# COMPARISON OF THE SIZE OF CELLS AND SOME HISTOLOGICAL FORMATIONS BETWEEN WHALES AND MAN 

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INTRODUCTION, MATERIAL AND METHODS
Cells and histological formations constructing the huge bulk of the whale's body are not so large as one might suppose. They are of the similar size to those of other mammals including man. Probably the size of cells is determined by some biological factors which are, although unknown yet, rather common in the animal kingdom. The present writers, following the histological studies of whales, happened to be attracted to this notable similarity of cell size among whales and man and tried to examine this similarity precisely and statistically.

Several kinds of histological preparations of whales and man were used for this purpose. Whales used comprise the right whale (Balaena gracialis Bonnaterre)**, blue whale (Balaenoptera musculus L.), fin whale (Balaenoptera physalus L.), sei whale (Balaenoptera borealis Lesson), one kind of the beaked whale (Berardius bairdii Stejneger) and one kind of the dolphin (Lagenorhynchus obliquidens Gill), all of which were adult. Each of the specimens taken from these materials was embedded in celloidin, sectioned fifteen $\mu$ in thickness and stained with hematoxylin and eosin. Measurements of nerve cells and fibres were, however, made on the preparations stained by the Pal-carmin method.

In order to explain the method of statistical calculations, table 1 is to be referred to, in which the results of observations and calculations are shown. The first column gives the items of investigation, which includes several kinds of cells and histological units. For the measurements such cells were chosen at random that appeared to be cut through the center approximately. At the same time nearly round cells as possible were selected and two diameters of each cell, being at right angles to each other, were measured by the micrometer. Then the arithmetic average of these two values was got to represent the size of this cell. The same holds good for such structures as the lung alveoles, Langerhans islets, renal corpuscles, etc. As to the muscle and nerve fibres,

[^0]the thickness of each fibre was measured to show its size.
Following the second and third columns which tell the species of whales and the axis of measurement respectively, the fourth column $(N)$ gives the sample size or the number of cells examined. Column 5 ( $\bar{x}$ ) shows the sample mean or the arithmetic average of the measurements, which is represented by $\sum_{i=1}^{N} x_{i} / N$. The unit of these figures is always " micron.' While the sixth column ( $S$ ) indicates the total variance given by $\sum_{i=1}^{N}\left(x_{i}-\bar{x}\right)^{2}$, two following columns ( $s^{2}$ and $u^{2}$ ) state the sample and standard variances respectively. These two variances are given by $S / N$ and $S /(N-1)$.

Column 9 gives the confidence interval for ' $m$ ' or the mean of the mother population. The significance level $\alpha$ for the figures is 0.05 . It means that the mean of the mother population lies within this interval with the probability of $95 \%$. It is computed by the form

$$
\operatorname{Pr} .\{\bar{x}+u \sqrt{F / N} \geqq m \geqq \bar{x}-u \sqrt{F / N}\}=1-\alpha . \quad(\alpha=0.05)
$$

' F ' is to be got by checking the table of F -distribution ( $n_{1}=1, n_{2}=N-1$ ).
Column 10 shows the critical regions for the samples, indicating that the measurements of all the sample must be, with the probability of $95 \%$, within this region. It is computed by the form

$$
\operatorname{Pr} .\left\{\bar{x}+u \sqrt{\left.(N+\overline{1}) F / \bar{N} \geqq x_{i} \geqq \bar{x}-u \sqrt{(N+1) F / N}\right\}=1-\alpha . \quad(\alpha=0.05), ~}\right.
$$

The last column gives the result of the statistical comparisons. Supposing that two samples are to be compared, of which the sizes and standard variances are $M, N$ and $u^{2}, v^{2}$ respectively, the first step of the statistical test is to get ' $F_{0}$ ' given by $u^{2} / v^{2}\left(u^{2}>v^{2}\right)$ as well as the ' $F$ ' value from the $F$-distribution table, the degrees of freedom ( $n_{1}, n_{2}$ ) being $M-1$ and $N-1$. If ' $F_{0}$ ' is larger than ' $F^{\prime}$ ' $\left(F_{0}>F\right)$, it means that the comparison of these two samples is statistically impossible $(X)$. For the null-hypothesis that these two belong to one and the same mother population can be abandoned with the danger of $5 \%$. If ' $F_{0}$ ' is less than ' $F$ ' $\left(F_{0}<F\right)$, the second step of the test is to be taken. After calculating the common standard variance $w^{2}$ which is given by $\left(n_{1} u^{2}+n_{2} v^{2}\right) /\left(n_{1}+n_{2}\right)$ or $\left(S_{x}+S_{y}\right) /(M+N-2)$, ' $F_{0}{ }^{\prime}$ should be got by the following form.

$$
F_{0}=(\bar{x}-\bar{y})^{2} M N / w^{2}(M+N) .
$$

$S_{x}, S_{y}$ and $\bar{x}, \bar{y}$ represent the total variances and sample means of the two samples to be tested. Then the ' $F$ ' value is to be got by
TABLE 1. SIZE OF CELLS AND CELL AGGREGATES OF WHALES AND MAN.




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[^1]checking the $F$-distribution table, $n_{1}$ and $n_{2}$ being 1 and $M+N-2$ respectively. If ' $F_{0}$ ' is larger than ' $F$ ' $\left(F_{0}>F\right)$, it means that there is statistically a rational difference between these two samples ( + ), while in case $F_{0}<F$, it is shown that there is no rational difference at all between these two ( - ).

## RESUL'TS

All the results of observations and calculations are shown in table 1. Each of the items will be explained briefly. Accompanying figures and graphs are to help the explanation.


