a small dose of neostigmine again
but this time, as you see, there is no change.
And if we give a larger dose still,
the contractions quickly reduce to nil.
From this, of course, you will deduce
that neostigmine is no use
for succinylcholine overdose,
nor indeed, as this trace shows,
for too much decamethonium.

I'm sure you've not found it hard to follow
all the facts so far but, as you must already know,
there's an electrical side to this story,
so just have a look at this micro slide
which, when it's greatly magnified,
shows the nerve endings on a muscle.

00:05:36:00

Now, observe what happens when

an impulse comes along the nerve.
Note first that the outside of the nerve
is positively charged relative to the inside,
that is until an impulse passes
when the outside briefly negative becomes.
In this way nervous impulses hustle
quickly down towards the muscle.
And here a similar process acts
whenever a muscle is caused to contract.
The only difference in this case
is that the change in electrical state
is accompanied by physical action,
namely a contraction.

These electrical impulses you may recall
are very rapid and very small,
but they've all been measured frequently,
and here's the set-up for you to see.
In Ringer solution a frog muscle's placed;
the nerve is traced
and laid across two electrodes with wires attached.
Stimulated through these, the muscle contracts.
An earth lead is added, the bath run dry.
Two recording electrodes are placed nearby.
And the impulses which these receive
are visible on the CRT and photographed simultaneously.

<Animated man to camera>
But potential changes on a single end plate
are far less simple to demonstrate
and so back to our diagram we'll go. *<Narration over animated film>*
And here we can show
how the acetylcholine slightly reduces

the end plate potential until it produces,
by this action,
the muscular impulse and contraction.
The oscilloscope tube should make it quite clear.
You see the potential diminishing here
and when it is reduced to a critical fraction,
a spike marks the start of both impulse and contraction.
The basic principle being made plain,
let's try out our relaxants over again.
Tubocurarine first: now we've said that this acts like a block
but, in fact, this is only partly true –
for some acetylcholine does get through,
but not enough to reduce potential
to the low level essential.
This, since acetylcholine is partly stopped,
is what is termed competitive block.
So, we see on the oscilloscope
a potential reduction, quite remote
from the height at which it could produce a spike.

Succinylcholine and decamethonium, on the other hand,
act rather differently for both of these can produce
end plate potential to the critical values and, in fact,
cause the muscle to contract.
But, having done so they simply remain,
and you cannot excite the muscle again.
What's more, this reduced potential spreads
quite a little beyond the end plate's edge.
You will not be surprised then that what we have shown
as depolarisation block is known.
The oscilloscope, we know, will obviously show
first a spike of normal height
and consequential reduced potential.

<To camera>
Now for our labourers to reap the fruits.
Let's put our relaxants into two groups:
competitors and depolarisers,
but some don't quite belong to either.
And one more thing against this plan
is that some depolarisers can
act as competitors and vice versa.
Just why these compounds act this way,
it's really very hard to say,
though if you look at their molecules,
you may see what one might describe
as a sort of family likeness.
They all look rather complicated
and are of a similar size and shape.
Two quaternary nitrogen atoms in each appear,
known for about a hundred years
to be a characteristic of agents producing muscular block.
Acetylcholine follows a similar pattern
but with only one quaternary nitrogen atom,
and its only half their size.
But in spite of much surmise,
no one knows whether to attach
much significance to these facts.

And there now just a word before I go –
there's one more thing you ought to know
about suspected overdose.
If ever you meet this situation *<image of man lying unconscious on operating theatre>*
give artificial respiration.
If after this it's still not plain,

you'd better see the film again.

<End credits>

<In addition to those already listed at beginning of transcription>

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