Effect of high doses of nicotine in pigs
I. Changes of the electrocardiogram

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With 15 figures and 4 tables

Summary

Pigs in which venous catheters were positioned for long-term use were injected i.v. with high doses of nicotine in physiol. saline. The LD_{50} was 2.656 mg/kg body weight. Clinical symptoms were mainly: forced respiration, muscular tremor to tetanoid spasms, cyanosis of the skin, salivation and sometimes vomiting. The degree and duration of symptoms were dose-dependent.

Ecg changes in anaesthesized pigs following intravenous nicotine injections of 0.126 mg/kg and 0.378 mg/kg at 15 minutes' interval were immediately commencing disturbances of the heart rate in form of bradycardia and asystolia. After 5 sec we observed extrasystoles, tachycardia, sino-auricular block and AV-block of first and second degree as well as a number of T- and P-changes. Changes of the ecg were observed generally for 10 to 15 min, however, the T-wave remained sometimes negative or biphasic-preterminal negative for some hours.

Naturally, there is very little information about ecg changes in man due to severe acute nicotine intoxication. However, there are numerous ecg studies on the effect of nicotine in heavy smokers. An excellent review of this subject is given by v. Ahn (1). An increase in the heart rate by 10 to 25 beats per minute and a flattening of the T-waves by not exceeding 1–2 mm were found to be typical electrocardiographic findings following deep cigarette smoke inhalation. These findings were more pronounced after intravenous injection of 2 mg of nicotine. Patients with angina pectoris showed extrasystoles, negative or biphasic T-waves and depression of the ST segment following smoking or intravenous injection.

v. Ahn (1) investigated the effect of cigar and cigarette smoke as well as pure nicotine in two doses in young men (smokers and nonsmokers) during hypoxia. The hypoxia-test showed a flattening of the T-waves in spite of constant heart rate. Smoking during hypoxia resulted in a further flattening of the T-waves and a slight depression of the ST segment. Intravenous injection of nicotine provoked essentially the same ecg changes
as smoking. Injection of 1 mg of nicotine during hypoxia resulted in excessive hyperventilation of short duration; injection of 3 mg produced in some cases euphoria, in other cases signs of intoxication in the form of acroparesthesiae, nausea and vomiting.

According to Schievelbein (2) there was an increase of blood pressure and heart rate following nicotine application. Changes of the ecg were not described.

Acute nicotine poisoning in man has been recorded only in a few cases. Ecg changes observed in acute nicotine poisoning in man could of course only be recorded with delay. Ecg changes comprised bradycardia, arrhythmias, depression of ST segment, low and isoelectric T-waves (3). Sinus bradycardia, arrhythmias of the extrasystole type, sino-auricular block, paroxysmal auricular fibrillation have been reported but also tachycardias, high T-waves and depressed ST segments (Erstickungs-T) (4, 5, 6).

All investigated cases of nicotine poisoning provoked temporary ecg changes. There is nothing to indicate that nicotine in large doses could cause myocardial damage or infarction.

The effect of nicotine on ecg changes has been studied mainly in cats, rabbits, rats and guinea pigs (6, 7, 8, 9). Ecg changes may be summarized as follows (11):

1. bradycardia of 10 to 20 minutes' duration with simultaneous arrhythmia
2. tachycardia, extrasystoles, sino-auricular block, auriculo-ventricular block
3. very high, sharp T-waves, AV-block of first degree

Altogether it may be said that findings are manifold, partly very different or even contradictory.

As far as we know, the effect of nicotine on the ecg in pigs has not been investigated yet. In the following it is reported on an experiment with pigs having received high doses of nicotine.

**Material and method**

28 SPF-pigs of German landrace (farmers: Schaumann, Hülsenberg) with a body weight of about 30 kg were used for the LD₅₀ study. For the determination of the LD₅₀, animals were injected i.v. with a logarithmically increasing dose beginning at 0.126 mg/kg body weight.

10 animals of the same strain (body weight between 32 and 62 kg) were used for electrocardiographic studies. These animals received intravenous nicotine injections of 0.126 and 0.378 mg/kg body weight at 15 minutes' interval.

Nicotine was injected via venous catheters implanted into the vena jugularis externa according to the technique of Marshal et al. (10). A natrium nitrate solution or Liquemin® in physiol. saline (1:10) was used for preventing thrombosis.

Nicotine in physiol. saline was injected at three different concentrations: 3%, 1% and 0.3%. The different concentrations were chosen because of the rapidly commencing effect of nicotine.