That the alterations in systemic blood pressure represent a direct interaction between drug and brain tissue is confounded by the recognition that changes in cerebral arterial tonus can modify peripheral vascular responses (Kaneko, McCubbin & Page, 1960; Mitchell, Sciven & Rosendorff, 1975). Dyer & Gant (1973) have shown that mescaline constricts umbilical vasculature and it may be inferred that systemic blood pressure changes observed in this study may reflect mescaline action at the cerebral vascular level.

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Effect of non-steroidal anti-inflammatory drugs on the tetrazolium reductase activity of leucocytes

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One property of non-steroidal anti-inflammatory drugs (NSAIDs) is their inhibitory action on the migration and phagocytic activity of monocytes. In concentrations effective in clinical treatment they also inhibit the phagocytosis of starch particles and bacteria by polymorphonuclear cells (Di Rosa, Papadimitriou & Willoughby, 1971; Di Rosa, Sorrentino & Parente, 1972; Ruutu & Kosunen, 1972; Yi-Han Chang, 1972). The inhibitory effect extends to the chemotaxis of polymorphonuclear cells induced by fragments formed during complement activation. NSAIDs also inhibit the activation of lymphocytes by mitogens (Whitehouse, 1967).

We wanted to know whether clinical treatment with some NSAIDs influenced circulating neutrophil granulocytes which play a part in the non-specific defence against microorganisms and in the development of inflammatory reactions. The reduction of nitrotetrazolium blue (NBT-test, Baehner & Nathan, 1967, 1968) has been frequently used to assess the functional state of phagocytes. Another substrate for the estimation of tetrazolium reductase activity that is particularly suited to quantitative photometric examination is iodonitrotetrazolium (INT) (Lokaj & Oburková, 1974). To our knowledge the possibility of influencing the NBT-test by NSAIDs has received only brief mention (Douwes, 1972).

For our purpose we used blood samples from patients of either sex who were being treated for post-traumatic conditions or milder forms of degenerative diseases of the locomotor system and who were otherwise clinically healthy. Their ages ranged from 35–65 years. Groups of five patients were treated with NSAIDs for two weeks. The drugs used were: acetylsalicylic acid—3 g day^{-1}

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azapropazone (Prolixan Siegfried, Switzerland)—900 mg day^{-1}, clofezone (Perclusone Mack FRG—equimolar compound of phenylbutazone and clofexamide) 900 mg day^{-1}, Eumotol [Bumadizon-Byk-Gulden, FRG-butyl-malonyl-mono-(1,2-diphenyl hydrazide)], 330 mg day^{-1}.

Blood, heparinized, was collected before and after one and two weeks treatment and leucocytes separated by sedimentation in dextran. For phagocytosis rice starch (Amylum oryzae, Czechoslovak Pharmacopeia) was used. The reductase activity was estimated using INT (2,*p*-iodophenyl-3-nitrophenyl-5-phenyl-tetrazolium chloride, Lachema) as substrate in the test according to Lokaj & Obůrková (1974). The formazan obtained was extracted with acetone and assessed photometrically at 485 nm. The extinction (A_{485}) was calculated per 1×10^6 neutrophil granulocytes estimated in the haematological preparation from the original cell suspension.

We also wanted to know if changes in the reductase activity were reversible after treatment was stopped and for that purpose 5 patients were treated daily with 3 g of acetylsalicylic acid for one week and had no treatment for a second week.

The results are summarized in Table 1. Treatment with acetylsalicylic acid, azapropazone and clofezone after seven days led to a decline of the metabolic activity of peripheral polymorphonuclear cells, which was manifested by a reduced tetrazolium reductase activity. Eumotol had a slighter effect on the INT-test but there was a decline in the activity of phagocytozing polymorphonuclear cells. A decrease in reductase activity was also detected after two weeks treatment but the values did not differ substantially from those after seven days treatment. Seven-day treatment with acetylsalicylic acid led to a reduction of reductase activity; after subsequent seven days without the drugs normal values returned (Table 1).

Table 1. *Effect on INT reductase activity of treatment with non-steroidal antirheumatic drugs and after stopping treatment with acetylsalicylic acid.* Values are the differences in absorbance between non-phagocytozing and phagocytozing cells—A_{485}.

Treatment	Before treatment	After one week's treatment	After two week's treatment
Acetylsalicylic acid (3 g day^{-1})	0·050 ± 0·003	0·014 ± 0·002*	0·008 ± 0·003*
Azapropazone (900 mg day^{-1})	0·064 ± 0·006	0·020 ± 0·005*	0·015 ± 0·002*
Clofezone (600 mg day^{-1})	0·054 ± 0·002	0·016 ± 0·002*	0·012 ± 0·002*
Eumotol (330 mg day^{-1})	0·092 ± 0·005	0·062 ± 0·002*	0·054 ± 0·002*
Acetylsalicylic acid 3 g day^{-1})	0·055 ± 0·002	0·030 ± 0·004*	0·052 ± 0·002 (after seven days without treatment)

* Statistically significant difference $P < 0·02$ in comparison with the values before treatment.

The tetrazolium reductase activity of leucocytes reflects those metabolic changes which lead to the formation of microbicidal substances, in particular hydrogen peroxide and the superoxide radical (Nathan, 1974). Under normal conditions non-phagocytozing cells reduce tetrazolium salts only to a slight extent. This spontaneous reduction is enhanced in some pathological conditions, especially during bacterial infections.

NSAIDs are known to uncouple oxidative phosphorylation and to reduce the biogenesis of ATP. These drugs also inhibit dehydrogenases by competition for pyridine nucleotides which act as coenzymes (Whitehouse, 1965). This explains why the tetrazolium reductase activity of peripheral leucocytes is influenced during treatment with some NSAIDs.

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