The therapy (corticosteroids, resochin) did not influence either of the immunological reactions ($P > 0.05$) mentioned. There was no significant relation between either of the immunological reactions and the duration of the rheumatoid arthritis.

At an interval of three weeks after the skin testing a significant rise of antistreptolysine O titre occurred simultaneously with antistreptokinase in only one of all our patients with rheumatoid arthritis.

Discussion. In order to explain the inhibition of skin reaction in patients with rheumatoid arthritis, two postulates may be considered: the desensitization of delayed hypersensitivity and immunological hyporeactivity. There is no evidence favouring the first possibility. The mechanism of desensitization is immunologically specific and as yet we have no basis for a special disposition to desensitization in rheumatoid patients. More acceptable is the second possibility, that the inhibition of delayed hypersensitivity is a general reaction of rheumatoid subjects. EPSTEIN and JESSAR[9] demonstrated the decrease of reactions to conjugated antigens of chemical compounds. Although different antigens were used, our results are in agreement with this report.

The increase of antistreptokinase titres might be caused by recent streptococcal infection. With respect to the lack of clinical symptoms, to the negative throat cultures and to the negative responses in antistreptolysine O titre, the above-mentioned possibility may be rejected. The failure to demonstrate antistreptolysine O rise consistent with antistreptokinase is evidence that no kind of non-specific antibody response occurred.

The increased specific antistreptokinase antibody responses in rheumatoid patients could be interpreted as indicating that a considerable proportion of rheumatoid subjects have had contact with this antigen either fairly recently or on numerous occasions – or that these patients had for some other reason been able to respond immunologically to the minimal dose of the skin testing antigen better than the other patients.

Our results are in agreement with generally accepted immunological hyper-reaction in rheumatoid subjects. MEISELAS et al.[5] showed in patients with rheumatoid arthritis an increased antibody response to Brucella vaccine, and GREENWOOD and BARR[4] to tetanus toxoid.

In conclusion, it should be emphasized that immunological reaction in rheumatoid patients undergoes a change: symptoms of delayed hypersensitivity are inhibited but the specific antibody response is, however, increased. Whether this discrepancy of immunological reaction has some relation to the pathogenesis of rheumatoid arthritis remains for further work to elucidate.

Zusammenfassung: Es wird über die immunologische Reaktivität von Patienten mit progressiver Polyarthritis berichtet. Nach Injektion von 25 E Streptokinase (Präparat Dornokinase) zeigten die Patienten eine gewisse Dissoziation der immunologischen Vorgänge: Herabsetzung der Hautreaktionen und erhöhte spezifische Antikörperreaktion.

V. HOUBA, M. ADAM,
J. MALEČEK, and B. TESÁREK

Research Institute for Rheumatic Diseases, Prague (Czechoslovakia), May 15, 1964.

[9] W. L. EPSTEIN and R. A. JESSAR, Arthr. Rheum. *2*, 178 (1959).

