AAEC/E565

AAEC/E565

# AUSTRALIAN ATOMIC ENERGY COMMISSION
## RESEARCH ESTABLISHMENT

## LUCAS HEIGHTS RESEARCH LABORATORIES

# TECHNETIUM-99 LEVELS IN PERTECHNETATE SOLUTIONS FROM (n,$\gamma$) AND (n,f) MOLYBDENUM-99 GENERATORS

by

P.W. MOORE

April 1983

ISBN 0 642 59768 5

AAEC/E -- 565.

AUSTRALIAN ATOMIC ENERGY COMMISSION
RESEARCH ESTABLISHMENT

LUCAS HEIGHTS RESEARCH LABORATORIES

# TECHNETIUM-99 LEVELS IN PERTECHNETATE SOLUTIONS FROM (n,$\gamma$) and (n,f) MOLYBDENUM-99 GENERATORS

by

P.W. MOORE

## ABSTRACT

There is increasing evidence that, in some radiopharmaceutical kits, $^{99}$Tc has an adverse effect on the imaging and labelling performance of $^{99m}$Tc. For example, labelling efficiency with red blood cells can be affected when $^{99}$Tc to $^{99m}$Tc (99/99m) ratios exceed about 4:1.

The 99/99m ratio in a target is about 13.5:1 after a seven-day irradiation in a nuclear reactor. The ratio increases slightly during the time needed for processing. With the chromatographic generators used in hospitals, up to 90 hours may elapse between the final wash stage of manufacture and the first elution, during which time, 99/99m ratios can

increase to about 90:1. If elution efficiencies are high and the time between elutions is between 12 and 24 hours, ratios in the generator, hence in the eluates, will drop in two or three elutions to acceptable levels. However, with poor elution regimes, ratios may actually increase with each elution.

In the case of ready-to-inject pertechnetate solutions, the critical time at which 99/99m ratios increase rapidly is the time between elution and use. If production conditions are poor, ratios may increase to more than 600:1 by the time of use. With better conditions and production schedules, $^{99}$Tc levels at the time of use are comparable to those from chromatographic generators.

National Library of Australia card number and ISBN 0 642 59768 5

The following descriptors have been selected from the INIS Thesaurus to describe the subject content of this report for information retrieval purposes. For further details please refer to IAEA-INIS-12 (INIS: Manual for Indexing) and IAEA-INIS-13 (INIS: Thesaurus) published in Vienna by the International Atomic Energy Agency.

CHROMATOGRAPHY; EFFICIENCY; ISOMERIC NUCLEI; ISOTOPE PRODUCTION; NUCLEAR DECAY; PERTECHNETATES; RADIOISOTOPE GENERATORS; RADIOPHARMACEUTICALS; SOLVENT EXTRACTION; TECHNETIUM 99; TIME DEPENDENCE

## ACKNOWLEDGEMENT OF COPYRIGHT

# CONTENTS

(Continued)

## 1. INTRODUCTION

On average, seven out of eight atoms of molybdenum-99 ($^{99}$Mo) decay radioactively to the metastable isomer of technetium-99 ($^{99m}$Tc). This isomer decays with a half-life of 6.02 hours to $^{99}$Tc, which then decays with a half-life of 2.14 x $10^5$ years to $^{99}$Ru. One in eight $^{99}$Mo atoms decays directly to $^{99}$Tc. Consequently, with increasing time an increasing amount of $^{99}$Mo and $^{99m}$Tc is converted to $^{99}$Tc. Since the activities of the two technetium isomers depend upon the number of atoms of each and their respective half-lives, the activity of $^{99}$Tc is negligible in comparison with that of $^{99m}$Tc even when it is present in amounts that might be ten or a hundred times greater. However, from the chemical point of view, the two isomers are the same, and the $^{99}$Tc cannot be ignored when there is competition between the two for limited amounts of chemical and biological reactants.

Smith and Richards [1976] reported that $^{99m}$Tc labelling efficiencies begin to decrease when more than 1.48 x $10^{14}$ atoms (24 ng) of Tc are added to red blood cell (RBC) labelling kits containing a nominal 1 μg of stannous ion ($Sn^{++}$). They pointed out that this quantity is usually exceeded in ready-to-inject pertechnetate ($TcO_4^-$) solutions and may also be a problem with generators unless the Tc growth times are carefully controlled. Smith and Richards argued that various factors decrease the amount of available $Sn^{++}$ inside the blood cells to a small excess above that required to reduce the $TcO_4^-$ to the quadrivalent state. When larger amounts of $Sn^{++}$ are added to make up this loss, the excess $Sn^{++}$ combines with plasma proteins and, if not removed before the addition of $TcO_4^-$, will reduce some of the $TcO_4^-$ outside the blood cells. Since the reduced species do not cross the cell membrane, low labelling efficiencies result.

In the same year, Porter et al. [1976] reported that 3 x $10^{15}$ atoms of $^{99}$Tc (500 ng) was the maximum amount that could be added to a $^{99m}$Tc-human serum albumin kit and still maintain the radiochemical purity above 90 per cent. Subsequently, Srivastava et al. [1977] reported reduced labelling yields with some commercial lung agents when the number of Tc atoms added to the kits exceeded certain values. With one agent, the yield fell sharply above 6 x $10^{14}$ Tc atoms (100 ng). Since 1 GBq of pure $^{99m}$Tc weighs 5.14 ng, a test involving 200 MBq of $^{99m}$Tc reduces labelling yields if the ratio of $^{99}$Tc to $^{99m}$Tc (hereafter called the 99/99m ratio) exceeds about 100:1. For a test involving 500 MBq of $^{99m}$Tc, 99/99m ratios above 40:1 cause reduced labelling. Srivastava et al. also monitored ready-to-inject $TcO_4^-$ from four suppliers over several months. They found that $^{99}$Tc levels varied in a manner that was characteristic of the particular source (i.e. $^{99}$Tc levels were related to manufacturing conditions) and commented that it was not uncommon for the amount of $^{99}$Tc to exceed the reducing capacity of the usable stannous ion in several commercial radiopharmaceutical kits.

Maddalena and Domel [1981] have studied the causes of poor bone-imaging and RBC labelling obtained with certain $TcO_4^-$ solutions. They have found that of all the possible impurities in solvent-extracted $TcO_4^-$ only $^{99}$Tc has a significant effect on RBC labelling. They have shown that labelling efficiencies begin to decline at about 25 ng of Tc/μg $Sn^{++}$, the same level as was found by Smith and Richards [1976]. A test involving 1 GBq of activity therefore shows a decrease in labelling efficiency when the ratio of 99/99m exceeds about 4:1. It also follows that an in vitro test, which measures either the point or the extent of decrease, can be developed and used as a method for determining $^{99}$Tc in $TcO_4^-$ solutions.

