

# ΠΡΑΚΤΙΚΑ ΤΗΣ ΑΚΑΔΗΜΙΑΣ ΑΘΗΝΩΝ

ΣΥΝΕΔΡΙΑ ΤΗΣ 4<sup>ΗΣ</sup> ΦΕΒΡΟΥΑΡΙΟΥ 1954

ΠΡΟΕΔΡΙΑ ΓΡΗΓΟΡΙΟΥ ΠΑΠΑΜΙΧΑΗΛ

ΠΡΑΞΕΙΣ ΚΑΙ ΑΠΟΦΑΣΕΙΣ ΤΗΣ ΑΚΑΔΗΜΙΑΣ

ΑΝΑΛΗΨΙΣ ΤΗΣ ΠΡΟΕΔΡΙΑΣ

Ὁ Πρόεδρος κ. **Γρηγ. Παπαμιχαήλ**, ἀναλαμβάνων τὰ καθήκοντά του, ἀπή-  
θυνε τὸν κάτωθι χαιρετισμὸν πρὸς τὰ μέλη τῆς Ἀκαδημίας :

*Κύριοι συνάδελφοι,*

*Ἐνεκεν ἀσθενείας μὴ δυνηθεὶς νὰ παρασιῶ κατὰ τὴν ὑπὸ τοῦ διαπρεποῦς  
προκατόχου μου κ. Κουρέα κατάθεσιν τῆς προεδρίας τῆς Ἀκαδημίας, σήμερον  
τὸ πρῶτον παραλαμβάνων παρ' αὐτοῦ τὴν προεδρικὴν ἔδραν, καὶ πάλιν πολλὰς  
ὁμολογῶ χάριτας πρὸς τὴν Ὀλομέλειαν, ἀγαθυνθεῖσαν διὰ τῆς τόσον τιμητικῆς  
δι' ἐμὲ ψήφου της νὰ μὲ τάξῃ εἰς τὴν θέσιν ταύτην. Εἶπε δὲ δι' ἐμὲ τιμὴ ὅτι  
διαδέχομαι ἐπιφανέστατον συνάδελφον μετὰ περισσῆς συνέσεως καὶ ἄκρας εὐστο-  
χίας διευθύνοντα τὰ τῆς Ἀκαδημίας, ὅθεν καὶ ἀναδειχθέντα ἄξιον τῶν θεομῶν  
συγχαρητηρίων καὶ εὐχαριστιῶν τοῦ ἡμετέρου σώματος.*

ΕΚΛΟΓΗ ΤΑΚΤΙΚΟΥ ΜΕΛΟΥΣ

Δι' ἀπολύτου πλειοψηφίας ἐξελέγη τακτικὸν μέλος ἐν τῇ τάξει τῶν Θετικῶν  
Ἐπιστημῶν πρὸς πλήρωσιν ἔδρας τῶν ἰατρικῶν ἐπιστημῶν ὁ κ. **Γεώργιος  
Φωτεινός**, ὁμότιμος καθηγητῆς τῆς Ἱατρικῆς Σχολῆς τοῦ Πανεπιστημίου Ἀθηνῶν.

ΑΝΑΚΟΙΝΩΣΕΙΣ ΜΗ ΜΕΛΩΝ

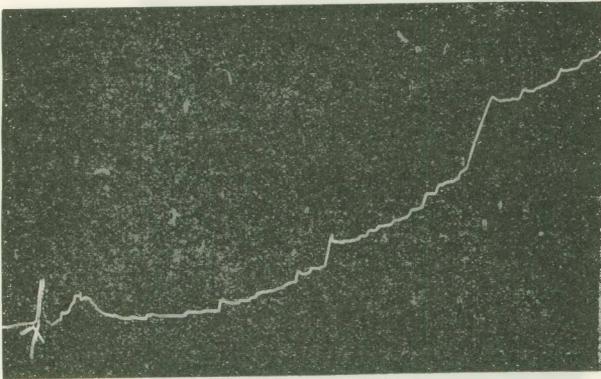
ΦΑΡΜΑΚΟΛΟΓΙΑ. — **Spasmogenic action of the antihistaminic drugs  
on leech muscle**, by *N. Klissianis*. \* Ἀνεκοινώθη ὑπὸ τοῦ κ. Γεωργ.  
Ἰωακείμογλου.