Fig. 1. Average means of the cell sizes.
Hepatic cells (Figs. 1, 2.)
Not only the microscopical appearances but also the size of the hepatic cells is quite similar to each other among the right whale, blue whale and man. The sample means of the longitudinal and transversal diameters are $18.6 \mu$ and $13.9 \mu$ for the right whale, $18.3 \mu$ and $14.9 \mu$ for the blue whale, and $18.0 \mu$ and $14.4 \mu$ for man. The averages of these


Fig. 2. Size distribution of hepatic cells.

- -. Right whale
.---. Blue whale
- -. Human


Size of cells ( $3.0=4 \mu$ )
Fig. 4. Size distribution of adrenal cortical cells.
.—. Right whale
-. Humąn


Fig. 3. Size distribution of heart muscle fibres.
....... Sei whale
.-. Human


Size of cells ( $1.0=13 \mu$ )
Fig. 5. Size distribution of fat cells (in the gastric submucosa).

- Right whale
.-. Human
two diameters are also of high similarity, being $16.3 \mu, 16.5 \mu$ and $16.3 \mu$ respectively. Furthermore, it is illustrated in figure 2 that these cells of whales and man show very similar mode of distribution of the size. The statistical comparison revealed that there were no rational differences among these three populations of cells.

Heart muscle fibres (Figs. 1, 3)
As shown in figure 3, muscle fibres constructing the heart of the sei whale and man are almost the same size in their thickness. The sample means are $10.7 \mu$ and $10.6 \mu$ respectively and the distribution curve for each takes a similar shape and position. The statistical calculations showed that no rational differences in thickness were recognizable between these two groups of muscle fibres.

Purkinje fibres (Fig. 1)
Contrary to the high similarity of the thickness of ordinary heart muscle fibres between the sei whale and man, Purkinje fibres present remarkable difference in size between these two species. The former, of which the average thickness is $37.1 \mu$, exceeds the latter by more than $10 \mu$. That the whale's heart is provided with very thick Purkinje fibres is interesting, when it is reminded of that the hearts of ungulates have also remarkably thick Purkinje fibres.

Cortical cells of the adrenal gland (Figs. 1, 4)

Adreno-cortical cells in the deep layer abutting on the medulla were measured. Although the sample means of these cells are not so different from each other between the right whale and man, their mode of distribution is noticably different. (Fig. 4) Necessarily a rational difference was encountered by the statistical comparison.


Fig. 6. Size distribution of parietal cells of the gastric mucosa.

- _. Right whale
.--.. Blue whale
.-...-. Fin whale
........ Sei whale
-..Human

Fat cells (Figs. 1, 5)
Fat cells in the gastric submucosa of the right whale and man showed a remarkable discrepancy in their sizes, the former being nearly twice as large as the latter. Their modes of distribution are also discrepant to such an extent that the statistical comparison turned out to be impossible.

Parietal cells of the gastric gland (Figs. 1, 6)
Parietal cells in the gastric mucosa were compared among the sei, fin, blue, right whale and man. Generally speaking these cells showed a considerable uniformity in size, the sample means ranging from $16.8 \mu$ in man to $19.9 \mu$ in the right whale. Figure 6 illustrates diagrammatically the mode of distribution for each species. According to the statistical calculations, however, the comparison of these whales and man gives rather un-uniform results. For in some cases there is no rational difference ( $f . i$. between fin and sei whale or man), while in some other cases there is rational differences ( $f . i$. between sei and


Fig. 7. Size distribution of spinal root fibres (large medullated fibres).

| - ventral root <br> . dorsal root | Human |
| :---: | :---: |
| ntral root rsal r. | Lagenorhynchus |
| ventral r <br> dorsal r. | Berardius |

blue, right whale or man, between right and fin whale or man), and still in other cases the comparison is impossible ( $f$. i. between blue and fin, right whale or man).

Spinal root fibres (Figs. 1, 7)
Thick-medullated fibres of the cervical nerves were chosen at random and measured in their thickness for the Berardius, Lagenorhynchus and man. The sample mean of the ventral root fibres as well as of the dorsal ones is largest in the Berardius and smallest in man, that of the Lagenorhynchus taking the mediate value in both groups of fibres. If the ventral root fibres are compared with the dorsal fibres, the former always exceed the latter in thickness. Hence the distribution curve for the ventral fibres takes a position left to that for the dorsal fibres for each of the species examined. (Fig. 7).

The results of the statistical comparisons among these six groups of nerve fibres are rather irregular. In some cases it was revealed that the comparison was impossible ( $f . i$. between the ventral root fibres of Berardius and those of Lagenorhynchus or man, between the dorsal


Fig 8. Size distribution of nerve cells of the hypoglossal nucleus.
-+++• Sei whale

- Human - Mouse
root fibres of Lagenorhynchus and those of Berardius or man). In other cases, however, the comparison turned out to be possible, although rational differences were recognized in most cases.

Nerve cells (Figs. 8-13)
Nerve cells in the hypoglossal and trigeminal mesencephalic nuclei as well as the Purkinje cells in the cerebellum were measured and examined in the sei whale, man and mouse. The average of the longitudinal and transversal diameters of each cell was used for the statistical calculations. As shown in figures 8,9 and 10 , in every item of the invesitigation it was made clear that the brain of the sei whale was furnished with the largest cells and the mouse's were smallest, while the human materials were of the intermediate size. Statistical relations in size among these groups of nerve cells are not so intimate. So far as the size is concerned, most of them seem to belong to special kind of population.


Fig. 9. Size distribution of the Purkinje cells.
$\cdot+++$. Sei whale

- Human
...... . Mouse

When those three kinds of cells are compared to each other in each of the species examined, the cells of the hypoglossal nucleus are largest and the Purkinje cells are smallest for both the sei whale and mouse.


