identification of the virus was 3 to 10 days, depending on the number of passages before positive agglutinations of red cells were obtained. With about 5 to 10% of the throat washings it was possible to identify the virus within 3 to 4 days, using either the amniotic or allantoic inoculation. Zephiran at a concentration which would not inactivate the virus was not consistently effective in removing bacteria. It is quite possible that different results in ferrets, hamsters, and chick embryos would be obtained with throat washings from patients with influenza B.

Summary. During the epidemic of influenza A in 1943-44, throat washings from military personnel were tested in ferrets or hamsters, or in both species, and a smaller number of the same washings were inoculated into chick embryos.

None of the throat washings from 23 persons in whom response to serological tests for influenza A virus was negative produced antibodies to that virus after intranasal inoculation in ferrets.

Of 30 throat washings from persons showing positive response to serological tests for influenza A virus, 17 (56.7 ± 9.05%) produced in ferrets an increase in antibodies to the virus. With 2 exceptions all ferrets showing an increase in antibodies also developed fever 2 to 3 days after inoculation. Four of 41 ferrets showing no increase in antibodies had similar febrile reaction.

Thirty, or 56.6 ± 6.81% of 53 throat washings from persons with known cases of influenza A were positive in hamsters, a result identical with that obtained in ferrets. Twelve throat washings that were negative in ferrets produced no antibody response in hamsters.

Seventeen throat washings shown to contain influenza A virus by tests in ferrets or hamsters were inoculated into chick embryos by the amniotic route. Of these, 7 (41.2 ± 11.9%) infected the embryos. Virus was demonstrated in 4 throat washings in the first passage and in 3 in the second, but usually 1 or 2 additional amniotic or allantoic passages were necessary before the virus reached sufficient titer to be positively identified as influenza A.

In 2 of 13 unfiltered throat washings inoculated into the allantois of chick embryos, virus was demonstrated on first passage.

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Electrocardiographic Changes in Epidemic Parotitis (Mumps).*

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In January, 1943, a 20-year-old white sailor entered the hospital with epidemic parotitis and on the fifteenth day of his illness complained of constant retrosternal pain and of dizziness on arising. His pulse rate was 35 per minute and the electrocardiogram revealed complete heart block with prolongation of the QRS interval (0.12 sec.). He improved rapidly and by the eighth day following the onset of his angina the electrocardiogram was normal. Early this year, another 20-year-old white sailor, under treatment for mumps, developed precordial pain and palpitation on the seventh day of illness. The pulse rate fell to 28 per minute and the electrocardiogram showed 3:1 heart block. Three days later, another electrocardiogram revealed complete auriculo-ventricular dissociation. His condition slowly improved and by the 77th day following the onset of his cardiac pain the elec-

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trocardiogram had returned to normal. In both instances the leucocyte counts and sedimentation rates were elevated during the acute phase. A review of the literature revealed no reference to any similar observations. Hence, a study of the electrocardiographic findings in mumps was undertaken, in order to determine the incidence, variations and prognostic significance of the electrocardiographic changes.

Method. Electrocardiographic tracings were taken on a series of 104 adults with mumps during the height of an epidemic early in 1944. Standard limb leads and chest lead CF4 were used in all cases. In 46 of these patients serial electrocardiograms were made at intervals of 2 to 4 days. This study was correlated with determinations of the sedimentation rate and with blood counts. In addition, a careful search was made for clinical evidence of cardiac involvement.

Results. Significant electrocardiographic findings were observed in 16 of the 104 patients (15.4%). In 4 of these, the P waves became diphasic or inverted in one or more leads. In 2 individuals, prolongation of the P-R interval was noted. In 1 instance, the QRS complex in CF4 became inverted, and in another, the voltage in the limb leads decreased. Two patients showed considerable elevation of the S-T segments in CF4, and in 1 of these the S-T segment was bowed upwards. In 1 subject the S-T segment became depressed beyond normal in leads II and III. Changes in the T waves were observed in all of the 16 patients; in 11 of these they were noted in two or more leads. The T waves became tiny, diphasic or inverted and with serial electrocardiograms the evolutionary stages in the development of T wave inversion were demonstrable. T wave abnormalities occurred with essentially the same frequency in all 4 leads. In 14 out of the 16 patients with electrocardiographic changes more than one abnormality was found; in the remaining 2, the T wave changes were decisive. No specific electrocardiographic pattern was recognizable in this study.