Action of the antihistaminic drugs on all living structures are of great  
importance. This is because other actions of the antihistaminic drugs can

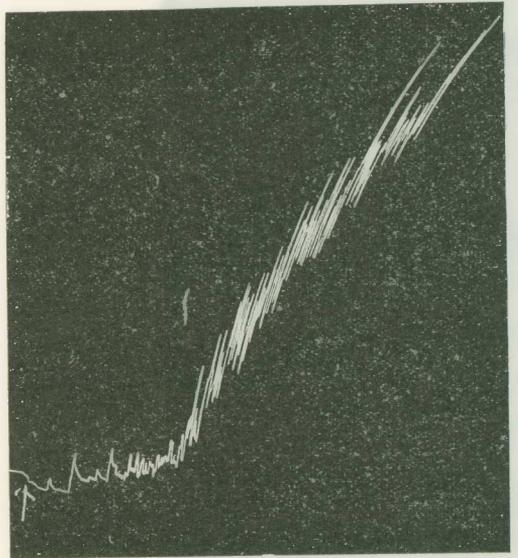
\* Ν. ΚΛΕΙΣΙΟΥΝΗΣ: Ἐρευναι περὶ τῆς σπασματικῆς ἐνεργείας τῶν ἀντιισταμινικῶν  
ἐπὶ τοῦ μυὸς τῆς βδέλλας.

also be involved in the antihistaminic effect and not only the specific one against histamine for ex. counteraction of allergic manifestations can also be explained through other actions of these drugs than the antihistaminic. The specificity of the antihistaminic action has been corroborated through many facts. It is well known that antihistaminic effect includes also an anticholinergic action, but this anticholinergic action cannot explain the antihistaminic effect. For ex. benadryl acts in the gut as an anticholinergic as well as against barium contraction. But these effects do occur at a benadryl concentration which is much higher than the action of benadryl against histamin<sup>1)</sup>. Another fact which does not indicate that the antihistaminic action on smooth muscle is a spasmolytic one is that in many smooth muscle structures as gut, uterus, in vitro as in vivo, some antihistaminics act as spasmogenics<sup>1)</sup>. To test these phenomena we have made experiments on blood leeches, which are very insensible to histamine. We have worked in the way described by Joachimoglu<sup>2-3)</sup>. The sensitivity of the leeches varies, some of them react slowly. To increase sensitivity we used to let the leeches some days before experiments suck blood from the belly of a lightly narcotised cat. We have used the following drugs: 1) Benadryl Dambergis (Beta dimethyl aminoethylbenzhydryl ether hydrochloride), 2) Neo-antergan Specia (N-p methoxy benzyl -N- dimethylaminoethyl- a- aminopyridine), 3) Phenergan Specia (N-dimethylamino -2- propyl 1 phenothiazine), 4) Pyribenzamine citrate Dambergis (N- benzyl-N- dimethylethyl- a- aminopyridine). All the drugs used were in powder form. Only the back muscular layer of the leech was used. This was cut in pieces which were degaglionated and fixed in a bath of 50 c.c. of Ringer (\*) A Gimbal level was used for recording the contractions. The removal of the ganglia was verified, because the level wrote in the beginning a lightly ascending or horizontal line. At this point we added to the bath one of the above mentioned drugs i. e. benadryl in a concn. of 1 to 1000. After a little time we observe that the muscle starts contractions which are recorded very strong by the level, (curve 2 and 5). This action is so strong that even after many washings from the antihistaminic the muscle continues carrying out small contractions. The same we can observe with a concentration of 1 0/100 N- autergan (curve 1 and 6). The limit of the minimal acting dose of be-

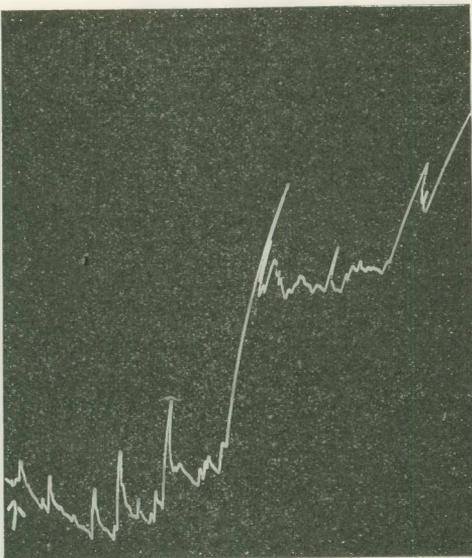
(\*) Ordinary Ringer was applied. (6g NaCl, 0,075 g. KCl, 0,1 g. NaHCO<sub>3</sub>, 0,1 g. CaCl<sub>2</sub>, H<sub>2</sub>O 1000 c.c.).



