As was to be expected, prognosis in the elder patients was less good than in the younger, for the power of recuperation diminishes with age and osteo-arthritic changes are more prone to occur. Also as a rule the elder patients have been subjected to more numerous attacks.

By combining the two groups the results of operation were: Good, 35 cases (70 per cent.); fair, 11 cases (22 per cent.); poor, 4 cases (8 per cent.). Hence the prognosis is not by any means assured, but I believe these figures indicate a fair average of the results that may be expected if cases are "followed through" after operation. This is particularly necessary with internal derangements of the knee-joint, as cases apparently cured may relapse after a period of freedom. In one patient in this series who was apparently cured the condition suddenly recurred after an interval of nine months of strenuous life.

Prognosis should be especially guarded where attacks have been frequent and in the elderly. On the other hand, when once attacks have become established insecurity of the joint and osteo-arthritic changes are a natural sequence and may be diminished or controlled by removal of the offending cartilage.

REFERENCES.

¹ Sir D'Arcy Power: *BRITISH MEDICAL JOURNAL*, January 14th, 1911. ² Von Bergmann: *Operative Surgery*. ³ Rendle Short: *Bristol Medico-Chirurgical Journal*, 1912, 52. ⁴ Sir Robert Jones: *Annals of Surgery*, December, 1909.

THE ANTISEPTIC ACTION OF THE STYRYL-PYRIDINES AND STYRYL-QUINOLINES.*

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THE formation of styryl-quinoline derivatives by the condensation, in presence of piperidine, of p-dimethylamino-benzaldehyde and quaternary salts of quinaldine and lepidine was noticed by König,⁴ and, later, Barbier¹ and König and Treichel⁵ described a number of substances of this type. Recently Mills and Pope⁶ described the preparation of a similar kind of compound from α -picoline methiodide, and also recorded the fact that this material, like the cyanines, possesses photosensitizing properties. The similarity in structure between these substances and those of the isocyanine type, together with observations made by us showing that the antiseptic potency of the isocyanines was increased by simplification of the quinoline portion of the molecule, suggested the possibility that the styryl compounds might also exhibit antiseptic activity. The relation between the two types will be apparent from the appended formulae:

Preparation of the Styryl Compounds.

One molecule of p-dimethylamino-benzaldehyde and 1 molecule of the quinaldine methiodide were dissolved in alcohol, and the solution boiled for three to four hours after the addition of a small quantity of piperidine. The dyestuff, which crystallized on cooling, was in some cases recrystallized from alcohol. This further purification, however, did not increase the antiseptic potency.

These bodies have the advantage over the cyanines of being much more easily and rapidly prepared, and are obtained in much better yields. The following compounds were tested:

- 2 p-dimethylamino-styryl-pyridine methiodide;
- 2 p-dimethylamino-styryl-quinoline methiodide and ethiodide;
- 2 p-dimethylamino-styryl-6 aminoquinoline methiodide (base and hydrochloride);
- 2 p-dimethylamino-styryl-6 methylquinoline methiodide and methochloride;
- 2 p-dimethylamino-styryl-6 methylquinoline allobromide;
- 2 p-dimethylamino-styryl-6 methoxyquinoline methiodide and the corresponding ethoxy compound;
- 2 p-dimethylamino-styryl-7 aminoquinoline methiodide hydrochloride.

Antiseptic properties were determined, as previously described.^{2,3}

To 1 c.cm. of culture medium were added varying amounts of the substances to be tested along with 0.1 c.cm. of a 1 in 1,000 dilution in saline of a twenty-four-hour culture of the organisms (*Staphylococcus aureus* or *B. coli*) in peptone water. As test media (a) 0.7 per cent. peptone water with a pH value of about 7.2, and (b) undiluted ox serum (previously heated at 56° C.) were employed. The mixtures were then placed at 37° C., and were examined after forty-eight hours for the presence or absence of growth, which was determined in each instance by the appearance of turbidity in the fluid, and also by subculturing a loopful on agar.

In the case of *Staphylococcus aureus*, the sterilizing concentration of the above-named substances lay between 1 in 200,000 and 1 in 1,000,000 both in peptone water and in serum, except with 2 p-dimethylamino-styryl-pyridine methiodide, which was distinctly weaker (1 in 40,000 was required to produce sterility in both media). Toward *B. coli* the antiseptic action was never greater and usually somewhat weaker than toward *staphylococcus*. For *B. coli* the most powerful compounds were 2 p-dimethylamino-styryl-6 methylquinoline methochloride and methiodide (sterilizing concentration in both media, 1 in 100,000 to 1 in 200,000). The occurrence of long zones of inhibition between concentrations which permit of active growth and those which sterilize completely is a feature of this group of compounds. In no case did the presence of serum cause a marked decrease in antiseptic power for either organism.

The toxicity of several compounds of the series was tested for mice; the tolerated dose was 1 c.cm. of 1 in 5,000 to 1 in 15,000 dilution for animals weighing 20 grams. Where lethal doses had been given there were no characteristic lesions in any organ.

The methochloride and methiodide of 2 p-dimethylamino-styryl-6 methylquinoline and the ethochloride and ethiodide of 2 p-dimethylamino-styryl-quinoline were tested on mice infected with *Tryp. brucei*; but with the maximal doses tolerated there was no effect on the course of the infection.

The chemical variations in the series involve merely alterations in side-chain substituents, apart from the pyridine compound. The substitution of a simple pyridine nucleus for a quinoline nucleus caused slight reduction of antiseptic power. Alterations in the side-chain occupying the 6- position are not very marked in their effect; the 7-amino derivative does not differ significantly in its action from those substituted in the 6- position.

Thus it is shown that substances belonging to the group of styryl-quinoline compounds are very powerful antiseptics.

REFERENCES.

- ¹ Barbier: *Bull. Soc. Chim. Paris*, 1920, vol. 27, p. 427. ² Browning, Cohen, and Gulbransen: *BRITISH MEDICAL JOURNAL*, 1922, April 1st.
- ³ Browning, Cohen, Gaunt, and Gulbransen: *Proc. Roy. Soc., B*, 1922, vol. 93, p. 329. ⁴ König: *Journ. f. prakt. Chem.*, 1912 (ii), vol. 86, p. 172.
- ⁵ König and Treichel: *Journ. f. prakt. Chem.*, 1921 (ii), vol. 102, p. 63.
- ⁶ Mills and Pope: *Trans. Chem. Soc.*, London, 1922, vol. 121, p. 946.

A REPORT received by the United States Public Health Service at Washington shows a remarkable reduction in the infant mortality rate in Springfield and Campbell Townships, Green County, Missouri, since the establishment of a whole-time county health department. In 1918 the infant death rate in these two townships was 105 per 1,000. The county health department was organized that year. In the following year the infant death rate in the two townships dropped to 96 per 1,000. In 1920 it was 85, in 1921 it was 76, and in 1922 it was 61. This reduction of 42 per cent. in four years is regarded as a striking example of what may be accomplished in infant welfare by carrying out, with economy and efficiency, a well balanced general programme of health work affecting all age-sex groups in a community with a well administered health department under the direction of a whole-time health officer.

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