In all but one patient the electrocardiographic abnormalities were observed on the fifth to the tenth day of illness, and in the majority of these were present on the eighth or ninth day. In 1 subject an abnormal tracing was found on the twentieth day. The changes were transitory in 14 patients and returned to normal in 2 to 35 days. However, in most instances the curves were normal in 4 to 8 days. In the remaining 2 patients electrocardiographic evidence of progressive improvement was observed, but residual changes persisted for 3 months and 5 months respectively.

Precordial pain, either alone or with dyspnoea and palpitation, developed in 4 patients and in 2 of these antedated the appearance of the electrocardiographic abnormalities. A soft blowing systolic murmur became audible at the mitral area in 2 patients but disappeared in 2 months. The sedimentation rate was elevated in 5 individuals and a slight leucocytosis was found in 4.

Comment. Cardiac involvement in epidemic parotitis has generally been regarded as a rare complication and, when observed, has been described as an endocarditis or pericarditis. That mumps may also produce myocarditis was originally suspected by Pujol[1] and by Barbato[2] from clinical observations, but no proof of their contention was presented. Later, Manca[3] described an instance of acute interstitial fibrinous myocarditis which he regarded as a characteristic reaction to the mumps virus. Since the completion of this work, Wendkos and Noll[4] reported a single instance of mumps with T wave changes and prolongation of the P-R interval.

It is evident from the present study that myocardial involvement in mumps is not a rare event and that the electrocardiographic changes are similar to those observed in rheumatic fever. Moreover, the occurrence of delayed A-V conduction time in epidemic parotitis casts further doubt on the specificity of this finding and raises the question of its reliability in the diagnosis of rheumatic fever. Rather, it is added confirmation of the belief that the myocardium is susceptible to involve-

1 Pujol, M., *Arch. de med. et pharm. mil.*, Paris, 1918, **69**, 527.

2 Barbato, M., *Rif. Med.*, 1925, **41**, 1109.

3 Manca, C., *Arch. ital. di anat. istol. pat.*, 1932, **3**, 707.

4 Wendkos, M. H., and Noll, J., Jr., *Am. Heart J.*, 1944, **27**, 414.

ment not only in rheumatic fever and mumps but in other forms of generalized bacterial or virus infections as well. These implications and other aspects of the problem will be dealt with in greater detail in the final report.

Summary. 1. Two isolated cases of epidemic parotitis accompanied by electrocardiographic evidence of complete heart block are reported. 2. In a subsequent study of 104 consecutive cases of epidemic parotitis in adults, evidence of myocardial involvement was observed in 16 instances (15.4%). In all but 2 patients, the electrocardiographic changes were transitory and of short duration. The broad implications of these findings are discussed briefly.

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Inhibition of Drug Precipitation in the Urinary Tract by the Use of Sulfonamide Mixtures. I. Sulfathiazole-Sulfadiazine Mixture.*

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Serious toxic effects of sulfonamides upon the kidneys have appeared only after introduction of N^1-heterocyclic derivatives of sulfanilamide. Preference of these compounds over sulfanilamide in human therapy is based primarily on their wider range of antibacterial activity. Two representatives of this group, sulfathiazole and sulfadiazine, are employed at present as the "drugs of choice" whenever sulfonamide therapy seems indicated, despite their poor solubility if compared with the mother substance sulfanilamide. Hence renal concrement formation—a complication unknown from sulfanilamide—has become a serious problem worthy of the most careful attention.

The present investigation deals with the possibility of lessening the danger of renal concrement formation by the employment of sulfonamide mixtures. Solubility studies with N^1-heterocyclic derivatives of sulfanilamide revealed that these compounds are soluble in one and the same solution nearly to the extent of their separate solubilities; in other words, a saturated solution of sulfadiazine, for instance, can still be further almost fully saturated with sulfathiazole. This finding applies even to compounds which are structurally as closely related as sulfadiazine and its monomethyl and dimethyl derivatives (sulfamerazine and sulfamethazine). Table I illustrates these observations. Almost identical results were obtained in solubility studies with normal human urine.

Since even closely related sulfonamides, when present simultaneously in the same solution, do not influence each other appreciably with regard to their particular solubilities, the danger of intrarenal drug precipitation from the sulfonamides comprising the mixture should be only as great as if each compound had been administered alone, and in the partial dosage contained in the mixture. On the other hand, it seemed probable that in using combinations of different sulfonamides having similar or identical therapeutic indications, the antibacterial effect would largely correspond to the total concentration of free sulfonamide.

The validity of these contentions was investigated in toxicity experiments with albino rats and with the help of *in vitro* antibacterial studies. Sulfathiazole and sulfadiazine were selected for the initial series of experiments, because these compounds are at present most frequently employed, have almost the same therapeutic indications, and cause renal complications in about the same percentage of

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