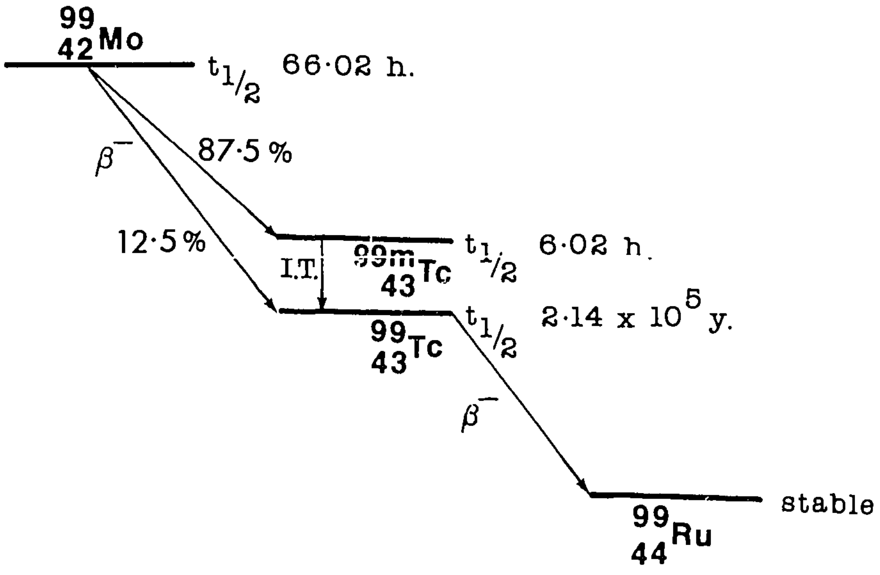
If the 99/99m ratio proves to be more important than is generally realised, a number of questions need to be answered:

- What levels of $^{99}$Tc may be expected under normal conditions of use?
- Does ready-to-inject $TcO_4^-$ have greater amounts of $^{99}$Tc than $TcO_4^-$ from a hospital chromatographic generator?
- How much build-up of $^{99}$Tc occurs at different stages of production?
- What can be done to reduce the amount of $^{99}$Tc, and what is the cost in terms of yield and inconvenience?

This report seeks to answer these questions by analysing the various production stages of a process starting with $(n,\gamma)^{99}$Mo, and by providing graphs from which 99/99m ratios can be determined at each stage under particular production conditions. Most of the information and all of the conclusions reached here are equally applicable to a process starting with (n,f)$^{99}$Mo.

## 2. $^{99}$Mo and Tc GROWTH AND DECAY

The decay of $^{99}$Mo and its daughters is shown below in simplified form [after Lederer et al. 1968]. The decay scheme shown in a later (7th) edition gives a branching ratio of 86.81:12.85. This does not materially alter any of the calculations or conclusions in this report. It can be seen from the decay scheme that, in a strict sense, $^{99m}$Tc can never be obtained in the carrier-free state because of the branching decay of $^{99}$Mo. Another way of looking at this is to say that $TcO_4^-$ solutions are already 70 minutes old when eluted because the amount of $^{99}$Tc in a fresh eluate is the same as it would be if $^{99m}$Tc was the only direct product of $^{99}$Mo decay and the eluate was allowed to decay for 70 minutes.



Unfortunately, decay schemes do not immediately convey much idea of the relative amounts and activities of each nuclide formed. To appreciate this, it is assumed that the $^{99}$Mo activity of a molybdenum oxide target is 40 GBq $g^{-1}$ $MoO_3$ (1.08 Ci $g^{-1}$) after a seven-day irradiation in a high flux reactor such as the AAEC's reactor HIFAR. The number of atoms of $^{99}$Mo giving this activity can be calculated using equation (3.2). The value of $R_1$, the rate of formation of $^{99}$Mo, can also be calculated from equation (3.2). Using this value, the number of atoms of $^{99m}$Tc and $^{99}$Tc may then be calculated using equations (3.5) and (3.6).

A mass balance shows the following:

| Nuclear Species | | atoms/g $MoO_3$ |
|---|---|---|
| $^{99}$Mo | at t = 7 days | = 1.371 x $10^{16}$ |
| $^{99m}$Tc | | = 0.107 x $10^{16}$ |
| $^{99}$Tc | | = 1.441 x $10^{16}$ |
| total $^{99}$Mo formed | | = 2.919 x $10^{16}$ |
| total Mo present | | = 4.184 x $10^{21}$ |
| initial $^{98}$Mo | | = 1.021 x $10^{21}$ |

This shows that only one atom in every 35 thousand of the target $^{98}$Mo atoms is activated in the reactor. Of those activated, approximately 53 per cent decay before the irradiation is complete. Since 87.5 per cent of these decays produce $^{99m}$Tc, more than 92 per cent of the $^{99m}$Tc also decays. By contrast, it can be shown that only one $^{99}$Tc atom in every 16.5 million decays during this period.

A similar situation applies in the case of $^{99}$Mo produced by the fission of $^{235}$U. As in the (n,γ) reaction, $^{99}$Mo is produced at a constant rate and 53 per cent of it decays over a seven-day irradiation to the same products in the same proportions. Three or four isotopes of molybdenum are formed by various reactions, and although the $^{99}$Mo is therefore not strictly carrier-free, it has a specific activity of several million GBq $g^{-1}$. A $UO_2$ target enriched to 1.8 per cent in $^{235}$U, when irradiated for seven days in the HIFAR reactor, produces about 90 GBq of $^{99}$Mo $g^{-1}$ of $UO_2$, which represents approximately six per cent of the fission product yield.

Some time after removal of the $MoO_3$ or $UO_2$ targets from the reactor, a situation is reached in which the rate of formation of $^{99m}$Tc exactly balances the rate of decay. The $^{99m}$Tc is then said to be in transient equilibrium with the $^{99}$Mo. Under these conditions, the $^{99m}$Tc activity declines with the 66-hour half-life of the parent $^{99}$Mo although, of course, the $^{99m}$Tc continues to decay with its characteristic six-hour half-life.

The number of atoms of $^{99m}$Tc in equilibrium with $1.371 \times 10^{16}$ atoms of $^{99}$Mo, calculated using equation (5.1), is $1.204 \times 10^{15}$, and the activity of the $^{99m}$Tc, calculated using equation (5.2), is 38.51 GBq. A comparison of values calculated from equations (3.5) and (5.1) shows that during the irradiation the $^{99m}$Tc is not in equilibrium with the $^{99}$Mo. During this period the number of atoms of $^{99m}$Tc, and the $^{99m}$Tc activity, increase from about 62 per cent of the respective equilibrium values after the first day to about 89 per cent after 7 days and about 91 per cent at saturation (i.e. at $t \gg t_{\frac{1}{2}}$). The ratios at any time during the irradiation depend only on the time and the half-lives of the parent and daughter nuclides.

The number of $^{99m}$Tc atoms at equilibrium is slightly less than one eleventh of the number of $^{99}$Mo atoms (the ratio of half-lives) and the activity of the $^{99m}$Tc is 96.28 per cent of the $^{99}$Mo activity. In the absence of branching, the number ratio would be slightly more than one eleventh, and the activity would be 110 per cent of the $^{99}$Mo activity (the number ratio equals the half-life ratio and the activities become equal only when the half-life of the parent is very much greater than that of the daughter). Because of its longer half-life, $^{99}$Tc is never in equilibrium with either parent. The number of $^{99}$Tc atoms increases slowly over some months and then declines over many centuries.