Fig. 10. Size distribution of nerve cells of the trigeminal mesencephalic nucleus.
$\cdot+++$ Sei whale

-     - Human
........ Mouse


Fig. 11. Size distribution of nerve cells of the sei whale.

- Nucl. nervi hypoglossi
.—. Purkinje cells
.-..... Nucl. mesencephalicus V


Fig. 12. Size distribution of nerve cells of man.
-_. Nucl. nervi hypoglossi
.-. Purkinje cells
....... Nucl. mesencephalicus V


Fig. 13. Size distribuition of nerve cells of the mouse.

- Nucl. nervi hypoglossi
-_. Purkinje cells
- Nucl. mesencephalcus V


Size of alveoles ( $1.0=13 \mu$ )
Fig. 14. Size distribution of alveoles of the lung.
.-. Right whale
... Human


Fig. 15. Size distribution of the pan-creas-acini.
.-. Right whale
$. \infty=-$. Blue whale
.-. Human
...... Right whale (embedded in paraffin)

In the case of man, however, the cells of the hypoglossal nucleus are smallest, although the order in size of other two kinds of cells is the same as in the sei whale and mouse. (Figs. 11, 12 and 13)

Alveoli of the lung (Fig. 14)
The pulmonary alveoli of the right whale are by far larger than those of man, the sample mean of the inner diameters being $276.6 \mu$ and $170.7 \mu$ respectively. The distribution mode is also quite different from each other and the comparison is statistically impossible.

Pancreatic acini (Fig. 15)
Outer diameters of the pancreatic acini of the blue, right whale and man are fairly alike, the sample means being approximately $35 \mu$ in each case. Their distribution modes are, as shown in figure 15, also similar to each other so extremely that they can be regarded statistically, so far as the size is concerned, as belonging to one and the same mother population.

In the preparations of the right whale pancreas embedded in paraffin the acini were smaller than those in the celloidin preparations. This decrease in size is apparently due to the shrinkage. As the sample mean for the paraffin preparations is $32 \mu$ compared to $35.3 \mu$ in the celloidin preparations, the decrease is calculated to be $9.3 \% .^{1)}$ Because of this decrease in size the distribution curve for the paraffin preparations is shifted to the left considerably. The shape of the curve itself is however almost the same as that for the celloidin preparations, thus resulting merely in the rational difference statistically.

## Langerhans islets

The Langerhans islets of the right whale pancreas are on the average a little larger than those in the human pancreas. The sample means of the measurements are $144 \mu$ for the former and $125 \mu$ for the latter. Their distribution shows an irregular curve in both cases and the statistical comparison turned out to be impossible.

Renal corpuscles
Malpighian corpuscles of the right whale kidney are exceeded slightly in size by the human equivalents. Furthermore the distribution for the right whale represents a steeper curve than that for the human material. The curve for the latter is provided with a broader foot contour.

Relation in size between the nucleus and cell body
By the measurement of the adreno-cortical cells and the parietal cells of the gastric glands their nuclei were measured too. The average

[^2]sizes given by the arithmetic mean of the length and width of nuclei as well as of cell bodies are in table 2. The ratio between these two values seems to be approximately the same for each kind of cells of


Fig. 16. Comparison of the size of cell-bodies and nuclei of the adrenocortical cells

- : Right whale $O$ : Man


Fig. 17. Comparison of the size of cell-bodies and nuclei of the parietal cells of the gastric gland.
whales and man. In the adreno-cortical cells the proportion of the nucleus to the cell body is nearly $50 \%$ in both the right whale and man. The same ratio is shown to be considerably smaller and less than $40 \%$ in the parietal cells for man and every kind of whales examined.

The scatter diagrams in figures 16 and 17 are to show the correlation in size between the nuclei and the cell bodies. Judging from these diagrams there seems to be no simple relationship between these two. The cell bodies are by far more variant in size than the nuclei within them.

TABLE 2. RATIO IN SIZE BETWEEN THE NUCLEUS AND CELL BODY.

| Item | Species | Cell body $(\mu)$ | Nucleus $(\mu)$ | Ratio |
| :---: | :--- | :---: | :---: | :---: |
| Adreno- <br> cortical <br> cells | Right w. | 11.7 | 5.3 | $2.2: 1=1: 0.45$ |
| Man | 12.9 | 6.3 | $2.1: 1=1: 0.49$ |  |
| Parietal | Sei w. | 17.6 | 5.4 | $3.2: 1=1: 0.31$ |
| cells of | Fin w. | 17.2 | 6.0 | $2.9: 1=1: 0.35$ |
| the | Blue w. | 18.3 | 6.8 | $2.7: 1=1: 0.37$ |
| gastric | Right w. | 19.9 | 6.6 | $3.0: 1=1: 0.33$ |
| gland | Man | 16.8 | 5.8 | $2.9: 1=1: 0.35$ |

## HISTORICAL REVIEW

Cell size in general*
Since Schleiden and Schwann enunciated the cell-theory in 1838-1839, the cell has attained and kept its position as the most fundamental and essential subject in the fields of biology. More than half a century has elasped, however, before the problem of the size of this tiny mass of jelly-like substance called protoplasm attracted the notice of scholars. For it was Julius Sachs (1893) who for the first time paid special attention to the fact that the cells forming big plants are not necessarily larger than those of small plants. Amelung (1893), Strasburger (1893) and Rabl (1899) followed Sachs and Driesch (1900) mentioned of "the law of fixed largeness of the organ cells." It would be paraphrased that not the cell size but the number of cells of organisms varies in proportion to the body size. Studying on the Crepidula (gastropod) and rabbit respectively, Conklin (1912) and Painter (1928) reached to the same conclusion that the equivalent cells of animal bodies are, regardless of the individual variations in body size, almost the same.

