$$\Sigma (x_1-\bar{x}_1)(y-\bar{y}) = 0{,}947\cdot 1871+0{,}897\cdot 2134+\ldots \ldots+0{,}582\cdot 1889-3{,}953\cdot 10417/5 = 5{,}927.$$

$$\Sigma (x_2-\bar{x}_2)(y-\bar{y}) = 0{,}660\cdot 1871+0{,}435\cdot 2134+\ldots \ldots+0{,}016\cdot 1889-1{,}383\cdot 10417/5 = -69{,}114.$$

Die entsprechenden Werte werden eingesetzt

$$0{,}084209\, a(c+z)+0{,}143281\,(b-az) = 1 \text{ bzw. } 0;$$
$$0{,}143281\, a(c+z)+0{,}285367\,(b-az) = 0 \text{ bzw. } 1;$$

nach Auflösen der 2 Sätze von je 2 Gleichungen erhält man die inverse Matrix

$$\begin{bmatrix} 81{,}5104 & -40{,}9259 \\ -40{,}9259 & 24{,}0529 \end{bmatrix}.$$

Nach (5) sind dann

$$a(c+z) = 81{,}5104\cdot 5{,}927+(-40{,}9259)\cdot(-69{,}114) = 3309;$$
$$b-az = (-40{,}9259)5{,}927+24{,}0529(-69{,}114) = -1905.$$

Für die Berechnung der Standardfehler sind nach (7)

$$s^3 = [1871^2+\ldots+1889^2-10417^2/5-3309\cdot 5{,}927-(-1905)(-69{,}114)]/2 = 5{,}5$$

und nach (6)

$$s_{a(c+z)} = \sqrt{81{,}5104\cdot 5{,}5} = 21{,}2;$$
$$s_{(b-az)} = \sqrt{24{,}0529\cdot 5{,}5} = 11{,}5.$$

Da $\lambda_M = 0{,}0542$ und $\lambda_T = 0{,}416$ sind, ist $z = 1{,}15$; c wurde für die gegebene Zählanordnung zu 0,5 bestimmt, das heisst, bei gleichen absoluten Aktivitäten wird zweimal soviel La^{140} wie Ba^{140} gezählt.

Durch Einsetzen dieser Werte erhält man

$$a\,(0{,}5+1{,}15) = 3309 \pm 21{,}2$$
$$a = A_{M0} = 2005 \pm 13$$

und

$$b - 2005\cdot 1{,}15 = -1905 \pm 11{,}5$$
$$b = A_{T0} = 401 \pm 12.$$

Es liegt somit für La^{140} ein Unterschuss von rund 80% vor.

Ist $\lambda_T \gg \lambda_M$, so werden

$$\lambda_T/(\lambda_T-\lambda_M) \approx 1 \quad \text{und} \quad \exp(-\lambda_M t) \approx 1$$

und (2) vereinfacht sich zu

$$y = a\,(1+c)+(b-a)\,x_2. \tag{8}$$

Es sind hierbei

$$a = \frac{\bar{y}-\bar{x}_2\,\Sigma (x_2-\bar{x}_2)(y-\bar{y})/\Sigma (x_2-\bar{x}_2)^2}{1+c}; \tag{9}$$

$$b = a+\Sigma(x_2-\bar{x}_2)(y-\bar{y})/\Sigma(x_2-x_2)^2. \tag{10}$$

Kann die Strahlung der Muttersubstanz mit Hilfe entsprechender Folien vollkommen unterdrückt werden, so dass $c = 0$ wird, und ist $\lambda_T \gg \lambda_M$, so ergibt sich für (2) eine weitere Vereinfachung zu

$$y = a+(b-a)\,x_2. \tag{11}$$

b berechnet sich nach (10) und a nach

$$a = \bar{y}-\bar{x}_2\,\Sigma (x_2-\bar{x}_2)(y-\bar{y})/\Sigma(x_2-\bar{x}_2)^2. \tag{12}$$

Für die Differenz $|b-a|$ in (8) und (11) berechnet sich der Standardfehler nach

$$s_{b-a} = \sqrt{\frac{\left[\Sigma y^2-(\Sigma y)^2/n-\dfrac{[\Sigma(x_2-\bar{x}_2)(y-\bar{y})]^2}{\Sigma(x_2-\bar{x}_2)^2}\right]/(n-2)}{\Sigma(x_2-\bar{x}_2)^2}} \tag{13}$$

Der Standardfehler von a und damit auch b ist dadurch gegeben, dass man für y in (9) und (12) den Standardfehler berechnet, der gleich der Wurzel aus dem Zähler im Wurzelausdruck (13) ist.