## 3. PRODUCTION OF $^{99}$Mo BY THE IRRADIATION OF $MoO_3$ IN A REACTOR

The 'law of diminishing returns' usually imposes the condition that reactor irradiation times are limited to two or three product half-lives, hence for $^{99}$Mo, a seven-day irradiation is usual.

The rate of $^{99}$Mo production during irradiation is the difference between the rates of formation and decay. If, initially, there is no $^{99}$Mo present, the number of atoms of $^{99}$Mo ($N_1$) at any time (t) during irradiation is given by

$$N_1 = \frac{R_1}{\lambda_1}(1-e^{-\lambda_1 t}) \tag{3.1}$$

where $R_1$ is a constant equal to the rate of formation of $^{99}$Mo atoms, $\lambda_1$ is the decay constant for $^{99}$Mo defined by the relationship, $\lambda = \ell n2/t_{\frac{1}{2}}$, and $t_{\frac{1}{2}}$ is the half-life.

The activity (A) of a radioactive substance is given by the relationship

$$A = -\left(\frac{dN}{dt}\right) = \lambda N$$

hence

$$A_1 = \lambda_1 N_1 = R_1\left(1-e^{-\lambda_1 t}\right) \tag{3.2}$$

Since the rate of formation of $^{99m}$Tc is 87.5 per cent of the rate of decay of $^{99}$Mo,

$$R_2 = 0.875\ R_1\left(1-e^{-\lambda_1 t}\right) \tag{3.3}$$

where $R_2$ is the rate of formation of $^{99m}$Tc. The net rate of production of $^{99m}$Tc is the difference between the rate of formation and the rate of decay, and is therefore given by

$$\frac{dN_2}{dt} = 0.875\ R_1\left(1-e^{-\lambda_1 t}\right) - \lambda_2 N_2 \tag{3.4}$$

Integrating for the boundary condition that $N_2 = 0$ at time $t_o$ gives

$$N_2 = \frac{0.875}{\lambda_2} R_1\left(1-e^{-\lambda_2 t}\right) + \frac{0.875}{\lambda_2-\lambda_1} R_1\left(e^{-\lambda_2 t} - e^{-\lambda_1 t}\right) \tag{3.5}$$

Since the total number of $^{99}$Mo atoms formed at time t is equal to $R_1t$, and the decay of $^{99}$Tc is negligible, the number of atoms of $^{99}$Tc is

$$N_3 = R_1t - (N_1 + N_2) \tag{3.6}$$

Giving $R_1$ the convenient value of 1 (the units are arbitrary), the relative numbers of atoms of the three nuclides after different irradiation times are calculated using equations (3.1), (3.5) and (3.6). The results of these calculations are shown in Figure 1, where the number of atoms is given by the ordinate value, not the area under the curve. The figure clearly shows the increase in the relative amount of $^{99}$Tc in the target with irradiation time. The amount of $^{99}$Tc, expressed as a ratio of the $^{99m}$Tc, is shown in Figure 2.

It can be seen that a typical seven-day irradiation produces in the target a 99/99m ratio of 13.5:1. This is greater than the level which causes a reduction in RBC labelling but is of no consequence if all the technetium is separated from the $^{99}$Mo by extraction, filtration, or washing during subsequent processing. However, it has a considerable influence on 99/99m ratios in early eluates if only part of the technetium is removed.

## 4. THE 99/99m RATIO RESULTING FROM $^{99}$Mo DECAY

Inevitably, some hours elapse between the time at which the target is unloaded from the reactor and a production stage at which separation of at least part of the Tc from the $^{99}$Mo occurs. The 99/99m ratio at that stage is higher than at the time of unloading.

Equations describing the relative numbers of nuclides in a radioactive decay series are well known and may be obtained from Bateman's general equation for the number of nuclei of the nth product. Applying the general equation to $^{99}$Mo and the two Tc daughers gives

$$N_1 = N_1^0 e^{-\lambda_1 t} \tag{4.1}$$

$$N_2 = 0.875\, N_1^0 \frac{\lambda_1}{\lambda_2-\lambda_1}\left(e^{-\lambda_1 t} - e^{-\lambda_2 t}\right) + N_2^0\, e^{-\lambda_2 t} \qquad (4.2)$$

$$N_3 = 0.875\, N_1^0 \left(1 + \frac{\lambda_1}{\lambda_2-\lambda_1} e^{-\lambda_2 t} - \frac{\lambda_2}{\lambda_2-\lambda_1} e^{-\lambda_1 t}\right) +$$

$$0.125\, N_1^0 \left(1 - e^{-\lambda_1 t}\right) + N_2^0 \left(1 - e^{-\lambda_2 t} + N_3^0\right) \qquad (4.3)$$

where

$$\left.\begin{array}{l} N_1^0\\ N_2^0\\ N_3^0\\ N_1\\ N_2\\ N_3 \end{array}\right\}\text{is the number of atoms of}\left\{\begin{array}{l} \left.\begin{array}{l} {}^{99}\text{Mo}\\ {}^{99m}\text{Tc}\\ {}^{99}\text{Tc} \end{array}\right\}\text{at time } t = 0\\ \left.\begin{array}{l} {}^{99}\text{Mo}\\ {}^{99m}\text{Tc}\\ {}^{99}\text{Tc} \end{array}\right\}\text{at time } t \end{array}\right.$$

$$\left.\begin{array}{l} \lambda_1\\ \lambda_2\\ \lambda_3 \end{array}\right\}\text{is the decay constant for}\left\{\begin{array}{ll} {}^{99}\text{Mo} & = 0.0105\ \text{h}^{-1}\\ {}^{99m}\text{Tc} & = 0.1151\ \text{h}^{-1}\\ {}^{99}\text{Tc} & = 0 \end{array}\right.$$

For the special case where $N_2^0 = N_3^0 = 0$, the 99/99m ratio is obtained by dividing equation (4.3) by equation (4.2). The resulting expression can be simplified to

$$\frac{99}{99m} = \frac{N_3}{N_2} = \frac{11.43 + e^{-\lambda_2 t} - 12.43\, e^{-\lambda_1 t}}{e^{-\lambda_1 t} - e^{-\lambda_2 t}} \qquad (4.4)$$

In Figure 3 the 99/99m ratios calculated from equation (4.4) are plotted against time. This figure can be used to determine 99/99m ratios in irradiated $MoO_3$ at various times after removal from a reactor. For example, the ratio at A' is 41:1, 48 hours after A when it was 20:1. The calculation is appropriate only in cases where the relative amounts of $^{99}$Mo and $^{99m}$Tc have not been altered by removal of Tc. Using this method, the increases in the 99/99m ratio with elapsed time t', after unloading from the reactor for selected ratios in the target at unloading time, are plotted in Figure 4. It can be seen that the ratio increases more rapidly with time when the initial ratio is higher.