Meanwhile, Hardesty (1902) stated, based upon the measurements of Cavazzani (1891) and Bühler (1898), that the variations in the size-of cell-bodies of the spinal ganglia are not directly proportional to the variations in the size of the body of the animal, though in general the larger animal possesses larger cells. According to his own measurements of nerve cells in the spinal cord for several mammals, however, the average mean diameter of the cell-bodies of the columna anterior in

[^3]the intumescentia cervicalis turned out to decrease gradually through a series of mammals of diminishing body weight. His observations showed further that the volume of the cell-body varies more nearly in proportion to the body size of animals and the volume of the entire neuron bears a still more constant ratio to the bulk of the animal body.

Comparative examinations of the cell size of several kinds of mammals led Levi (1905) to a noteworthy conclusion as follows. According to him, there are two categories of cells, one of which comprises such cells that show a notable uniformity in size all through the animals, while the cells of the second group vary in proportion to the body size. Epithelial and glandular cells belong to the first group and the large ganglion cells represent the typical example of the second group. Levi tried to explain the difference in relation to the histogenesis of each cells. For the cells of the first group maintain the potentiality of cell division during the whole life of animals, while the second ones lose the possibility early in the development. Observations of Obersteiner (1913) on Purkinje cells of the cerebellum of the sei whale, elephant and mouse gave the same relationship between the cell size and body size. Ganglion cells of the invertebrates were, however, shown by Erhard (1912) to vary capriciously and independently of the body size. Even for mammals he denied the intimate correlation between the size of cells and animal bodies.

Hatai (1902) measured the nerve cells in the spinal ganglia of the white rat and noticed the increase of cell size following the growth of animal. According to Pfuhl (1932), same kind of growth of the hapatic cells was reported by several authors for man and animals; Harting (1845) and Toldt-Zuckerkandl (1876) for man, Kretschmar (1914) for the pig, Plenk (1911) for the rat, Heiberg (1907) for the mouse and Illing (1905) for domestic animals. Akiyama (1928) made a similar observation for the adrenocortical cells of the white rat. According to Berezowski (1910) the epithelial cells of the intestinal villi were observed to grow and lengthen too. Detailed investigation of the growth of cell size was made later by Rohrbacher (1927), who stated that each kind of cells has its specific size particular to the growth stages of animals.

Another factor influencing the cell size was pointed out by Chambers (1908), who noticed that the frog developed from a small ovum had smaller cells than the frog from a larger ovum. So it is possible, as Wassermann (1929) said, "dass bis zu einem gewissen Grad die difinitive Zellgrösse auch durch die Grösse der Ursprungszelle, des Eies, bestimmt sein kann."

The last and important matter to be considered in relation to the cell
size is the quantitative correlation among the cell, the nucleus and the chromosomes. R. Hertwig (1903) was the first to notice the constancy of the ratio in volume between the cytoplasm and the nucleus and he established the theory of the nucleo-cytoplasmic relation or the karyoplasmic ratio (Lehre der Kern-Plasma-Relation). Erdmann (1908, 1909), Koehler (1912) etc. followed Hertwig and developed his theory. Erhard (1912) too stated that "die Grösse der Kerne (der Ganglienzellen) richtet sich nach der Grösse der Zellen, nur haben Zellen mit reichlicher Nisslsubstanz stets kleine, solche mit wenig oder gar keinem Tigroid stets grosse Kerne.'**

Deviations of the nucleo-plasmic relation were studied by several authors such as Erdmann (1911), Lanz (1926), Stieve (1926), Tretjakoff (1928), etc. Excepting pathological cases, most of these changes of the nucleo-plasmic relation were apparently connected to the fluctuations of the hormonal condition. The functional hypertrophy is another element which causes the shifting of this relation in favour of the cytoplasm. According to Bucher (1948) the nucleo-plasmic relation changes as the aging progresses, resulting smaller nuclei in the cells of higher ages.

Studying upon the chromosomes of the sea-urchin larvae, Boveri (1905) found the parallelism between the cell size and the number of chromosomes or the amount of chromatin in the nucleus. Thus the cell body, nucleus and chromosomes are shown to be in quantitative correlation to one another, although no one knows whether one of these three takes the initiative in determining the volume or size of the others.

Such a harmonious balance prevailing in the intracellular structures fascinated Heidenhain (1907-) and he called it "syntonischer Zustand" or "Syntonie" or "Kanon der Teile und des Systems." The idea of "Syntonie" has developed hand in hand with that of the "dividing bodies" ("Teilkörper ") such as protomeres, histomeres and histosystems. For both of these ideas represent important constituents of his famous "synthetische Morphologie" or "Synthesiologie." By means of these unique ideas Heidenhain tried to grasp the biological principle prevailing in the intra-, extra-, as well as the "supra"-cellular structures of the living body.

At least one part of Heidenhain's hypothetical theories was proved by fact, when Jacobj (1925) found the rhythmical variations of nuclear volumes in the hepatic cells of rats and mice. The so-called Jacobj's law or "das rhythmisches Verdoppelungswachstum" of the nuclear volume was tested and accepted by Voss (1928), Clara (1928, 1930) and

[^4]many other scholars. Jacoby (1935) himself investigated later on many kinds of human cells and classified them into a series of classes, in which the nuclear volumes increase by doubling. Standard nuclear size for each class is as follows.

| Class | Diameter $(\mu)$ | Volume (cub $\mu$ ) |
| :---: | :---: | :---: |
| K $1 / 8$ | 3.25 | 18 |
| K $1 / 4$ | 4.1 | 36 |
| K $1 / 2$ | 5.2 | 72 |
| K 1 | 6.5 | 144 |
| K 2 | 8.2 | 288 |
| $\vdots$ | $\vdots$ | $\vdots$ |
| K 16 | 16.4 | 2304 |

In recent years new attention has been paid to Jacobj's doubling phenomenon of the nuclear volume. For some of the histochemical studies showed a parallelism between the nuclear volume and the DNA amount. (cf. Swift, 1953 ; Alfert, 1955 etc). New methods of precise caryometry are also being devised. (f.i. Bucher, 1954.) At the same time the nucleo-cytoplasmic relationship of $R$. Hertwig is increasing its importance in the fields of modern biology (cf. Frankenhauser, 1952; Hämmerling, 1953 etc.), and the ratio between nucleus and nucleolus too is becoming an interesting subject. (cf. Junqueira and Hirsch, 1956.)*

So far is the review of the literature on the problem of cell size in general. Concerning the items of the present writers' investigation some supplemental survey of the history will be added.

