choice of scientific endeavor. A treatment of the history or philosophy of science should perhaps include a discussion of the effects of fashion upon scientific progress.

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Histamine in Tissue Mast Cells

THE granular basophil cells of the tissues were first clearly described by Paul Ehrlich (*1*) and named "mast cells" in the belief that the characteristic metachromatic granules develop in certain mesenchymal cells under conditions of hypernutrition (*2*). As Ehrlich observed, the cells are common in the loose connective tissues, especially near small blood vessels.

Sixty years later Scandinavian workers showed that the metachromatism of the mast cell granules is due to heparin (*3*), a finding that has since received substantial support from the high anticoagulant activity of pathological tissues abnormally rich in mast cells (*4, 5*). It thus seemed that "one of the old problems of histologists, the riddle of the metachromatic granules in the mast cells of Ehrlich" has been solved (*6*).

One curious anomaly remained. It had been known for long that in certain shock states in the dog not only heparin (*7*) but also histamine (*8*) is released in quantity from the liver. With this in mind a series of investigations was undertaken to re-examine the status of the mast cell in relation to the tissues and to determine what, if any, is its role in the elaboration and release of histamine.

It was first observed (*9*) that the granules in some of the mast cells of the rat stain positively for alkaline phosphatase and the suggestion was made that the enzyme may be concerned in the formation of the metachromatic material by which mast cells are generally recognized. A further study of conditions in the rat (*10*) supports the idea that these phosphatase-positive mast cells are young cells whose chief source of origin is from undifferentiated mesenchymal precursors in the adventitia of small blood vessels. However, in the rat such vessels often have one or more muscle coats and as the mast cells mature they tend to migrate away from the vessels into the tissues and there slowly lose their granules. Any secretion from the mature cells must thus permeate the tissues before it enters the blood.

The effects of histamine liberators on the mast cells of the rat were next examined (*11*) and it was observed that following rapid intravenous injection of a lethal dose of the fluorescent histamine liberators, stilbamidine or 2-hydroxystilbamidine, fluorescent diamidine can often be demonstrated in the cytoplasm of peritoneal mast cells. If the same dose is given slowly the initial trapping of the diamidine is missed, the mast cells having undergone vacuolization and disruption. Similar though less violent disruption of mast cells follows the injection of agar-activated rat serum, the so-called "anaphylatoxin" of Bordet (*12*). The disruption caused both by diamidines and anaphylatoxin can be prevented by premedication with an antihistamine drug.

These findings so clearly imply that the mast cells are themselves concerned in the phenomenon of histamine release that pharmacological assays for histamine were made on a large series of normal and pathological tissues which varied widely in their content of mast cells (*13*).

Preliminary studies (*14*) indicated that there exists a strong positive correlation for histamine, mast cells, and heparin in those tissues for which values for heparin are available (*6*). Holmgren and Wilander (*3*) found their highest content of mast cells and heparin in ox liver capsule but it now appears that ox pleura is an even richer source of mast cells and this material also gave the highest value for histamine (200–280 μg/g tissue) of any normal tissue so far examined (*15*). The Scandinavians did not estimate the heparin content of lung in view of possible interference from chondroitin sulphate. However, through the kindness of S. W. Stroud, Boots Pure Drug Company Limited, Nottingham, beef lung pleura and parenchyma were assayed for heparin. It is, therefore, of some interest that he finds considerably more heparin in beef pleura (24,000 units per lb) than in the underlying parenchyma (16,000 units per lb). Thus the high mast cell content of ox pleura reflects both the amount of heparin and the amount of histamine which it contains.

Since the strongest evidence for the role of the mast cells as "heparinocytes" rests on the exceptionally high heparin content of mast cell tumours (*4*) it was clear that the present hypothesis of the mast cell as a "histaminocyte" would likewise stand or fall on the findings for histamine in mast cell tumours. After a search extending over some years no less than four mast cell tumours were recently encountered. Two were from children and two from dogs. All four tumours were extremely rich in histamine, a pleomorphic mast cell tumour from a child yielding the unprecedented value of nearly 1 mg (1000 μg) histamine per gram of tissue (*13, 15*). There thus appear to be some grounds for the belief that not only do tissue mast cells contain heparin: they are also rich in histamine.

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Bilateral Reversal of Internal Organs of the Cat

VARIATIONS in the arrangement of blood vessels in mammals are rather common, particularly in the venous system. A complete reversal of all organs, however, is quite uncommon. Gribble (*1*) states that he has seen only one such animal among the many cats he has examined in the past few years. The present specimen is the only example this author has seen in an aggregate of about six years' experience with cat dissections. A brief description of the organs affected follows.

The esophagus followed the trachea on the right side until it passed the origin of the bronchi where it proceeded slightly to the right of the mid-line to enter the stomach.

The entire stomach was located to the right of the median line with the pyloric end on a line below the enlarged cardiac end. The greater curvature lay at the extreme right while the lesser curvature was located in a medial position.

The duodenum proceeded to the left and then turned caudad, following the left lateral margin of the abdominal cavity.

The liver presented a reversal in position. The larger portion lay on the left side. The smaller portion occupied the right side. The common bile duct passed caudad on the left side to enter the duodenum.

The pancreas was reversed end for end to correspond to the general reversal of the abdominal viscera. The spleen lay along the greater curvature of the stomach which placed it on the right side of the body.

The kidneys seemed to be in a normal position, the left lying about 1 cm farther caudad than the right.

The left lung was larger.

A complete reversal in the position of the heart was encountered, the apex directed to the right. This of course reversed the positions of the heart chambers. The major blood vessels conformed to this shift. The aorta emerged from the right ventricle and made its arch to the right instead of the left. The innominate, carotids, and subclavians were likewise reversed. A corresponding reversal was found with the veins.

It is interesting to note that only the structures within the peritoneum and mesenteries have been affected. The kidneys, lying retroperitoneally, apparently were unaffected. In this respect the animal reported here differs from that reported by Gribble (*1*).

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Olfactory Thresholds in the International Critical Tables

PROBABLY the most extensive and available collection of olfactory thresholds is contained in the International Critical Tables (*1*), and researchers quite often check their own threshold results against the data therein. In compiling the data, Zwaardemaker has translated them all into a common unit, molecules per cc of air. The method of translation is given as follows:

"The olfacty of an odor is the threshold or minimum perceptible concentration expressed in gms per cc which multiplied by $6.06 \times 10^{21}/M$, where M is the molecular weight, gives molecules per cc." (*1*, p. 360.)

Unfortunately, the formula given is in error. Avogadro's number, which should be the basis of this calculation, is about 6.023×10^{23}. The fraction in the second decimal place is of very little importance, but the exponent is quite important. It seemed that the exponent given in the formula in the tables might be a typographical error, but calculations based on several thresholds taken from the original Henning (*2*, p. 411) resulted in the numbers found in the tables. The thresholds in the tables are, therefore, in error by a factor of 100, that is, it would require 100 times the number of molecules per cc indicated to reach threshold. Perhaps this is one reason why olfactory thresholds have seemed hard to duplicate!

It is, fortunately, very easy to correct the errors in exponents. The thresholds in the tables are given in the form $A \times 10^x$ molecules/cc. The values of x need only be increased by 2 in each case to give the correct value.

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