Figure 3 can also be used to determine the 99/99m ratio in a generator at time t after all the Tc has been removed in a production or elution step. This is done simply by re-starting at zero time. For reasons discussed in Section 5, Figure 3 cannot be used if only some of the Tc is removed.

## 5. THE EFFECT OF ELUTION CONDITIONS ON THE 99/99m RATIO IN ELUATES

### 5.1 Introduction

The discussion which follows makes two assumptions: first, the two Tc isomers are eluted in the proportions in which they are present in the generator;* and second, elution of a generator is mathematically equivalent to solvent extraction of a molybdate solution, hence the findings are equally valid for both systems.

### 5.2 Why Elution Affects the 99/99m Ratio

Consider a situation in which $^{99m}$Tc is essentially in equilibrium with $^{99}$Mo in a generator with a 99/99m ratio of 10:1; this is the condition at point B in Figure 3. Technetium-99m is formed at the same rate that it decays, and the 99/99m ratio, if not disturbed by elution, increases with time in accordance with the main curve. If the generator is eluted with an efficiency of, say, 70 per cent, the 99/99m ratio in the generator no longer follows this curve because the $^{99m}$Tc is no longer in equilibrium with the $^{99}$Mo. Since the rate of formation of $^{99m}$Tc is proportional to the number of $^{99}$Mo atoms and the rate of decay (effectively the rate of formation of $^{99}$Tc) is proportional to the now smaller number of $^{99m}$Tc atoms, $^{99m}$Tc is formed at a faster rate than it decays, with the result that $^{99m}$Tc 'grows in' until equilibrium is once more established.

---

* This assumes that conditions are conducive to isotopic exchange. Bonnyman [1983] has suggested that poor elution efficiencies of chromatographic generators are usually due to the reduction and hydrolysis of $TcO_4^-$ on the column which could prevent exchange of adsorbed $^{99}$Tc with fresh $^{99m}TcO_4^-$. In these circumstances, the 99/99m ratio in the eluate is the same as that in a generator with 100 per cent elution efficiency. Unfortunately, no study has yet been undertaken to determine the extent of exchange in generators in relation to elution efficiency.

The change in the 99/99m ratio with time is now given by the curve BB'. If another elution is performed 24 hours later at C, the subsequent change in the ratio with time is given by the curve CC'. Curves BB' and CC' are drawn from calculated values for an elution efficiency of 70 per cent. The actual shapes of these curves vary with the elution efficiency.

The 99/99m ratio at the next elution can be calculated by finding suitable values for $N_2^o$ and $N_3^o$ in equations (4.2) and (4.3), which represent the conditions immediately after elution. These values are equal to (1 - fractional elution efficiency) multiplied by the $N_2$ and $N_3$ values at that elution. The ratio of $N_3/N_2$ can then be calculated for t equal to the time interval between elutions. However, the problem is more easily managed without computer aid, and the solution is more informative if another method is adopted. This approach makes use of the fact that the amount of $^{99}$Tc formed between elutions depends on whether $^{99m}$Tc growth between elutions represents a late or early stage of the $^{99m}$Tc growth curve, i.e. whether the amount of $^{99m}$Tc is approaching the equilibrium value. Less $^{99}$Tc is formed in an early stage (on the steep part of the growth curve) than in a late stage (on the flat part of the growth curve).

## 5.3 A Simple Approach to the Problem

Under transient equilibrium conditions, the following relationships hold

$$N_2(\text{eq.}) = \frac{0.875\ \lambda_1}{\lambda_2-\lambda_1} N_1 \tag{5.1}$$

and

$$A_2(\text{eq.}) = \frac{0.875\ \lambda_2}{\lambda_2-\lambda_1} A_1 \tag{5.2}$$

where $N_2$(eq.) is the number of atoms of $^{99m}$Tc in equilibrium with $N_1$ atoms of $^{99}$Mo; and $A_2$(eq.) is the activity of the $^{99m}$Tc in equilibrium with the activity ($A_1$) from $N_1$ atoms of $^{99}$Mo.

If $N_2^o = 0$, dividing equation (4.2) by (4.1) gives

$$\frac{N_2}{N_1} = \frac{0.875\ \lambda_1}{\lambda_2-\lambda_1}(1 - e^{-(\lambda_2-\lambda_1)t}) \tag{5.3}$$

and, since $\frac{N_2}{N_1} = \frac{\lambda_1}{\lambda_2}\frac{A_2}{A_1}$

$$\frac{A_2}{A_1} = \frac{0.875\ \lambda_2}{\lambda_2-\lambda_1}(1 - e^{-(\lambda_2-\lambda_1)t}) \tag{5.4}$$

On combining equation (5.1) with (5.3) and (5.2) with (5.4)

$$\frac{N_2}{N_2(eq.)} = \frac{A_2}{A_2(eq.)} = 1 - e^{-(\lambda_2-\lambda_1)t} \tag{5.5}$$

A graph of this equation against time (Figure 5) shows the rapid initial increase in the number of atoms of $^{99m}$Tc and the $^{99m}$Tc activity, followed by a progressively slower increase as equilibrium is approached.

Let us reconsider the problem discussed earlier. If a generator in which the $^{99m}$Tc is in equilibrium is eluted with 70 per cent efficiency, the condition after elution is represented by point P on the curve, and is the same condition with respect to $^{99m}$Tc that would have been reached by allowing $^{99m}$Tc to grow for 3.4 h from zero. The condition at the next elution, 24 hours later, is given by Q at t = 27.4 h. Choosing a convenient value for $N_1^o$, values of $N_1$ and $N_2$ for t = 3.4 and 27.4 can be calculated using equations (4.1) and (4.2). The difference in the $N_1$ values gives the total number of Tc atoms formed between elutions, and the difference in the $N_2$ values gives the net increase in the number of $^{99m}$Tc atoms. The number of $^{99}$Tc atoms formed may then be calculated by subtracting the number of $^{99m}$Tc atoms from the total number of Tc atoms. This may then be expressed as a percentage of the total technetium produced by $^{99}$Mo decay between elutions. If the calculation is repeated for different elution efficiencies, and the resultant values plotted against elution efficiency, as in Figure 6, a linear relationship is obtained. If the procedure is repeated for a number of elution intervals, the curves all meet the ordinate axis at the same point.

Figure 6 clearly shows that, even under the best elution regimes, the amount of $^{99m}$Tc decaying is more than 50 per cent of that formed between elutions. Since most of the $^{99m}$Tc in the generator would have been formed since the previous elution, it can be said that more than half of the $^{99m}$Tc decays before it is eluted. As was expected, the amount that decays is greater for low elution efficiencies and long intervals between elutions. With very low elution efficiencies, more $^{99}$Tc is formed than can be accounted for by $^{99}$Mo decay; this means that there is a net loss of $^{99m}$Tc in the generator between elutions. The common intercept at 108.78 occurs because $N_2$(eq.)/$N_1$ = 0.0878 (equation 5.1) and $N_2$(eq.) and $N_1$ decay with the same half life. If no elutions are performed on a generator in equilibrium, the amount of $^{99}$Tc formed in any period is equal to 100 per cent of the $^{99}$Mo decay during that period plus 8.78 per cent due to a reduction in the $N_2$(eq.) value.