Hepatic cells
Several works on the quantitative study of the hepatic cells and nuclei have been mentioned already. Data given for the human hepatic cells are as follows.

| v. Ebner (1899) | $18-26 \mu$ in diameter |
| :--- | :--- |
| Bucher (1948) | $20-25$ |
| Kopsch (1955) | $18-35$ |
| Bargmann (1956) | $13-30$ |

Average means of the cell size for several animals were tabulated by Pfuhl (1932) in the following way. Apparently the hepatic cells show a fairly uniform size among animals.

[^5]SIZE OF HEPATIC CELLS (PFUHL, 1932)

| Animal (adult) | Cell $(\mu)$ | Nucleus $(\mu)$ | Author |
| :---: | :---: | :---: | :---: |
| Rat | 23.0 | 8.0 | Plenk |
| Rabbit | 25.7 | 8.3 | Schlater |
| Cat | 21.1 | - | Illing |
| Dog | 20.0 | $7-8$ | Auerbach |
| Horse | 26.3 | - | Illing |
| Pig | 26.5 | - | " |
|  | 21.4 | - | " |
| Ox | 23.3 | - | Kretschmar |
| Goat | 23.6 | - | Illing |
| Sheep | 29.0 | - | Baum |
|  | 21.5 | - | Illing |
|  | 20.7 | - | " |

Heart muscle fibres and Purkinje fibres
For the detailed survey of the literature Benninghoff (1930) and Häggqvist (1931, 1956) are to be referred to. Measurements of the width of the human cardiac fibres were reported as follows.

| Letulle (1897) | $5-25 \mu$ |
| :--- | :--- |
| v. Ebner (1899) | $9-22$ |
| Marceau (1904) | $5-40$ (average 20) |

The size of the human heart muscle fibres in relation to the aging was studied very extensively by Schiefferdecker (1916). According to him, the muscle fibres as well as the nuclei increase in size with aging.

For animals Schiebler's data (1953) will be cited.

| Animal | Ordinary fibres of <br> the heart muscle | Purkinje fibres |
| :---: | :---: | :---: |
| Ox | $10 \mu$ | $35-45 \mu$ |
| Calf | 10 | $18-32$ |
| Pig | 10 | $20-26$ |
| Dog | 10 | $14-20$ |
| Cat | 10 | 11 |

Notable uniformity seems to be prevailing in the size of heart muscle fibres, while the size of Purkinje fibres varies from one animal to another. According to Hirai (1943), however, the heart of such animals as with higher activity is made of compact bundles of thinner muscle fibres.

SIZE OF HEART MUSCLE FIBRES (HIRAI, 1943)

| Animals with | higher activity | Animals with lower activity |
| :---: | :---: | :---: |
| Wild dog | $157 \pm 5.3 \mu$ | Rabbit $\left\{\begin{array}{l}211 \pm 9.4 \mu \\ 225 \pm 10.5\end{array}\right.$ |
| Dog | $182 \pm 5.8$ |  |
| Japanese spaniel | $181 \pm 7.1$ | Mouse $\left\{\begin{array}{l}224 \pm 9.0 \\ 234 \pm 9.5\end{array}\right.$ |
| Hare | $178 \pm 5.8$ |  |
| Water rat | $\left\{\begin{array}{l}185 \pm 6.3 \\ 189 \pm 5.4\end{array}\right.$ |  |

Davies and Francis (1952) studied comparatively the hearts of mammals of various kinds and said that the ordinary myocardical fibres in all the animals examined showed a remarkable uniformity in diameter. On the other hand the fibres of the conducting system showed considerable difference in size among animals, the Purkinje fibres always exceeding the fibres of the atrio-ventricular bundle. Furthermore they examined the relationship between the size of the Purkinje fibres and the duration of QRS of the electrocardiogram for each animal, and got the suggestion that in hearts of thicker muscle fibres of the conducting system the cardiac impulse spreads through the ventricles at a higher rate than in those of thinner fibres.

DIAMETERS OF THE HEART MUSCLE FIBRES. (DAVIES AND FRANCIS, 1952)

| Animal | Atrio-ventr. <br> bundle <br> $(\mu)$ | Subendocardial <br> Purkinje <br> fibres $(\mu)$ | Ventricular <br> myocardium <br> $(\mu)$ | QRS <br> $(1 / 100$ sec.) $)$ |
| :--- | :---: | :---: | :---: | :---: |
| Horse | 35 | 88 | 12 |  |
| Cow | 30 | 40 | $"$ | 7 |
| Human | 11 | 18 | $"$ | 9 |
| Wallaby | 36 | 40 | $"$ | 8 |
| Sheep | 30 | 40 | $"$ | 3.5 |
| Dog | 12 | 18 | $"$ | 3 |
| Cat | 9 | 15 | $"$ | 4 |
| Rabbit | 10 | 14 | $"$ | 4 |
| Rat | 9 | 13 | $"$ | 3 |
| Swan | 35 | 44 | 9 | 2 |
| Pigeon | 11 | 12 | 8 | 3 |
|  |  |  |  | 2.7 |