A. CATSCH

Institut für Strahlenbiologie an der Reaktor-Station Karlsruhe, 11. Juni 1958.

Summary

A simple and time saving numerical method is described permitting the rapid determination of mother to daughter ratios in biological specimens containing radionuclides.

Informations - Informationen - Informazioni - Notes

COGITATIONES

An Hypothesis to Explain the Relation Between the Synthesis and Release of Animal Viruses from Infected Cells and the Lipid Content of the Viruses

Infectious particles of animal viruses are released from their host cells by one of two mechanisms—continuous release of small amounts of virus over a long period of time or the burst-like release of a large number of particles. The viruses released by the continuous process are all sensitive to ether, whereas those released in a burst are resistant to ether and other lipid solvents. The available relevant data are listed in the Table for virulent viruses.

The continuous release process has been most carefully analyzed for the myxoviruses. They are released from their host cells a few minutes after they become infectious, although they may remain on the external surface of the cell for some time before being released into the surrounding medium[1]. This has been confirmed by several electron microscopic studies[2]. Similar studies have been made with the equine encephalitis viruses. Western equine encephalitis is continuously released directly into the medium without remaining on the cell surface[3].

Herpes simplex is released by a continuous process[4]. Although this has not been corroborated by electron microscopy[5], the closely related Herpes B virus has been

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The release mechanism and lipid content of some typical virulent animal viruses. The + and − in the table of kinetic studies and electron microscopic studies (EM) refer to confirmation or lack of confirmation of the proposed release mechanism.

I. Continuous release process

Virus and Virus-group	Kinetics	EM	Lipid content	Evidence that lipid is an essential component
(A) *Myxoviruses*				
Influenza	+[6]	+[10]	~23%[16]	Ether sensitive[21]
Fowl plague	+[7]	+[11]	~24%[17]	Ether sensitive[22]
Newcastle disease	+[8]	+[12]	~27%[18]	Ether sensitive[29] and phospholipase sensitive[23]
Mumps		+[13]	Not investigated	Ether sensitive[29]
(B) *Encephalitis*				
WEE	+[3]		~40%[19]	
EEE		+[14]		Ether sensitive[29]
(C) *Herpes*				
Herpes simplex	+[4]	−[5]	Not investigated	Ether sensitive[29]
Herpes B	+[25]	+[25]	Not investigated	Ether sensitive[29]

II. Burst-like release process*

Virus and Virus-group	Kinetics	EM	Lipid Content	Evidence that lipid is a non-essential component
(A) *Poliomyelitis*	+[28]		None	Resistant to butanol and other lipid solvents[24]
(B) *Pox-group*				
Vaccinia		+[27]	5·7%[20]	Resistant to ether[29]
Fowl pox		+[15]		

observed at the surface of infected cells where the particles are apparently completed[25].

That polio virus is released by a burst has been directly demonstrated by studying the release kinetics from individual infected cells[26].

The pox-viruses seem to be completely synthesized within the cell[27]. The growth kinetics of vaccinia suggest that there are large amounts of intracellular virus present during the multiplication[28], but critical experiments to distinguish between true intracellular virus and virus at the cell surface are still lacking. All the pox-viruses which have been tested, including vaccinia, are resistant to ether[29], even though vaccinia seems to contain a small amount of lipid. This may be located internally and hence protected from ether or the lipid may be a contamination.

In general it appears that the viruses which are sensitive to ether contain lipid as an essential component and only such viruses are released by the continuous release process.

