of Compazine, the next 5 drugs, in decreasing order of milligram potency (Thorazine, Vesprin, Compazine, Tentone, and Sparine), contain the dimethylamino group in place of the piperazine ring. 4. The only ineffective drug, (Pacatal) is the only one containing the piperidine ring.

It can therefore be concluded that of the 3 substituents at position 10, the piperazinylpropyl group is more effective than the dimethylaminopropyl group and that the piperidylmethyl group produces an ineffective drug. Trifluoromethyl is generally more effective than chlorine or other substituents at position two.

Our results show a striking parallel with the results reported by Ayd(6) comparing the milligram potency of these same drugs required for therapeutic control of a wide spectrum of psychiatric disorders in 4,000 ambulatory and hospital patients. The relative ranking of the 10 drugs for milligram potency was identical in both studies with the exception of Thorazine, which was less effective than Compazine and Vesprin in Ayd's study, and of Compazine, which Ayd found to be more effective than Vesprin and Tentone.

It may be concluded that the relative milligram potencies of phenothiazines are similar for pigment dispersion in the frog melanocyte and for therapeutic control of human psychiatric illness.

Summary. Nine phenothiazine ataraxic drugs were found to cause melanophore dispersion in the intact frog; one drug was shown to be ineffective. All drugs tested in hypophysectomized animals were without effect. The drugs, therefore, are effecting the release of MSH by direct action on the hypophysis or indirectly *via* brain centers. Minimal effective doses of the drugs were correlated with substitutions on the phenothiazine nucleus. A parallel with milligram potency for therapeutic control of psychiatric disorders is noted.

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Direct Recordings from Chronically Implanted Electrodes on the Specialized Conducting System of the Heart.* (26247)

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This laboratory has previously described a technic for studying conduction within the heart by utilizing electrodes placed at selected sites on the endocardium under direct vision during cardiopulmonary bypass(1,2, 3). Such studies, until recently, have been carried out only during acute experiments. It is now possible to implant multi-lead electrodes over the bundle of His, the Purkinje-papillary junctions and on other areas within the heart with complete recovery of the animal from the surgical procedure. Records from these intracardiac electrodes, as well as from surface electrodes on the atria and ventricles, can be monitored through external leads over extended periods of time.

Method. Adult mongrel dogs weighing 20-28 kg were anesthetized with an intravenous injection of a 2½% solution of thiopental sodium, intubated, and placed on a respirator.

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The right chest was entered through the bed of the fifth rib, tapes were placed around the superior and inferior venae cavae and the pericardium opened widely. Sterile plastic electrodes containing 5 contacts were sutured to the epicardium of the right atrium and the right and/or left ventricles. Animals were then placed on total cardiopulmonary bypass; a heat exchanger was incorporated in the circuit to control the temperature of the dog. The right atrium was opened, the bundle of His was located with an exploring electrode(2) and a permanent 5 contact recording electrode sutured in position. The right ventricle then was opened and a similar electrode sutured in position over the Purkinje-papillary junction of the anterior papillary muscle. Sterile leads from this latter electrode were brought out through the upper end of the ventriculotomy wound which was closed with interrupted cotton sutures. Sterile leads from the electrode over the bundle of His were brought out through the right auricular appendage. The animal was taken off perfusion and the right atrium closed with a running 4-0 arterial suture. Leads from the intra- and extra-cardiac electrodes were brought out to the surface of the dog and the chest incision closed in layers. The recording electrodes consisted of fine silver wires embedded in plastic plaques. Each of the 5 wires was insulated with a coating of teflon; the leads from each electrode were placed within a polyethlene tube and the entire unit sterilized. Electrograms were monitored on an Electronics for Medicine 8-trace oscilloscope and permanent records made on photographic paper moving at 200 mm/sec. Records from electrodes on and within the heart were filtered to eliminate low frequency components; filter settings are specified for each record.

Results. Electrograms recorded on the first postoperative day and the twentieth day through electrodes located on the right atrium, over the bundle of His and on the right ventricle are shown in Fig. 1. Also shown are records of leads I, II, and III obtained 5 months after electrode implantation. Fig. 2 shows tracings from another animal obtained 5 days after operation. In this experiment an additional electrode was placed on the Purkinje-papillary junction of the anterior papillary muscle of the right ventricle. Inspection of the records in both figures reveals activity recorded through the electrode on the right atrial appendage (A_1,A) clearly precedes the P wave of lead II and atrial activity recorded through the electrode located over the His bundle (A_2) appears during the initial part of the P wave. The time required for activity to spread from the region of the pacemaker to the vicinity of the A-V node is 20-40 msec. The deflection recorded from the bundle of His (H) appears midway in the P-R segment (Fig. 1, first day, Fig. 2) and indicates the usual subdivision of this segment into intervals associated with transmission in the A-V node and conduction in the His-Purkinje system. In Fig. 2 the electrogram recorded from Purkinje fibers at the Purkinje-papillary junction (P) is simultaneous with the beginning of the Q wave in lead II and electrical activity recorded from the papillary muscle (M) is present during this initial deflection of the electrocardiogram. The records obtained on one animal 20 days after implantation (Fig. 1) are included because they show an increase in P-R interval. The electrogram from the His bundle show that this change is due entirely to an increase in the time required for A-V transmission. There is also some change in the S-T segment and T wave of lead II; these changes did not persist, as can be seen from the electrocardiogram recorded 5 months after electrode implantation.