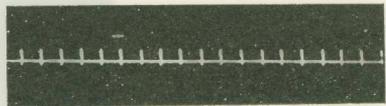
1) By ↑ addition of Neoantergan 1 ‰  
 1) Είς ↑ προσθήκη N-antergan 1 ‰



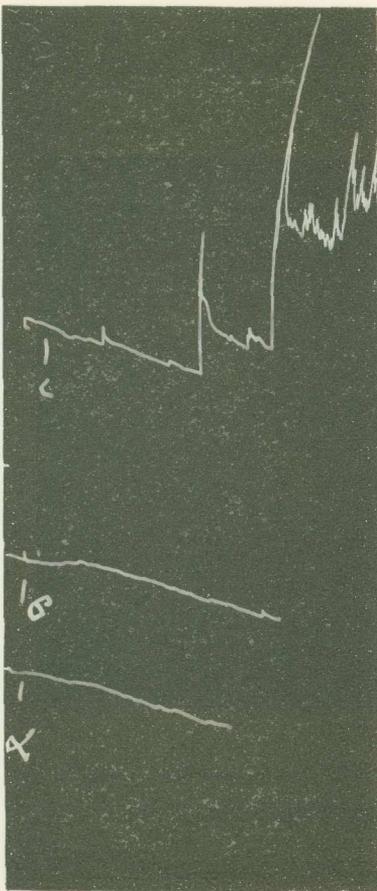
2) By ↑ addition of Benadryl 1 ‰  
 2) Είς ↑ προσθήκη Benadryl 1 ‰



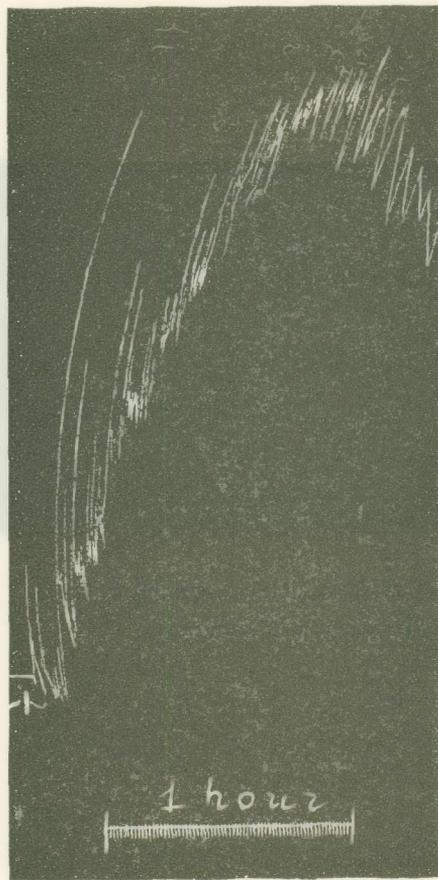
3) By ↑ addition of Pyribenzamine 1 ‰  
 3) Είς ↑ προσθήκη Pyribenzamine 1 ‰



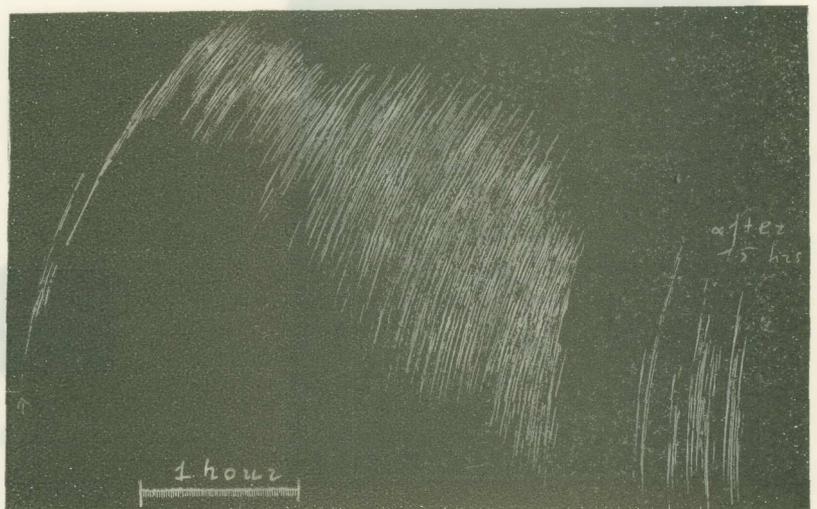
Time = 60"  
 Χρόνος = 60"



