to duration; (4) as to the mean pitch, the pitch actually heard tending to be approximately 6 per cent. of the extent of the vibrato below the center of the oscillation; (5) the vibrato, considering such facts as number of pulsations per second, the amplitude in pitch (each horizontal space representing a semitone), and regularity of the vibrato, and (6) the occurrence of mordents, as on the last syllable of "blooming" and the last syllable of "faded" by Alda. Numerous measures of subordinate elements for each of these factors may be made. Of special interest is the mode of glide, particularly within the tone itself, as on the words "the last" by Alda.

Here a single artist is taken as an example of a good singer. There are, of course, great differences among good artists; multiplying of illustrations brings out these features. We here simply wish to illustrate the principle.

In interpreting the relative performance of the two singers we must fall back upon a gradually accumulating series of norms which we are now building up for all these factors. For example, Helen's vibrato, which averages about five pulsations per second, is somewhat too slow as rated by our norms for artists. Alda's rate of about seven pulsations per second is approximately the most favored rate. On the other hand, the amplitude of Helen's vibrato is not quite as large as Alda's, or as the norms for artistic singers in general. This may or may not be in her favor. One of the writers is of the opinion that it is decidedly in her favor because the more subdued the vibrato the more pleasing it is to him.

But such subjective differences of opinion may now be gradually eliminated by two different processes: first, by measuring agreement in practice among the great artists; and second, by determining the best achievement of such artists under experimental control and submitting these to experimental analysis and evaluation from the point of view of experimental esthetics. This procedure of giving recognized artists the opportunity of perfecting performance with the aid of measuring instruments under fractionated procedure is the avenue through which we shall ultimately establish norms of artistic achievement.

When the other two factors, intensity and timbre, are recorded with the camera and added to our scientific musical score of performance, we shall have a comprehensive objective basis for the comparison of musicians and for the detailed quantitative account of musical value.

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SPECIAL ARTICLES

THE TREATMENT OF PATIENTS WITH ADDISON'S DISEASE WITH THE "CORTICAL HORMONE" OF SWINGLE AND PFIFFNER

THE preparation of an aqueous extract of the suprarenal cortex which would maintain the life of bilaterally suprarenalectomized cats indefinitely was announced by Swingle and Pfiffner in a brief article published in SCIENCE of March 21, 1930. Subsequently they have reported that by the administration of this extract they were able not only to revive comatose animals, on the verge of death from suprarenal insufficiency, but also to restore them to a normal condition and to keep them in perfect health by daily injections.

The significance of such an announcement and the interest aroused by the possibility of using this extract in clinical medicine are obvious. An extensive experience in the use of the so-called Muirhead regimen in cases of Addison's disease has convinced us of the futility of ordinary therapeutic measures in combating the crises of acute suprarenal insufficiency which develop in the course of this disease and of the great need for a more active cortical preparation which can be administered either hypodermically or intravenously. This point was further emphasized by a patient with Addison's disease who was brought to the hospital in a state of complete collapse, May 31, 1930. The outlook seemed hopeless under ordinary conditions, but as a last resort a telegram was sent to Drs. Swingle and Pfiffner and they forwarded a supply of cortical extract by air mail. The patient, who was in a state of typical collapse, was restored to activity within two to three days. A summary of the clinical history in this case follows:

The patient was a farmer, aged thirty-nine years, and first came to the clinic in January, 1930. He had had pleurisy with effusion eleven years previously and symptoms of Addison's disease had been present for eight months. He was in a critical state when admitted; he was in collapse, the systolic blood pressure was 78 mm of mercury, and the blood urea 48 mg for each 100 cc. Treatment was given with solutions of sodium chloride and glucose intravenously, and the Muirhead regimen was instituted. The patient improved slowly; he was dismissed from the hospital thirty-nine days after admission.