Light Sensitivity in the Amphipode, *Niphargus aquilex schellenbergi* Karaman

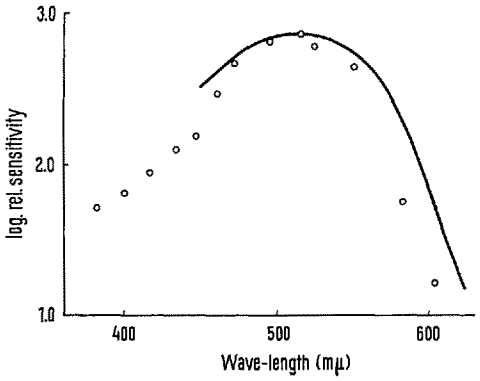
Amphipodes of the genus Niphargus are colourless, transparent arthropodes without lateral or medial eyes. They live in subsoil water in rock crevices (new red sandstone), coming to the surface in springs. Observations on the diurnal periodicity of Niphargus showed that light acts as a time giver[1]. In order to study the photic response of the amphipodes more specifically, 14 medium sized specimens (6–9 mm) were put into a flat test chamber of 3 cm diameter filled with spring water. One half of the chamber was in the dark, the other half was lit from above by a 1000 Watt xenon arc passed through a set of double interference filters and neutral density filters. Threshold determinations were made by counting the relative numbers of animals at the end of a 5 min stay in the dark and after 2 min in the light. During exposure to intense illumination, the organisms showed strong negative photokinetic reactions. In order to measure the absolute threshold, the light intensity was reduced in steps of 0.15 log unit until the organisms ceased to show any movement in response to light. With illumination by white light, the absolute threshold was at 3.5 lm/m^2 (about 10^6 times the absolute threshold of the human eye). No change of sensitivity was seen after the animals had been kept for several hours in darkness. However, the organisms showed slight signs of fatigue at the end of a 4 h experiment. Further, after several days, the sensitivity was found to be slightly increased, being constant during the later stages of the investigation.

Dividing the test chamber into two parts differentially illuminated by two beams of light, the organisms preferred the darker half of the chamber if the difference of illumination between the two parts was more than 17%. This ratio was fairly constant throughout the range of illumination, 3.5 to 2240 lm/m^2.

The results of measurements of the spectral sensitivity of Niphargus are shown in the Figure (circles, mean values of two days). Sensitivity is highest at 515 mμ and declines towards either side. Compared with the absorption spectra of known photopigments, the sensitivity data between blue and green are close to the absorption of lobster rhodopsin[2] (drawn-out line in the Figure). However, in the region of shorter and longer wavelengths, the sensitivity of Niphargus is definitely lower than the absorption spectrum of both lobster rhodopsin and visual pigment 515 mμ[3]. Since the spectral variation of the amount of

[1] K. MÜLLER, A. KURECK, and A. MÜLLER-HAECKEL, Naturwissenschaften *50*, 579 (1963).
[2] G. WALD and R. HUBBARD, Nature *180*, 278 (1957).
[3] H. J. A. DARTNALL, Brit. Med. Bull. *9*, 24 (1953).

light absorbed by visual pigment depends on the optical density of the pigment[3], the shape discrepancy between the sensitivity measurements and the absorption spectrum of lobster rhodopsin could be due to a low concentration of visual pigment in the unidentified photosensitive structure of Niphargus. An approximately equally high absolute light threshold (10 lm/m²) and low sensitivity to red light has been reported in *Niphargus orcinus virei*[4].



The circles show the relative spectral sensitivity of the negative photokinetic reaction of *Niphargus aquilex schellenbergi*. Equal quantum intensity spectrum 382–605 mμ. The absorption curve of lobster rhodopsin[2] is shown for comparison.

Zusammenfassung. Die absolute Schwelle der negativen Phototaxis der augenlosen, unpigmentierten Antipode *Niphargus aquilex schellenbergi* Karaman liegt bei 3,5 lm/m², die Unterschiedsschwelle gegenüber höheren Leuchtdichten beträgt 17%. Die zwischen 382 und 605 mμ bestimmte Spektralsensitivität zeigt ein Maximum bei 515 mμ.

A. KURECK

William G. Kerckhoff-Herzforschungsinstitut der Max Planck Gesellschaft, Bad Nauheim (Deutschland), May 25, 1964.

[4] R. GINET, Ann. Spéléol. *15*, 127 (1960).

Aufnahme von Thymidin durch Mastocytomzellen *in vitro* unter der Einwirkung von Podophyllumstoffen

Die DNS-Synthese wird durch Cytostatica aus der Reihe der alkylierenden Stoffe (N-Lost, Äthylenimine) gehemmt[1–3]; sie scheint jedoch durch Spindelgifte wie die Vincaalkaloide und Colchicin in therapeutischen Konzentrationen nicht beeinträchtigt zu werden[4,5].