The importance of elution frequency is also well illustrated in Figure 6. If the time interval between elutions is 48 hours, there is a net loss of $^{99m}$Tc between elutions if the elution efficiency is below 40 per cent, whereas if the elution interval is six hours, there is no net loss unless the elution efficiency drops below 13 per cent. Also, since 87.5 per cent of $^{99}$Mo decays produce $^{99m}$Tc, it can be seen from Figure 6 that, with an elution interval of 48 hours, more $^{99}$Tc than $^{99m}$Tc is formed between elutions unless the elution efficiency is above 97 per cent, whereas if the elution interval is six hours the amount of $^{99}$Tc formed does not exceed the amount of $^{99m}$Tc formed unless the elution efficiency is below 30 per cent.

## 5.4 Calculation of 99/99m Ratios

There is now sufficient information for 99/99m ratios in the eluates to be calculated for various initial ratios in a generator eluted with a chosen efficiency and frequency. The method and the basis for each calculation are shown in Table 1. The only point requiring further explanation is the calculation of the number of atoms of $^{99m}$Tc in a generator at elution time (column 3). This is done using the equation

$$N_2(\text{eq.}) = 0.0878\, Q_n N_1 \qquad (5.6)$$

derived from equation (5.1), where $Q_n$ is the ordinate of the point on the growth curve in Figure 5 for growth after the (n-1)th elution determined in the manner described above. If the time interval between elutions is constant, $Q_n$ achieves a constant value after the first one or two elutions, which is slightly less than the value of $Q_1$. The value of $Q_0$ for the generator in equilibrium is one.

Although for simplicity it is assumed that $^{99m}$Tc and $^{99}$Mo are in equilibrium until the final wash before the first elution cycle, it makes little difference to the 99/99m ratio in the first eluate if Tc is removed in a number of processing steps, provided that a suitable wash efficiency is used in the calculation and that the time interval between the steps is not longer than a few hours. If processing is prolonged, and there is substantial growth of $^{99m}$Tc between an extraction step and the final wash, the effects of extraction and washing on the 99/99m ratio should be calculated separately.

Figures 7 to 10 show the effect of elution efficiency on 99/99m ratios in eluates for elution intervals of 24 and 12 hours. Figure 11 shows the effect of the elution interval on 99/99m ratios in eluates for a constant elution efficiency of 70 per cent. The information in these figures may be summarised as follows:

(a) The 99/99m ratios decrease more rapidly when generators are eluted with high efficiency. Ratios can be reduced from 20:1 to 4:1 in two elutions if the elution efficiency is near 90 per cent. If elution efficiencies are below about 40 per cent and the elution interval is 24 h, 99/99m ratios have a tendency to increase with elution number rather than decrease.

(b) After a few elutions, the 99/99m ratio approaches a steady-state value that is characteristic of the elution efficiency and elution interval, and is independent of the initial ratio in the generator.

(c) The steady-state ratio is less for high elution efficiencies and short elution intervals.

(d) The 99/99m ratio reaches a steady-state value earlier when the elution efficiency is high.

(e) For a particular elution efficiency, the number of elutions required to reach a steady-state is the same for different elution intervals; this means that the time required to reach the steady-state is directly proportional to the elution interval.

Figure 12 shows the same data plotted differently to emphasise the importance of the elution interval in determining steady-state 99/99m ratios, especially at low elution efficiencies. With an elution interval of 24 h, the steady-state 99/99m ratio attains very high values at elution efficiencies below about 40 per cent, whereas if the elution interval is 12 h, low steady-state ratios are obtained at much lower efficiencies.

Figure 13 shows that the steady-state 99/99m ratio increases steadily with longer elution intervals. The figure indicates that if a 99/99m ratio of 4:1 is the maximum that can be tolerated in a Tc solution, elution intervals need to be as short as eight hours if the elution efficiency is only 30 per cent, 14 h if the efficiency is 50 per cent, 21 h if the efficiency is 70 per cent, and up to 30 h if the efficiency is 90 per cent.

### 5.5 Choosing a Better Elution Regime

Once a generator comes into use, a 24-hour elution cycle is the one most commonly used because it is convenient for both production and routine hospital use. If elutions are carried out at 12-hour intervals to keep $^{99}$Tc concentrations at acceptable levels, at least two daily shifts are required to elute the generator, and one of the two elutions is done at night when there is low demand for the product. Consequently, half the daily production is likely to be wasted. It is a much more attractive proposition to maintain a 24-hour cycle by eluting the generator at the start of a work period and washing it six hours later, towards the end of the the shift, thereby allowing an 18-hour 'grow-in' period for the next day.

Figure 14 compares 99/99m ratios for three variations of the 24-hour cycle. It is evident that the 12/12 and 6/18 hour cycles reduce 99/99m ratios much more effectively than the normal 24-hour cycle. The improvement is particularly marked when the elution efficiency is low. It is clear that these cycles also remove other elutable impurities, such as rhenium, caesium and silver isotopes much more effectively.

## 6. ELUTING FOR MAXIMUM $^{99m}$Tc ACTIVITY

It is felt intuitively that any improvement in quality due to eluting after shorter growth times is gained at the expense of $^{99m}$Tc activity in the eluate. Fortunately, the situation is much better than intuition might suggest. The first reason for this is easily overlooked by those who are used to thinking in terms of $^{99m}$Tc activity as a ratio of $^{99}$Mo activity or equilibrium $^{99m}$Tc activity (as in Figure 5). In both cases the denominator of the ratio is not constant, but decreases with time, and therefore tends to make the $^{99m}$Tc activity appear less at short times and greater at longer times.

An expression for $^{99m}$Tc activity at time t can be derived from equation (4.2). Since, by definition, $A_2 = \lambda_2 N_2$ and $A_1^o = \lambda_1 N_1^o$, equation (4.2) expressed in activities becomes

$$A_2 = 0.875\, A_1^o \frac{\lambda_2}{\lambda_2 - \lambda_1}\left(e^{-\lambda_1 t} - e^{-\lambda_2 t}\right) \qquad (6.1)$$

for $N_2^o = 0$.

The above point is illustrated in Figure 15 where the $^{99m}$Tc growth curve obtained using this expression with a suitable value of $A_1^o$ is compared with the curve for the expression for $A_2/A_2$(eq.) - see equation (5.5) and Figure 5. The $^{99m}$Tc activity for growth times in the range 14 to 22 h is considerably closer to the maximum $^{99m}$Tc activity than is indicated by the ratio curve. The maximum $^{99m}$Tc activity ($A_2$(max.)) occurs after a growth time of 22.9 h (the value of t for which $(d(A_2)/ dt) = 0$).

The $^{99m}$Tc activities are also greater than expected after growth times shorter than 24 h because growth after elution does not start at zero unless the efficiency of the elution was 100 per cent. As was discussed in Section 5, if the elution efficiency is between, say, 70 and 30 per cent, the $^{99m}$Tc activity is the same immediately after elution as it would be if it had grown from zero for 3.4 to 11.6 h. Under these conditions an elution interval between 19.5 and 11.3 h may be chosen (depending upon the elution efficiency) so that elution coincides with $A_2$(max.). The amount of $^{99m}$Tc is therefore higher than is obtained with a 24 h elution.