Progress at home on the Muirhead regimen was satisfactory for a while, but the patient was brought back to the clinic in a state of collapse, May 31. Treatment

with solutions of sodium chloride and glucose was instituted again, with only partial success. The extract of the suprarenal cortex sent by Drs. Swingle and Pfiffner arrived on the sixth day after the patient's admission to the hospital and treatment was begun with daily doses of 20 cc given subcutaneously. Within thirty-six hours a marked effect on appetite and strength was apparent. The patient, who had been so nauseated as to retain water with difficulty, now asked for wieners and sauerkraut and in lieu of the latter ate a double order of beefsteak with relish.

This extract produced considerable local irritation at the site of injection and because of the content of epinephrine could not be given intravenously in therapeutic doses. A further supply of the extract was not available at that time; therefore the patient was put back on the Muirhead regimen. He did well for a few weeks, but gradually failed and again went into collapse, from which the timely arrival of a fresh supply of extract sufficed to insure temporary recovery.

This cycle has been repeated three times in this case. The last time it was possible to use Swingle and Pfiffner's newest extract, which is free from epinephrine. This was given intravenously in divided doses in a quantity of 20 cc daily with a total dosage of 50 cc. Before its use the patient was excessively weak, bedridden, depressed, nauseated, losing weight and showed evidence of failing circulation. Within forty-eight hours he had taken a new lease on life, his appetite was excellent, his strength was greatly improved and he appeared to be in a state of perfect health. He gained 9 pounds in weight in the next eight days and has been in good condition since then.

Since that time it has been possible to observe the effect of the preparation on three other patients suffering from Addison's disease. The condition of one patient was not considered serious at the time of his examination and he was kept on the treatment for only four days. There were no spectacular changes during this period and the small supply of extract precluded its further trial. In the other two cases the clinical condition of the patients and the results obtained by treatment were similar in character to those observed in the first case. Metabolism studies were made in one case during the period of observation. The results will be reported later, but preliminary observations indicate disappearance of creatinuria and retention of nitrogen in consequence of the administration of the suprarenal extract.

The results in these cases convince us of the apparent efficacy of this cortical extract. There was no striking change in the blood pressure, but the disappearance of anorexia, increase of appetite to the point of hunger, the gain in weight and the definite feeling of increased strength and well-being were striking. As long as the preparation was administered, the results were all that could be desired. However, our supply of the preparation has been limited, so that we have not been able to observe the results following consistent dosage and continued administration. The first preparation was not free from epinephrine and caused local irritation when given subcutaneously. The later supply, however, is almost free from epinephrine; it is suitable for intravenous administration and is almost non-irritating locally. As has been shown, the immediate results in a crisis were excellent. Addison's disease, however, is chronic, and it will be necessary for several years to elapse before a final appraisal can be made of the value of this new therapeutic agent in its treatment.

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THE suprarenal cortical extract used intravenously by Dr. Rowntree on patients with Addison's disease represents the modification of our original aqueous preparation mentioned in an earlier communication to this journal.[1] This extract, 1 cc of which represents 30 gm of fresh beef cortex, contains only 0.3 per cent. of solids. The epinephrine content as measured by blood pressure assay on dogs is at most between 1:1,000,000 and 1:2,000,000. The method of fractionation used is based on our observation that, by the proper use of permutit, epinephrine can be practically quantitatively separated from the cortical hormone. The 70 per cent. alcohol-soluble fraction obtained by our previously described method[2] is simply filtered in alcoholic solution through an adequate amount of permutit which removes the epinephrine. Much inert material including most of the contaminating pigment is also removed by this fractionation step.

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ON THE CHEMICAL ALTERATION OF PURIFIED ANTIBODY-PROTEINS

DIAZONIUM salts of well-defined chemical compounds coupled to proteins have been used in the study of the relation of biological specificity to chemical constitution, in particular by Landsteiner[1] and his coworkers in the last two decades. It has usually been found that the coupled compound fully determines the

[1] SCIENCE, 72: 75–76, 1930.
[2] SCIENCE, 71: 321–322, 1930.
[1] Landsteiner and Lampl, *Biochem. Zeitschrift*, 86: 343, 1930.