the selector switch so that the sensitivity of the galvanometer can be adjusted.

After calibration, this circuit will measure the differences between the temperatures of the rats and that of the reference bath to ± 0.05°C. Each junction must be individually calibrated and will serve during daily use for about 10 days, failure being caused by rusting of the iron wire near the tip.

Specially designed potentiometers for use with iron-constantan thermocouples and containing automatic reference junction compensators are available commercially. Instruments of this type will afford greater convenience of measurement, but less sensitivity, than the circuit which has been described.

For use, the junctions are lubricated and inserted rectally to a depth equal to the length of the catheter tubing, and the end of the steel spring is firmly fastened with adhesive tape to the base of the rat's tail, which is first covered with a layer of gauze to minimize irritation. The adhesive tape is then covered with a piece of 40 mesh brass gauze (about 2¾ X ⅝ in. after the edges have been doubled over) which is held in place with 2 or 3 turns of wire.

After insertion of the thermocouples, the rats are returned to their cages, and the first readings may be taken about 30 minutes later. The junctions may be left in place for considerable periods of time. In the severest test to which the apparatus has been put, the temperatures of 9 rats were taken over 10 7-hour periods during 13 consecutive days. When the rats were sacrificed at the end of this time no lesions of the rectum or anus were found. Temperatures taken on a typical day are presented in Fig. 1.

Summary. 1. An apparatus for the measurement of the rectal temperatures of rats while they are free in their cages has been described. 2. An observed instability of readings which was presumably caused by reduction of heat loss or by excitation is avoided with this technic. 3. Typical results obtained at intervals during the day have been presented.

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Blood Concentration of P-chloro-xylenol in Man Following Parenteral, Percutaneous and Rectal Application.*

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It has been shown[1,2] that halogenized phenols and especially p-chloro-xylenol (3.5-dimethyl, 4-chlorophenol, referred to subsequently as CX), and its derivatives exert a chemotherapeutic effect in man, in urogenital and general septic infections. Because of local irritation large amounts of these substances cannot be administered parenterally. We have, therefore, availed ourselves of experience gained in estrogenic hormone therapy[3] and applied CX percutaneously. Concurrently, CX is introduced rectally. In this paper it will be shown that free CX appears in blood of patients treated with CX by various routes of administration. CX was determined in blood according to Zondek *et al.*[4]

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1 Zondek, B., *Nature*, 1942, **149**, 334.

2 Zondek, B., *J. Urology*, 1942, **48**, 747.

3 Zondek, B., *Klin. Wschr.*, 1929, **48**, 2229; *Schwz. Med. Wschr.*, 1935, **65**, 1168.

4 Zondek, B., Shapiro, B., and Hestrin, S., *Bioch. J.*, 1943, **37**, 589.

1. *CX in blood after intramuscular injection.* A 10% solution of CX in olive oil containing 2% anesthesin was employed. Other vehicles proved unsatisfactory. Doses of 10-20 cc (1 and 2 g CX respectively) were injected intragluteally into 12 healthy and diseased subjects. The blood was analyzed 2 to 6 times during the 48 hours following administration of the drug. In 3 cases no demonstrable amount of CX was found in the blood following administration of 1 g of CX, but in the other cases 1 mg% of CX was found 2-4 hours after the injection. The highest value found was 4 mg% 12 hours after injection in a case of hepatitis. With 2 g CX the blood content of CX was higher. In one case, 1.2 mg% was found 1 hour after injection, in 2 other cases 1.5 mg% and 3 mg% respectively 2 hours after injection. After 24 and 36 hours a concentration of 1 mg% was still demonstrated, whereas after 48 hours the blood contained no CX.

2. *Gastro-intestinal or rectal absorption of CX.* a. Stomach. CX on the tongue produces a numb sensation followed by burning. The oral administration of large quantities of this substance is therefore difficult. In one case it was possible to administer 10 g of CX dissolved in oil by this route without untoward after-effects. Blood analyses in this case gave the following results: after 1 hour—2 mg%; after 24 hours—1.4 mg%; after 48 hours—0. The blood concentration of CX after oral administration of 10 g does not exceed that obtained following intramuscular administration of 2 g of CX. We assume that this is due to removal of CX from the alimentary tract by the vena portae to the liver where by combination with glucuronate and sulfate it is rapidly inactivated.‡

b. Rectum. CX in 10% oil solution with 2% anesthesin can be administered rectally without injurious effect. Doses of 20 cc were administered once and twice daily, with a narrow catheter, backflow being prevented by closing the catheter with a clamp. Three patients were treated in this way. Following administration of 2.0, 2.5 and 4.0 g by this route, the following blood values were recorded: after 2 hours—traces, 1 mg% and 3 mg% respectively; after 24 hours—1 mg% and traces in the other cases; after 48 hours—traces in all 3 patients.

3. *Percutaneous administration.* Preliminary experiments indicated that large amounts of CX (10-30 g per day) can be administered percutaneously to man with no toxic effect. Eleven patients were treated percutaneously with 40% CX in alcohol-oil solution prepared by dissolving 100 g of CX in 100 cc ethanol and then adding an equal amount of olive oil gradually under continuous agitation. The results show that following percutaneous administration of a dose of 2 g, CX did not appear in demonstrable amount in the blood. After 5 g, traces were found, and after a dose of 8 g, 1 mg% CX was found after 3 hours, and 4 mg% after 24 hours. Following administration of larger doses (20 g), 4 mg% CX was demonstrable in the blood within one-half hour of the application and 1 mg% was still demonstrable in free form even after 72 hours.§

CX is thus resorbed by the skin, passes thence into the blood, and persists there for considerable periods of time. The prolonged presence of CX in the blood can probably be ascribed to the slow absorption of CX from the skin which thus acts as a depot.

4. *CX in the skin.* In conclusion it is of interest to note that skin treated with CX solutions or ointments remains sterile for 12 hours, a finding which in view of the known high disinfectant potency of CX is not unexpected. In performance of gynecological operations (Z.) the skin of the hypogastrium was vigorously anointed with 40% CX in oil-alcohol-solution 2-16 hours before operation. In one case 500 cm^2 of the skin was anointed

‡ Liver inactivates CX as will be reported elsewhere.

§ Unfortunately, we were unable to carry out similar experiments with CX-ointment, as our original American lanolin material was exhausted. In view of the greater bacteriostatic power of blood of patients who had received this CX-lanolin as compared with patients treated with CX-oil-alcohol solution it seems possible that the concentration of CX in the blood of these patients was correspondingly higher.

with 4.0 g CX 2 hours before operating. During operation 3 cm^2 of skin and subcutaneous tissue was removed and later analyzed. Without subcutaneous tissue it contained 2.5 mg CX, *i.e.* 10.4% of that applied to the area. In another case treated with 4.0 g CX on an area of 450 cm^2, 0.3 mg CX was found 15 hours after the inunction in 2.0 cm^2 skin, *i.e.* 1.7% of the CX applied. In the subcutaneous adipose tissue only 1-2 mg per g tissue were found. The findings show that CX penetrates into and through the skin.

Summary. The presence of free p-chloro-xylenol (CX) in the blood shows that this substance is resorbed after parenteral, oral, rectal, as well as percutaneous application. Only 1% of the amount of CX applied was detected in the blood. In percutaneous treatment, the skin acts as a depot from which CX is slowly resorbed into the blood, and as a result a prolonged circulation of CX in active form in the blood is obtained. The prolonged circulation of CX in the blood in active form following different routes of administration renders its chemotherapeutic efficacy in man comprehensible.