In terms of production, where $^{99m}$Tc is required at the same time each day, it is clear that if the generator is washed at an appropriate time after the daily elution, the time being dependent upon the washing efficiency, the 99/99m ratio is reduced more effectively than with a single daily elution, the activity of the $^{99m}$Tc reaches a maximum at the required time, and the yield of $^{99m}$Tc is very close to that for a 24-hour growth period. The technique is particularly useful when elution efficiencies are below about 70 per cent. The benefit is only slight, however, if elution efficiencies are above about 80 per cent and need only be used in these circumstances on the first day after build-up of $^{99}$Tc during transport or after standing for a prolonged time without elution. The times required for eluted or washed generators with various efficiencies to reach maximum $^{99m}$Tc activity for the next elution are shown in Figure 16.

It is worth noting that elution efficiencies will be overestimated if the calculation method (a) assumes that $^{99m}$Tc growth after elution starts from zero and (b) ignores $^{99m}$Tc growth during elution. If the elution efficiency is high, the time between elutions is considerably longer than 24 hours, and the time taken for the elution is no more than a few minutes, the overestimation will not be serious. However, under a variety of likely conditions it could be as much as five or ten per cent of the true efficiency.

## 7. DECAY OF $^{99m}$Tc AFTER ELUTION

The condition existing in the earlier stages, when the $^{99m}$Tc lost by decay is more or less restored by growth, ceases once $TcO_4^-$ is separated from the $^{99}$Mo by elution. The number of $^{99m}$Tc atoms, and consequently the $^{99m}$Tc activity, decline with a six-hour half-life instead of the 66-hour half-life of the earlier stages. As a result, 99/99m ratios increase more rapidly with time, although not at eleven times the former rate because the rate of production of $^{99}$Tc also declines with a six-hour half-life.

The decay of $^{99m}$Tc solutions with time is described by the equation

$$N_2 = N_2^o e^{-\lambda_2 t} \qquad (7.1)$$

from which the 99/99m ratio can easily be calculated since

$$N_3 = N_2^o + N_3^o - N_2 \qquad (7.2)$$

where $N_2^o$ and $N_3^o$ are values at the time of elution.

The data shown in Figures 17 and 18 may be calculated from equations (7.1) and (7.2) if $N_2^o$ and $N_3^o$ are given convenient values in the required ratio. Figure 17 illustrates the importance of low 99/99m ratios at elution in extending the useful life of $TcO_4^-$ solutions. If the 99/99m ratio at elution is low, it remains at acceptable levels for 20 hours or more, and the useful life of the solution is determined more by the $^{99m}$Tc activity than by the level of $^{99}$Tc in the solution. However, if the ratio is above about 10:1 at elution, it climbs in five to ten hours to ratios that could lead to poor labelling with some kits.

Figure 18 shows the same data plotted differently. In this form, the graph is useful for determining 99/99m ratios at times up to 24 hours after elution for any ratio at elution up to 24:1.

# 8. 99/99m RATIOS UNDER SPECIFIC PRODUCTION CONDITIONS

## 8.1 Introduction

To answer the questions posed at the beginning of this report, three methods for the production of $^{99m}$Tc are examined over a range of conditions that are appropriate to each of the methods.

The conditions chosen are described as 'poor, 'average' and 'ideal'. Conditions listed as poor characterise a process in which no attention has been paid to improving efficiencies and streamlining operations. These are by no means the worst possible conditions. Average conditions are those that are easily achievable at each stage; they are not midway between poor and ideal, and do not necessarily describe existing production conditions. Conditions listed as ideal describe a thoroughly optimised process with near maximum efficiencies and a tight but realistic timetable.

## 8.2 Discussion

Details of the conditions and the 99/99m ratios calculated for particular stages of production and use are given in Appendix A. This information clearly shows that, with respect to $^{99}$Tc, the quality of the product depends far more on the production conditions than on the production method. Although generally the solvent extraction method gives the highest ratios for each category, this is attributable to the inherently lower extraction efficiencies of the process. In all three cases, poor production conditions lead to high 99/99m ratios, whereas under the best conditions, all are capable of producing ratios of 4:1 or better.

The three methods each have stages at which $^{99}$Tc builds up; these should be controlled to keep 99/99m ratios at a minimum. With the ready-to-inject solutions, the critical period is the time between elution and use. Even moderate levels of $^{99}$Tc increase to very high levels if the time between elution and use exceeds about 24 hours. If more attention is paid to delivery times, quite satisfactory ratios can be obtained at the time of use.

With portable chromatographic generators, the critical time is between the final production wash and the first elution. Because hospitals demand early delivery of generators, the 99/99m ratio in the first elution is higher than those of the other two production methods. However, because of the shorter time between elution and use, the ratio does not increase to the same extent as in ready-to-inject solutions. Also, because of the usually high efficiencies of chromatographic generators, 99/99m ratios decrease considerably with the first one or two elutions.

If hospital staff can be convinced that it is in their interest to shorten the time between manufacture and use, a more sensible production timetable might result. In the ideal situation, $^{99}$Tc in the first eluate can be substantially reduced if the generator is washed on Sunday afternoon in preparation for use on Monday morning.

## 9. CONCLUSIONS

Specific conclusions and recommendations relating to each stage of production have been made in the preceding sections. The general conclusion to be drawn from this analysis is that production schedules and elution procedures currently in use have evolved without consideration being given to their effect on $^{99}$Tc levels in the final pertechnetate solution; consequently, if further study confirms the indications that high $^{99}$Tc levels have a deleterious effect on the imaging and labelling performance of pertechnetate with certain kits, schedules and procedures will need to be revised along the lines recommended above.

Analysis of three production methods reveals that no method has clear superiority over the others with respect to $^{99}$Tc levels since each method has critical stages at which $^{99}$Tc will increase to high levels if the controls are poor. It has been shown that the quality of pertechnetate solutions with respect to $^{99}$Tc depends on the standard of production, the timing of production, especially in relation to hospital use, and the efficiency and frequency with which generators are eluted or extracted.

## 10. REFERENCES

Bonnyman, J. [1983] - Int. J. Appl. Radiat. Isot. (in press).

Lederer, C.M., Hollander, J.M. and Perlman, I. [1968] - Table of Isotopes. 6th Ed. Wiley, N.Y.

Maddalena, D.J. and Domel, R. [1981] - private communication.

Porter, W.C., Dworkin, H.J. and Gutkowski, R.F. [1976] - J. Nucl. Med., 17:704.

Smith, T.D. and Richards, P. [1976] - J. Nucl. Med., 17(2)126.

Srivastava, S.C., Meinken, G., Smith, T.D. and Richards, P. [1977] - Int. J. Appl. Radiat. Isot., 28:83.