Die Podophyllum-Wirkstoffe SP-G[6] und SP-I[7] stellen Cytostatica vom Spindelgifttyp dar[8]. Als spezifisch auf die Mitosespindel wirkende Präparate sollten sie den Einbau von Thymidin, welcher üblicherweise als Parameter der DNS-Synthese gilt und nicht während der Mitose stattfindet, nicht stören. Ob dies der Fall ist, wurde in den im folgenden dargestellten Versuchen abzuklären versucht.

In Erlenmeyerkolben sich vermehrenden P-815-Mastocytomzellen wurden SP-G, SP-I und zum Vergleich N-Lost (Methyldi(β-chloräthyl)-amin; Dichloren) in verschiedenen, die Zellvermehrung vollständig hemmenden Konzentrationen zugesetzt. Die Zellkulturen standen $2^1/_2$ bzw. $6^1/_2$ h unter der Einwirkung der Cytostatica. ^{3}H-Thymidin wurde ihnen, sowie unbehandelten Kontrollkulturen, jeweils eine halbe Stunde vor Versuchsende in einer Konzentration von 0,08 μg/ml (= 0,9 μC/ml) zugegeben. Nach 30minütiger Inkubation mit Thymidin wurden die Kulturen in Eiswasser abgekühlt, die Zellen abzentrifugiert und in inaktiver Nährlösung (Basalmedium Eagle mit 10% Pferdeserum und 0,004‰ Folsäure) gewaschen. Hierauf erfolgte die Bestimmung der Radioaktivität im Sediment (dpm/mg Feuchtgewicht der Zellen). Aus diesen Zahlen lässt sich direkt auf den Thymidingehalt der Zellen schliessen (siehe Tabelle).

Da sich bei SP-G und SP-I keine Abhängigkeit der Beeinflussung der DNS-Synthese von der Konzentration des Wirkstoffes ergab, sind in der Tabelle die Resultate mit verschiedenen Konzentrationen zusammengefasst; die niedrigsten geprüften Gehalte sind so gewählt, dass sie eben noch eine totale oder subtotale Vermehrungshemmung zur Folge haben. Aus den Zahlen der Tabelle ist

Einfluss von 2 Podophyllumstoffen und einer alkylierenden Substanz auf den Thymidineinbau durch Mastocytomzellen *in vitro*. Konzentrationen: SP-G 0,63 bis 1,3 μg/ml; SP-I 0,63 bis 3,2 μg/ml; N-Lost (Dichloren) 0,1 μg/ml. P = Signifikanz der Abweichungen von den Kontrollen.

Cytostaticum	Versuchsdauer h	Veränderung des Thymidineinbaus gegenüber Kontrollen %	P
SP-G	$2^1/_2$	− 1,7	$> 0{,}4$
SP-I	$2^1/_2$	+ 11,0	$> 0{,}1$
SP-I	$6^1/_2$	+ 3,0	$> 0{,}4$
N-Lost	$2^1/_2$	− 31,5	$< 0{,}01$
N-Lost	$6^1/_2$	− 35,0	$< 0{,}01$

[1] G. PALME, E. LISS und F. WIEBEL, Naturwissenschaften *51*, 197 (1964).
[2] E. LISS und G. PALME, Naturwissenschaften *50*, 672 (1963).
[3] H. B. BREWER JR., J. P. COMSTOCK und L. ARONOW, Biochem. Pharmacol. *8*, 281 (1961).
[4] W. A. CREASEY und M. E. MARKIW, Biochem. Pharmacol. *13*, 135 (1964).
[5] TH. T. PUCK und J. STEFFEN, Biophysical J. *3*, 379 (1963).
[6] Benzylidenverbindungen der *Podophyllum-emodi*-Glucoside; Hauptkomponente ist Podophyllotoxin-β-D-benzylidenglucosid.
[7] Äthylhydrazid der Podophyllinsäure.
[8] H. STÄHELIN und A. CERLETTI, Schweiz. med. Wschr., im Druck.