An interpretation of the above observations can be derived from studies on the contribution of host cells to fowl plague virus components[30]. Preincubation of host cells with P^{32} leads to an increase in the specific activity

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* *Note added in proof.* The adenoviruses [Rowe *et al.*, Amer. J. Hyg. *61*, 197 (1955); H. S. Ginsberg, J. exp. Med. *107*, 133 (1958)] as well as Theiler's mous encephalitis (C. Henry and R. M. Franklin, unpublished data) also belong in group II.

of the phospholipid fraction of the virus which is grown on these cells without a concomitant increase in the specific labelling of the virus ribonucleic acid. Similar observations have been made during the P^{32} labelling of Newcastle disease virus[31]. This suggests that the virus lipid is obtained from the host cells as intact lipid material whereas the virus nucleic acid is newly synthesized from smaller components. The fact that the composition of the phospholipid fraction of several strains of influenza virus is the same as that of the normal chorioallantoic membrane[32] further supports this idea.

These facts lead to the following hypothesis: *viruses containing lipids as essential components are assembled from viral subunits or from vegetative forms at or near the cell surface and are completed by obtaining a protective external lipid coat from the lipid structures at the cell periphery as the particles pass to the external cell surface.* As a corollary to this, viruses which do not contain essential lipid components do not form a close union with the periphery of the cell but are completed within the cell and may be released in large amounts by a burst process.

It may be that each type of virus which is released continuously receives an equivalent outer shell of lipid material as it is being completed. It is striking that this hypothetical lipid shell has the same thickness of 40 Å for two unrelated viruses, fowl plague and equine encephalitis, as estimated assuming an average virus density of 1·1 and an average lipid density of 0·9.

Since cells infected with tumor viruses continue to divide, one would expect that these viruses are all released by a continuous process and hence contain essential lipid components. Except for the Rous sarcoma virus, little is known concerning the growth of tumor viruses. Infectious virus particles are continuously released from Rous sarcoma cells in tissue culture[33] and this virus is ether sensitive[29].

Of the other tumor viruses which have been studied, the following are ether sensitive: myxoma[29], fibroma[29], and the agent of mouse leukemia[34]; and the following are ether resistant: Shope papilloma[29], mouse parotid tumor agent[35], and mouse sarcoma agent[35]. The ether resistant Shope papilloma virus, identified by specific fluorescent antibodies, is located for the most part in the differentiating keratohyaline layer rather than in the actively multiplying tissue[36].

The fact that some tumor viruses are ether resistant suggests that they may behave like lysogenic phage, being released by a rare burst event. The ether sensitive tumor viruses may all multiply like the Roux sarcoma virus.

Although this survey is concerned with animal viruses, it should be pointed out that bacterial viruses are released by a burst mechanism and do not contain lipids. Plant viruses are also free of lipids but the release mechanism is a highly specialized process, the virus passing from cell to cell by means of plasmodesmata[37].

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Max-Planck-Institut für Virusforschung, Tübingen, 24. April 1958.

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Zusammenfassung

Eine Hypothese über die Synthese und die Freisetzung von tierpathogenen Viren wird entwickelt. Diejenigen Viren, die durch einen kontinuierlichen Prozess freigesetzt werden, werden an der Zellperipherie zusammengefügt. Beim Durchtritt durch die Zellmembran erhalten sie eine Schutzhülle aus Lipiden, die aus den in der Zellmembran lokalisierten Lipiden der Wirtszelle stammen. Alle derartigen Viren sind gegen Äther empfindlich und enthalten Lipide als essentiellen Bestandteil. Diejenigen Viren, die stossartig freigesetzt werden, werden dagegen im Innern der Zelle zusammengefügt und enthalten keine essentielle Lipid-Komponente. Diese Hypothese wird auch auf die Tumor-Viren angewandt.

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XXI. International Congress of Physiological Sciences (Physiology and Pharmacology)

Buenos Aires (Argentina), 9 to 15 August 1959

President: Professor BERNARDO A. HOUSSAY. Secretary's Office: XXI International Congress of Physiological Sciences, Facultad de Ciencias Médicas, Paraguay 2151, Buenos Aires, Argentina.

Corrigenda

B. L. VAN DER WAERDEN, *Erwachende Wissenschaft* (Ref. N. STULOFF). Exper. *14*, Fasc. 6, 228 (1958).

Die letzte Zeile des vorletzten Absatzes der Buchbesprechung muss richtig lauten: «Ursachen des Niederganges der griechischen Mathematik».

H. LINDE und K. MEYER, *Zur Konstitution des Resibufogenins und Artebufogenins*. Exper. *14*, fasc. 7, 238 (1958).

Auf Seite 239 ist in Formel VIII das H-Atom an C-14 *α-ständig* zu formulieren.