## TABLE 1
## CALCULATION OF 99/99m RATIOS IN ELUATES

$N_1$ = 1000 atoms at wash time
Wash efficiency = 70%
Elution interval = 12 hours

$N_2$ and $N_1$ in equilibrium before wash
Elution efficiency = 70%
Ratio $N_3:N_2$ at wash time = 20:1

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|
| Elution | $^{99}$Mo in Generator at Elution ($N_1$) | $^{99m}$Tc in Generator at Elution ($N_2$) | $^{99}$Tc in Generator at Elution ($N_3$) | $^{99}$Tc in Generator After Elution ($N_3'$) | $^{99}$Tc formed Between Elutions ($N_3''$) | Total $^{99}$Tc At Next Elution ($N_3'+N_3''$) | 99/99m This Elution |
| Wash | 1000 | 87.80 | 1756.00 | 526.80 | 82.88 | 609.68 | 20.00 |
| 1 | 881.6 | 61.77 | 609.68 | 182.90 | 73.08 | 255.98 | 9.87 |
| 2 | 777.2 | 53.23 | 255.98 | 76.80 | 64.40 | 141.20 | 4.81 |
| 3 | 685.2 | 46.93 | 141.20 | 42.36 | 56.77 | 99.13 | 3.01 |
| 4 | 604.1 | 41.37 | 99.13 | 29.74 | 50.05 | 79.79 | 2.40 |
| 5 | 532.6 | 36.47 | 79.79 | 23.94 | 44.17 | 68.11 | 2.19 |
| 6 | 469.5 | 32.15 | 68.11 | 20.43 | 38.85 | 59.28 | 2.12 |
| 7 | 414.0 | 28.35 | 59.28 | 17.78 | 34.37 | 52.15 | 2.09 |
| 8 | 364.9 | 24.99 | 52.15 | 15.65 | 30.24 | 45.89 | 2.09 |
| 9 | 321.7 | 22.03 | 45.89 | 13.77 | 26.60 | 40.37 | 2.08 |
| 10 | 283.7 | 19.43 | 40.37 |  |  |  | 2.08 |

2. from equation (4.1); t = elution number x elution interval
3. from equation (5.6)
4. previous column 7
5. $(1 - \frac{\text{elution efficiency}}{100})$ x column 4
6. from Figure 6 and column 2
7. column 5 + column 6
8. column 4/column 3