Pulmonary alveoles
According to the survey of literature by Bargmann (1936), the number of alveoles of the human lungs are $300-500$ millions and the total area of their internal surfaces amounts to $50-100$ square meter. The average diameters of the human alveoles reported by several authors are as follows. (Data marked with ${ }^{(1)}$ are cited from Bargmann, 1936.)

| Rossignol (1847)' | $200-250 \mu$ |
| :--- | :---: |
| Frey (1859) | $50-166.7$ |
| Kölliker $(1880)^{\prime}$ | $60-90$ |
| v. Ebner (1899) | $160-220-370$ |
| Schulze (1906) | 200 |
| Ogawa (1920) | $100-190$ |
| Wilson (1922)' | $75 \times 90 \times 125$ |
| Marcus (1928) |  |
|  | adult |
| Claus (1935)' | newborn |
|  | infant |
| Kopsch (1955) |  |
| Braus (1956) |  |
| Bargmann (1956) | $400-600$ |
|  | $100-60$ |
|  |  |

Concerning the lungs of various mammals, the extensive data given by Schulze (1906) and Marcus (1928) will be cited here. It would be added further that Fiebiger (1915) studied on the lung of a dolphin and stated the size of alveoles as $260 \times 140 \mu$.

MEASUREMENTS OF LUNG ALVEOLES. (SCHULZE, 1906)

| Animal | Diameter of <br> alveoles $(\mu)$ | Number of <br> alveoles | Respiratory area <br> (sq. meter |
| :--- | :---: | :---: | :---: |
| Cat | 100 | 400 millionas | 20 |
| Sloth | 400 | 6.25 | 5 |
| Man | 200 | 150 | 30 |
| Dolphin | 140 | 437 | 43 |

(Schulze regarded the difference of the respiratory area as indication of activity of animals.)
MEASUREMENTS OF LUNG ALVEOLES. (MARCUS, 1928)

| Animal | Volume of <br> lungs (ccm) | Respiratory <br> mass (ccm) | Diameter of <br> alveoles $(\mu)$ | Number <br> of <br> alveoles | Respirat. Resp. area (sq. cm.; <br> area <br> (sq. m.) | (sqer gr. of <br> body weight |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: |
| Dolphin | 50 | 40 | 200 | 5 millions | 1 | 31 |
| Mouse | 0.9 | 7.2 | 30 | 266 | 0.1 | 54 |
| Rat | 7 | 5.6 | 50 | 45 | 0.6 | 33 |
| Cat | 180 | 144 | 100 | 144 | 7.2 | 28 |
| Man | 1880 | 1500 | 150 | 444 | 50 | 7 |
| Bat | 3 | 2.4 | 25 | 160 | 0.5 | 100 |
| Galeopithecus | 10 | 8 | 150 | 2.5 | 0.3 | 10 |
| Young deer | 420 | 336 | 120 | 200 | 14.4 | 21 |
| Calf | 3050 | 2440 | 160 | 600 | 76.8 | 13 |
| Horse | 17500 | 14000 | 140 | 5000 | 500 | 11 |

## Renal corpuscles

Numerous papers have hitherto been published which treated directly or indirectly the size of the renal corpuscles of man and animala. Data given in those works will be arranged and tabulated as follows. (Values put in the brackets concern the corpuscles situated deep in the renal cortex. Data of authors with the mark (') or (") are cited from Möllendorff-1930- or Vimtrup-1928- respectively.)

| Man: | $217 \mu$ | Bowmann (1842) ${ }^{\prime}$ |
| :---: | :---: | :---: |
|  | 200 | Schweigger Seidel (1865) |
|  | 200-300 | Sappey (1879)' |
|  | 200-300 | Toldt (1888) |
|  | 213 (吕), 196 (우) | Eckhardt (1888) ${ }^{\prime \prime}$ |
|  | 237 | Külz (1899) ${ }^{\prime \prime}$ |
|  | 200: 300, 149-212 | Glantenay and Gosset (1901)' |
|  | 130:220 | v. Ebner (1902)' |
|  | 210 | Moore (1903) |
|  | 192:159 | Peter (1909) |
|  | 200-300 | Prenant (1911) ${ }^{\prime}$ |
|  | 176-212 | Moberg (1929) |



Porpoise (Phocaena communis):

|  | $130: 103$ | Peter (1909) |
| :--- | :--- | :--- |
|  | $" \quad: "$ | Inouye (1909) |
| Horse: | $270: 240(272: 240)$ | Roost (1912)' |
| Dog: | $256: 240(288: 272)$ | Roost (1912)' |
|  | $162: 127$ | Abe (1953) |
| White rat: | $127(62$, newborn $)$ | Kittelson (1917) |
|  | 124 | Arataki (1926) |
|  | $113: 91$ | Abe (1953) |

Supplemental data about the renal corpuscles will be added in the following.

| MEASUREMENTS OF THE RENAL CORPUSCLES. (PUTTER, 1927 AND MÖLLENDORFF, 1930) |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
| Animal | Surface of each glomerulus (sq. mm.) | Total no. of glomeruli in both kidneys | Total surface area of glomeruli (sq. cm.) | Relative glomeruli surface per gr. of body weight |
| Mouse | 0.087 | 10 thousand | nd 20.5 | $1.08 \mathrm{sq} . \mathrm{cm}$. |
| Rabbit | 0.101 | 285 | 288 | 0.144 |
| Cat | 0.144 | 460 | 662 | 0.221 |
| Sheep | 0.249 | 1010 | 2520 | 0.0718 |
| Man | 0. 293 | 1700 | 4950 | 0.0708 |
| Ox | 0.335 | 8050 | 27000 | 0.0600 |
| Pig | 0.425 | 1400 | 5980 | 0.089 |
| Echidna | 0. 183 | 180 | 330 | 0.165 |

According to " Biological Data" edited by Spector (1956) (Table 145), the volume of glomeruli (cub. mm.) per one gram of kidney is as follows, showing a considerable uniformity among animals and man; man: 29, cat: 28, dog: 40, elephant: 42, ground hog: 75, guinea pig: 42, monkey: 50, mouse: 21 , opossum: 49 , ox: 47 , rabbit: 46 , albino rat: 40 , kangaroo rat: 30, swine: 37.