Discussion. Electrograms recorded directly from different parts of the specialized conducting system through chronically implanted electrodes confirm certain results of acute experiments. For example, it is apparent that atrial excitation reaches the region of the A-V node early during the P-R interval of the electrocardiogram. Nodal delay occupies the latter part of the P wave and the initial part of the P-R segment while the latter part of this interval is associated with the spread of activity through the bundle of His and the major subdivisions of the Purkinje system (4). Also, activity in ventricular muscle fibers in the anterior papillary muscle is re-

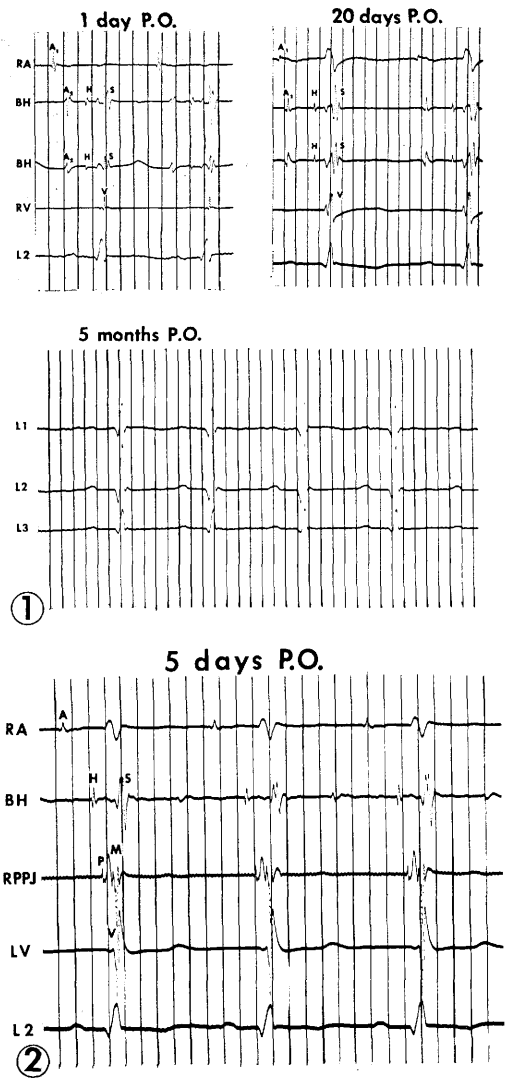

FIG. 1. Electrograms obtained 1 and 20 days following operation. Electrodes are positioned as follows: Right atrium near SA node (RA), bundle of His with 2 different filter settings (BH), right ventricle (RV) and a standard lead II electrocardiogram (L2). Components of electrograms are labeled as follows: A_1 = right atrium near SA node; A_2 = right atrium recorded at the His electrode; H = bundle of His; S = septum recorded at the His electrode, and V = right ventricle. Paper speed 200 mm/sec., time lines = 40 msec. Settings of low and high pass filters, in cps are for RA, 4/200; BH (line 2), 40/200; BH (line 3), 12/200; RV, 4/200; L2, 0.1/200. Polarity of His electrogram reversed in records obtained at 20 days; gain increased for upper trace. Leads I, II, III taken 5 mo following operation.

FIG. 2. Electrograms obtained 5 days following operation. Electrodes are positioned as follows: right atrium near SA node (RA), bundle of His (BH), Purkinje-papillary junction of right anterior papillary muscle (RPPJ), left ventricle (LV), and lead II of a standard electrocardiogram (L2). Components of electrograms not identified in Fig. 1 are labeled as follows: P = action potential from Purkinje fibers at Purkinje-papillary junction; M = action potential from underlying papillary muscle. Paper speed 200 mm/sec., time lines = 40 msec. Filter settings for RA, 12/200; BH, 40/200; RPPJ, 4/200; LV, 12/200; L2, 0.1/200.

corded during the initial deflection of the electrocardiogram(5). Measurement of the time required for transmission of activity through the A-V node and for conduction in the His bundle and Purkinje system is possible. Correlation of electrograms of the specialized fibers with the standard electrocardiogram is expected to add to the value of the latter in studying disturbances of rhythm and conduction in the intact heart.

Summary. By utilizing cardiopulmonary bypass, permanent electrodes with external leads have been sutured over the bundle of His and the Purkinje-papillary junction of the right anterior papillary muscle. For the first time this technic allows the activity of the specialized conducting system to be studied directly over extended periods of time and permits observations to be made not feasible in acute experiments.

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