## Effect of Mercury Derivatives of Fluorescein on the Fibrillation Threshold in Experimental Myocardial Infarction

Evidence of a rapid accumulation and long-term retention of mercury derivatives of fluorescein in the ischemia-damaged heart muscle has been established in previous papers. At the same time these substances clear fast both from the blood and the healthy myocardium. Thereby arises a high difference between the concentrations in the damaged muscle and in the healthy muscle and also between the levels in the damaged muscle and in the blood. The radioactive derivative that had proved in experiment to be most effective was called Mercurascan-$^{197}$Hg or -$^{203}$Hg according to the mercury isotope used. It was with the help of Mercurascan that it was for the first time possible to determine reliably the focus of myocardial infarction as a 'hot' area by in vivo scanning. Experiments with dogs as well as clinical tests indicated yet another clinically interesting property of Mercurascan, namely a lower occurrence of arrhythmias[1-3].

The experimental study was designed to verify whether application of mercury derivatives of fluorescein affects the occurrence of arrhythmias, particularly fibrillations.

*Methods and results.* Experiments were made with 17 dogs anaesthesized with Pentobarbital. During the experiment one-way ventilation of the dog by pure oxygen with absorbed $CO_2$ was carried out. Following thoracotomy, infarction was induced by ligating the ramus intraventricularis of the left coronary artery. Stimulation electrodes were inplanted into muscle fibers of the left ventricle in the following manner: $E_1$ electrode into the infarction focus, $E_2$ electrode into the healthy tissue and $E_3$ electrode into the border area between the two zones. Blood flow in the ischemic tissue was renewed 2 h after ligation; 30 min after the release of ligation the test substance was applied i.v. After another 30 min, measuring proper of the fibrillation threshold was resumed in the respective zones of the left ventricle's muscle. Measuring was repeated at 30-min intervals. In each experiment 2 dogs were studied simultaneously. One dog was given Mercurascan (0.5 mg/kg of body weight), the second placebo. The dogs were selected by lot.

The measuring proper of the heart's fibrillation threshold was carried out by alternate current (50 Hz). Current was turned on successively for an interval of 2 sec in the electrode circuits $E_1$, $E_2$ and $E_3$ against an indifferent large-surface electrode implanted in the subcutis of the chest. Measuring was started with standard 60/μA current increased leap-wise by 20/μA after 4 sec until irreversible arrest of circulation by fibrillation (or flutter) of the heart ventricles was induced. That value is referred to as the fibrillation threshold. Fibrillation of the ventricles was discontinued by a defibrillation discharge usually of 1 kV value applied directly to the myocardium. Thereafter the measuring was repeated.

The results are summarized in the Table. In instances where Mercurascan was applied i.v. 30 min after the release of ligation, a statistically significant rise of the threshold was registered in $E_1$ and $E_3$ electrodes as compared with the control, i.e. in $E_1$ electrodes implanted in the ischaemia-damaged zone and in $E_3$ electrodes in the border area between the 2 zones. On the other hand, the threshold did not rise in $E_2$ electrodes implanted in the zone not damaged by ischaemia.

*Discussion.* The ischaemic focus in the myocardium or the ischaemia-damaged tissue potentially increase the occurrence of extrasystoles or fibrillation of the ventricles. This is generally explained, on the one hand, by altered conductivity of the damaged tissue which therefore conduces to desynchronization of the myofibrils; on the other hand, by potential capacity of eddy currents of the damaged tissue to cause premature depolarization in the surrounding healthy tissue and thereby to contribute to fibrillation. In the therapy of fatal arrhythmias, it would be therefore of great advantage to block the unfavourable effect of the ischaemia-damaged tissue on the remaining tissues normally supplied with blood.

Owing to its tendency to accumulate and to fix only in the damaged muscle fibers, Mercurascan can be expected to act only in the ischaemic focus. This was also borne out by experiments which confirmed agreement between the distribution and retention of Mercurascan as well as its repressive effect on arrhythmias. After the application of Mercurascan, the fibrillation threshold values are significantly higher in the ischaemic area and somewhat lower in the zone surrounding the infarction focus. In the healthy muscle the values remain unchanged.

The action mechanism of the substance tested will be the subject of continued investigation. However, it appears from the basic series of our experiments that Mercurascan is capable of impeding the transmission of irritation from the ischaemia-damaged to the healthy tissue. This might have a favourable effect in the treatment of severe arrhythmia in the ischaemic heart disease.

*Zusammenfassung.* Experimentell wird an Hunden bewiesen, dass Fibrillationsschwellenwerte vom Ort des ischämischen Herdes und vom zwischen den zwei Zonen liegenden Raum durch Quecksilberderivate von Fluoreszein erhöht werden, diejenigen im gesunden Gewebe hingegen unverändert bleiben. Diese Befunde stimmen mit der Verteilung und Fixierung der Substanzen sowohl in geschädigtem wie auch in gesundem Myokardgewebe überein.

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Fibrillation threshold values

| Electrode | Without Mercurascan I (μA) | With Mercurascan I (μA) | Statistical significance for $P = 0.01$ |
|---|---|---|---|
| $E_1$ | 675 ± 87 | 2269 ± 187 | Significant difference |
| $E_2$ | 254 ± 15 | 258 ± 21 | Insignificant difference |
| $E_3$ | 376 ± 45 | 668 ± 72 | Significant difference |

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