## Langerhans' islets

Quantitative studies of the Langerhans' islets of man and animals were reviewed and surveyed extensively by Bargmann (1939) in $v$. Möllendorff's Handbuch der mikroskopischen Anatomie des Menschen, Bd. 6, 2 Teil, S. 209-. Among many papers treating this subject, merely the representative ones will be nominated here: Clark (1913) and Nakamura (1924) for man ; Bensley (1911) for the guinea pig ; Hess and Root (1938) for the white rat; Glaser (1926) for the mouse ; Clara (1924) for birds.

So far as the size of the Langerhans' islets is concerned, however,
the data of Heiberg (1909) are most extensive and some of them will be cited here.

AVERAGE DIAMETERS OF LANGERHANS' ISLETS. (HEIBERG, 1909)

| Animal | Long axis $:$ Short axis |
| :--- | :---: |
| Dog | $64: 43 \mu$ |
| Cat | $75: 54$ |
| Pig | $86: 64$ |
| Monkey | $122: 75$ |
| Sheep | $93: 54$ |
| Goat | $97: 54$ |
| Ox | $155: 75$ |
| Horse | $100: 64$ |
|  | $108: 86$ (cauda) |
| Pig | $75: 55$ (caput) |
|  | $75: 52$ (iobus dexter) |
| Ox | $158: 99$ (cauda) |
|  | $108: 82$ (caput) |
|  | $126: 82$ (lobus dexter) |


|  | DISTRIBUTION OF SIZE OF |  |  |  |  |  |  |  | L•ISLETS. (HEIBERG, 1909) |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Animal | below $75 \mu$ | $76-1.25$ | $126-175$ | $176-225$ | $226-275$ | $276-325$ | above 325 |  |  |
| Man | 23 | 38 | 23 | 10 | 4 | 1 | 1 |  |  |
| Mouse | 24 | 33 | 27 | 11 | 4 | 1 |  |  |  |
| Guinea pig | 35 | 37 | 18 | 8 | 2 |  |  |  |  |
| Dog | 64 | 28 | 7 | 1 |  |  |  |  |  |
| Cat | 48 | 40 | 11 | 1 |  |  |  |  |  |
| Pig | 50 | 34 | 13 | 2 | 1 |  |  |  |  |
| Horse | 24 | 47 | 18 | 5 | 5 | 1 |  |  |  |
| Sheep | 51 | 31 | 14 | 4 |  |  |  |  |  |
| Ox | 39 | 47 | 12 | 1 | 1 |  |  |  |  |

## DISCUSSION

Comparative observations of the cell size in whales and man revealed that some kinds of cells such as hepatic cells, adreno-cortical cells and parietal cells of the gastric gland as well as the heart muscle fibres show a considerable uniformity in the size. On the other hand there are other kind of cells which show a remarkable difference in the size between whales and man. The Purkinje fibres of the heart, fat cells, nerve cells and fibres represent examples belonging to the second catagory. A perusal of the pertinent literature suggests that the uniformity of size found in the cells of the first group holds good to a wider extent in the kingdom of animals, so far as the special attention is paid to
mammals. As Levi (1905) pointed out, probably the epithelial and secretory cells may be representatives of this group.

The literature tells at the same time that the variability of cell-size encountered in the second group prevails also among the equivalent cells of other mammals. It is an interesting and perhaps noteworthy fact that the nervous elements, especially larger ones, are the typical examples of this group.

Surveying the members belonging to the second group, it would be noticed that they are represented by relatively large cells. Also many of those cells are furnished with some special intracellular structures or inclusions such as Nissl bodies for the ganglion cells and the large drop of neutral fat for the fat cells. The extraordinary richness in sarcoplasm of the Purkinje fibres may be reminded of too. The ovum containing yolk granules as well as the cells of the sebaceous gland furnished with coarse droplets of fatty substance doubtlessly represents another example. Also the pigment cells in which the pigment granules accumulate belong to the same category.

Nissl bodies of the nerve cell are, however, not to be regarded as corresponding to fat drops, yolk substance, pigment granules and so on. For the latter are merely cellular inclusions, while the Nissl bodies are certainly a sort of important cellular constituent of the nerve cell. The examination of the nucleo-plasmic relation will be probably useful, at least to some extent, to discern between these two categories of intracellular structures. Cellular inclusions such as fat drops in the fat cells do not affect the correlation between the size of nucleus and the amount of the proper cytoplasm. So the nucleus of such a cell is rather small for the considerable bulk of its cell body. In the case of Nissl bodies, on the contrary, the correlation holds good between the nucleus and the total volume of the cytoplasm, resulting thus in such a cell as furnished with nucleus of a fairly largeness.

By the way the present authors have no knowledge as to whether the volume of the neurite and dendrites is to be taken into account when the nucleo-plasmic relation of the neuron is considered. If it should be, supposing that there are two nerve cells or perikarya of a similar size which are though provided with axon or dendrites of different length and numbers, the cell with longer and more processes must have a larger nucleus.