- 4) a - addition of  $BaCl_2$  1/100,000  
 b - addition of Neoantergan 1/30,000  
 c - addition of  $BaCl_2$  1/100,000 + Neoantergan 1/30,000
- 4) α = Προσθήκη  $BaCl_2$  1/100,000  
 β = Προσθήκη N-antergan 1/30,000  
 γ = Προσθήκη  $BaCl_2$ , 1/100,000 + N-antergan 1/30,000



- 6) By ↑ addition of N-Antergan 1:5,000  
 6) Είς ↑ προσθήκη N-Antergan 1:5,000  
 Χρόνος ----- 1 ώρα



- 5) By ↑ addition of Benadryl 1:5,000  
 Figure has been reduced to  $\frac{2}{3}$  of its size

- 5) Είς ↑ προσθήκη Benadryl 1:5,000  
 Χρόνος ----- = 1 ώρα

nadryl is 1 : 30,000. With N-antergan and Pyribenzamine this is 1 : 10,000, depending on sensitivity of the leeches. Addition of phenergan 1‰ to Ringer has not a such effect but this is not significant because Ringer gets at the same time turbid. The contractions are not counteracted when one adds histamine on the peak of the contractions. Atropine is also ineffective. This action can be explained through a stimulatory effect on the muscle or the nerve endings which after the removal of the ganglia remain in the muscle. To detect that, we have worked in a manner similar to one applied by Joachimoglu<sup>2)</sup>. We add to the bath a dilution of BaCl<sub>2</sub> 1/100,000. This causes no action on the muscle. After 1 hour during which the muscle was washed 4 times, we add to the bath a dilution of for ex. 1 : 30,000 N- antergan. No action occurs. After washing we add both these drugs at the above concentrations. We observe now a strong action, (curve 4). This proves that a dynamic synergism, exists between these two drugs and as it is accepted that BaCl<sub>2</sub> acts specifically on muscle fibers we have to assume that this also applies for this antihistaminic.

#### Conclusion

- 1) Antihistaminic drugs act spasmogenically on sensitive leech muscle.
- 2) The above action is a myotropic one.

#### ΠΕΡΙΛΗΨΙΣ

Ἡ ἐνέργεια τῶν ἀντιισταμινικῶν φαρμάκων ἐπὶ τῶν λείων μυϊκῶν ἰνῶν εἶναι σπασμολυτικὴ; Τοῦτο ἐσπουδάσαμεν ἐπὶ τοῦ μυὸς τῆς βδέλλας. Ἐχρησιμοποιήσαμεν πρὸς τοῦτο τὰ ἑξῆς ἀντιισταμινικά ὑπὸ μορφήν κόνεως: 1) Βεναδρούλη Δαμβέργης, 2) Νεοαντεργάνη Specia, 3) Φενεργάνη Specia, 4) Πυοιβενζαμίνη Δαμβέργης. Τεμάχια τοῦ ραχιαίου τμήματος τῆς βδέλλας μετὰ ἀφαίρεσιν τῶν γαγγλίων στερεοῦνται εἰς ποτήριον περιέχον 50 κ.ἔ. Ringer. Προσθήκη διαλ. 1‰ Βεναδρούλης προκαλεῖ ἰσχυρὰς συσπάσεις. Ἡ ἐνέργεια αὕτη φθάνει μέχρις ἀραιώσεως 1 : 30,000.

Εἰς τὴν Νεοαντεργάνη ἡ ἐνέργεια φθάνει μέχρις 1 : 10,000.

Ἐκ τῶν γενομένων πειραμάτων συνάγεται :

- 1) Ὅτι ἐπὶ τοῦ μυὸς τῆς βδέλλας τὰ ἀντιισταμινικά προκαλοῦν συσπάσεις.
- 2) Ὅτι πρόκειται περὶ ἀμέσου ἐνεργείας καὶ οὐχὶ περὶ ἐνεργείας ἐπὶ νευρ. ἀπολήξεων.

#### BIBLIOGRAPHY

- 1) Loewt E. R., Annals of the N. Y. Acad. of Sciences. 50, pg. 1149 - 1150. 1950.
- 2) G. Joachimoglu, Arch. f. exp. Path. and Pharm. 88. 1920. 364.
- 3) G. Joachimoglu - N. Klissunis, Schw. Med. Wschr. 78. 1948. 21. 519.