Returning to the earlier discussion, let us bring up a question. Is there any way to explain the above mentioned difference between two groups of cells in the animal tissues? This question is necessarily related to the problem of what is the definitive factors to determine the size of cells.

In the literature, various factors have been stated by many authors as influencing the size of cells. For instance the activity of animals, the rate of metabolism, the innate potentiality for further cell divisions, the size of animal body, the grade of growth and aging, functional influences such as due to hormons and training, etc. have been examined and their correlations to the cell size were proved to some extent. Probably each of those factors is working in its own way and the sum of them, in cooperation with still other innate factors, will determine the size of cells, although its detailed mechanism is at present far beyond our knowledge.

So far as the morphology is concerned, the quantitative correlation between the cell body and nucleus, which was noticed by Hertwig (1903), developed and elaborated by Heidenhain (1912-) and Jacoby (1925-) et al, seems to be of an important meaning. Especially Jacoby's phenomenon of the "rhythmical, doubling growth of the volume of nuclei" is astonishing and must be of a great importance.

Checking Jacobj's review table (1935), the present authors cannot avoid such a suggestion that the discrimination of two cell groups mentioned in the beginning of this chapter is related to the difference of respective classes of those cells. That is to say, cells of lower classes or of smaller nuclear volumes (f. i. $K^{1 / 8}, K^{1} / 4, K^{1} /$, $K 1$ ) belong to the first group of the present description, where the cell size shows a considerable uniformity among animals. On the other hand, cells of higher classes or of larger nuclear volumes ( $f . i . K 8, K 16$ ) are comprised in the second group, where the cell size varies from one animal to another. The higher variability of cell size found in the latter group is not difficult to understand, if it is taken into consideration that the standard nuclear volumes here are of high values. It is also easy to comprehend that the difference between those two groups of cells is not an absolute but relative one. For there can be intermediate classes of medium-sized cells ( $f . i . K 2, K 4$ ). Probably nerve cells of small and intermediate sizes represent examples of this category.

On the size of some large histosystems.
The digestion, respiration and elimination of wastes are three principal functions which are indispensable for keeping the vegetative life. In the protozoa like amoeba all of these functions take place through the body surface. In higher animals, however, each of these three functions is carried out in a special part of the body; the intestinal canal, lungs and kidneys. Thus the intestinal villi, pulmonary alveoles and the renal corpuscles may be regarded as specialized equivalents of the body surface of amoeba.

By the way measurements of the lung alveoles and renal corpuscles revealed that the size of these both shows considerable differences between whales and man. Judging from survey of the pertinent literature, a similar discrepancy of size seems to be prevailing widely among animals. Although the variations in diameter are quite irregular from animal to animal, the relative respiratory as well as glomerular surface per unit of the body weight is in nearly inverse proportion to the body size of animals. Supposing a cell or amoeba shaped like a ball, the relative surface per unit volume is given by $4 \pi r^{3} /^{3} / 4 \pi r^{3}=3 / r$. Thus it is also inversely proportional to the size of the body. Probably this is one of the reasons for the limitation of cell size. For, if it enlarges beyond a certain size, its surface cannot take in food and oxygen fast enough to maintain its bulk.

In spite of the variability among animals the average diameter of pulmonary alveoles as well as of renal corpuscles for every mammal falls in a limited range of some $50-300 \mu$. So we can still speak of a fairly uniformity in size for these histological structures. The pancreatic acini represent an example of a higher uniformity. According to Miziarsky (1900) the same relation was observed in the secretory alveoles of the parotis too.

To explain the size of these structures is as difficult as to explain the nature of the cell size. In his superb thinking way of "Synthesiologie", Heidenhain called those structures with a generic name " Histosysteme" (adenomeres, pneumomeres, etc.), and assumed that common biological factors for cell size would be responsible for determining the size of these "supra"-cellular units or systems too. The present writers have neither fact nor theory to develop the discussion further.

## SUMMARY

1. Several kinds of cells and histological structures were measured and compared statistically between whales and man. Historical review of the literature extended the comparison to other mammals.
2. Some kinds of cells such as hepatic cells, adreno-cortical cells, parietal cells of the gastric glands, heart muscle fibres, etc. were shown to have a fairly similarity in size among animals and man.
3. Nerve cells and fibres, fat cells, Purkinje fibres of the heart and so on were shown to belong to other category, where the size varies considerably from one animal to another.
4. The problem of cell size in general was discussed, with special remarks on the difference between two groups of cells just mentioned.

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    ** Brain Research Institute, University of Tokyo.
    *** With the special permission of the Japanese Government, this right whale was caught in May, 1956, for the scientific investigations. It was a female and 38 feet 4 inches in length.

[^1]:    ＊＊（1）at the level of rostral colliculus，（2）at the level of caudal colliculus．

[^2]:    1) According to Fujita (1947) the radii of the renal corpuscles of the rabbit were in the average $32.9 \mu$ in the paraffin preparations, $36.2 \mu$ in the celloidin preparations and $42.3 \mu$ in the frozen sections. Thus the decrease in size of the paraffin preparations compared to the celloidin ones was $9.1 \%$
[^3]:    * Among others, surveys of the pertinent literature by Chambers (1908), Wilson (1925), Wassermann (1928), Jacobj (1935), and Bucher (1954) are extensive and useful for reference.

[^4]:    * G. Hertwig (1931) stressed upon the necessity of carefullness in considering the nucleo-plasmic relations. For he showed clearly that the cytoplasm reacts to fixatives with irregular shrinkages of higher grade than the nucleus.

[^5]:    * It would be noteworthy that HsU (1954) studied in vitro on the chromosomes of human neoplasms and showed in graphs that the chromosome number distributes in the mode of doubling increase just like the nuclear volumes in Jacobj's graphs.