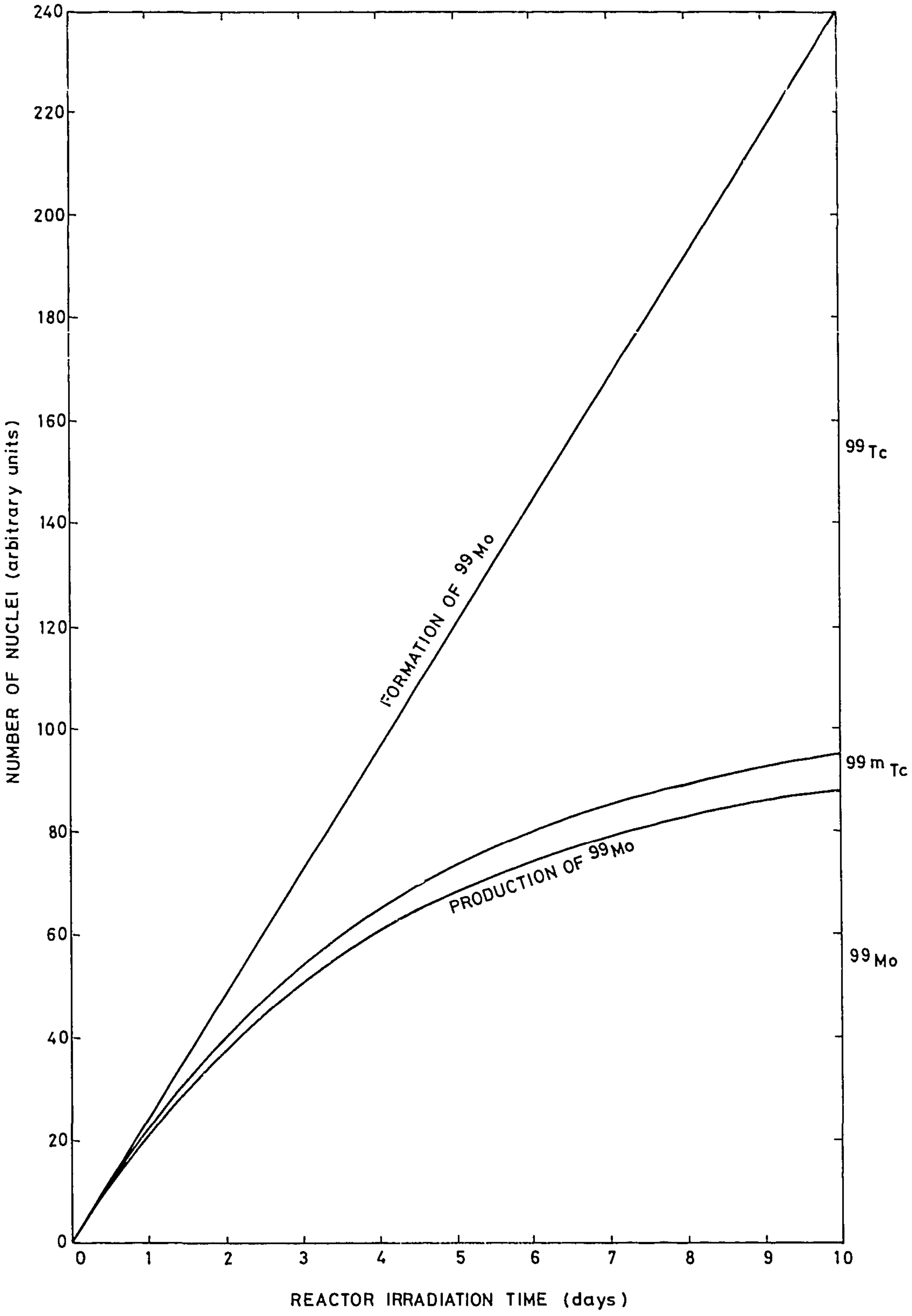


FIGURE 1. GROWTH OF $^{99}$Mo, $^{99}$Tc AND $^{99m}$Tc DURING IRRADIATION

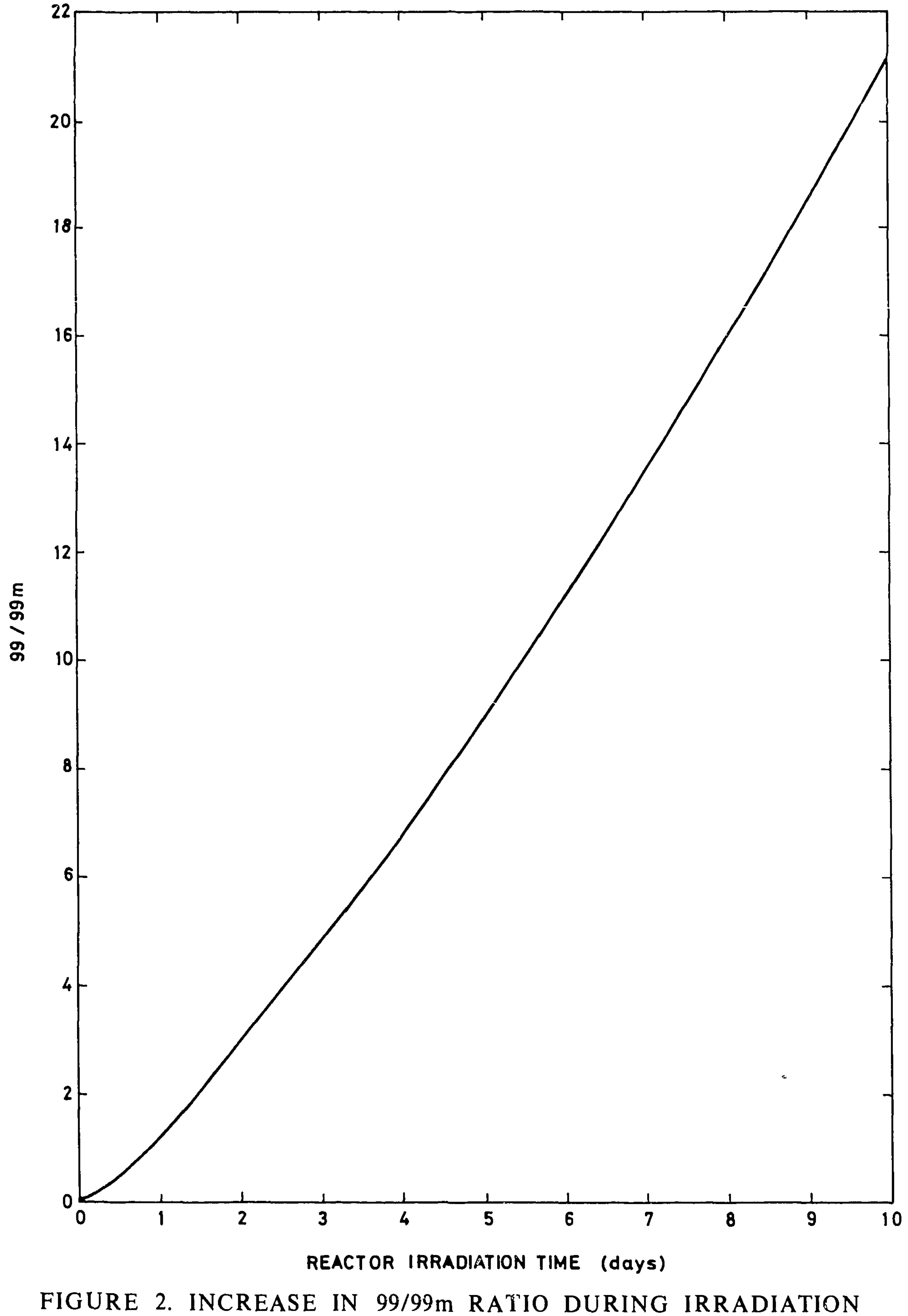


FIGURE 2. INCREASE IN 99/99m RATIO DURING IRRADIATION

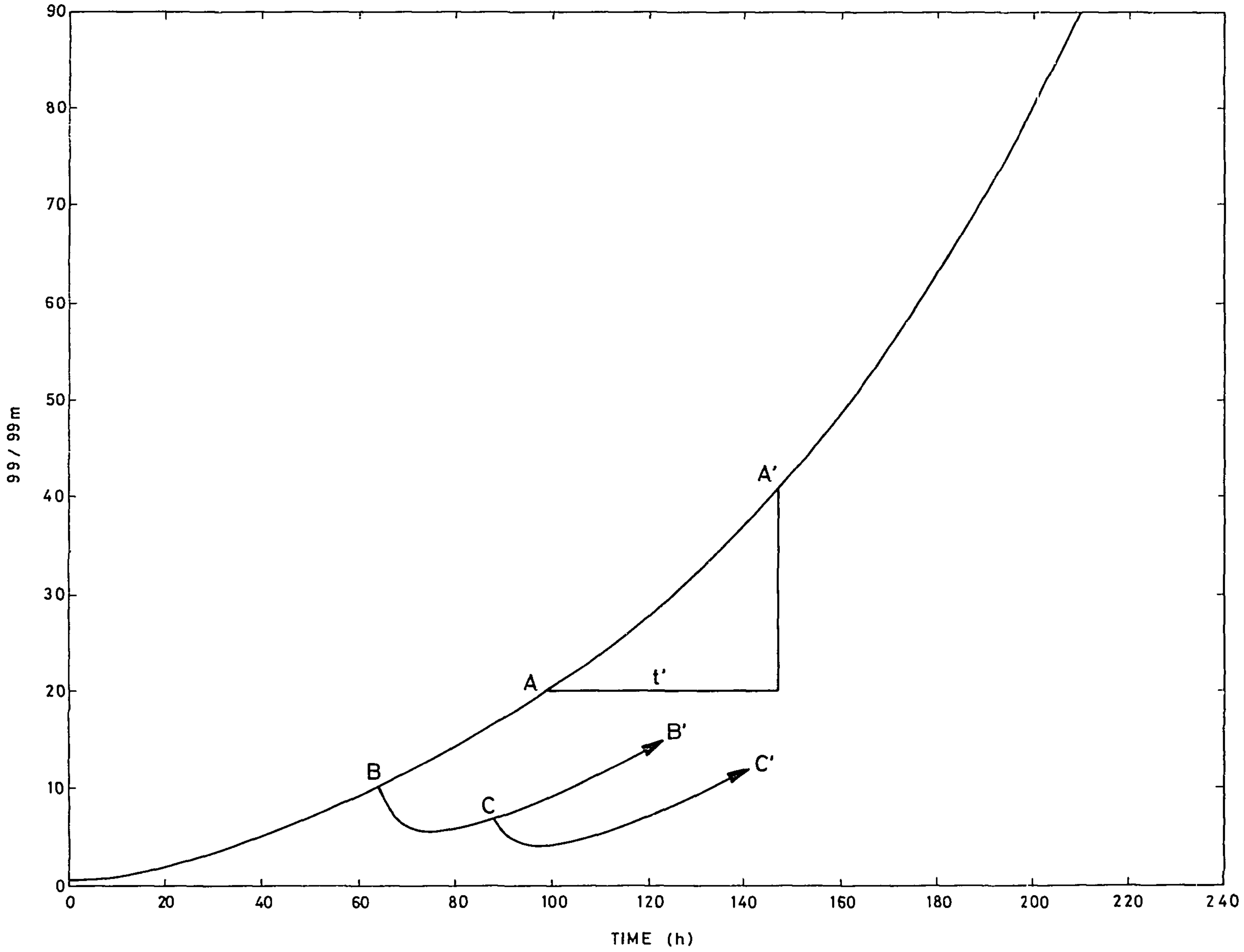


FIGURE 3. INCREASE IN 99/99m RATIO IN GENERATOR WITH TIME *t*

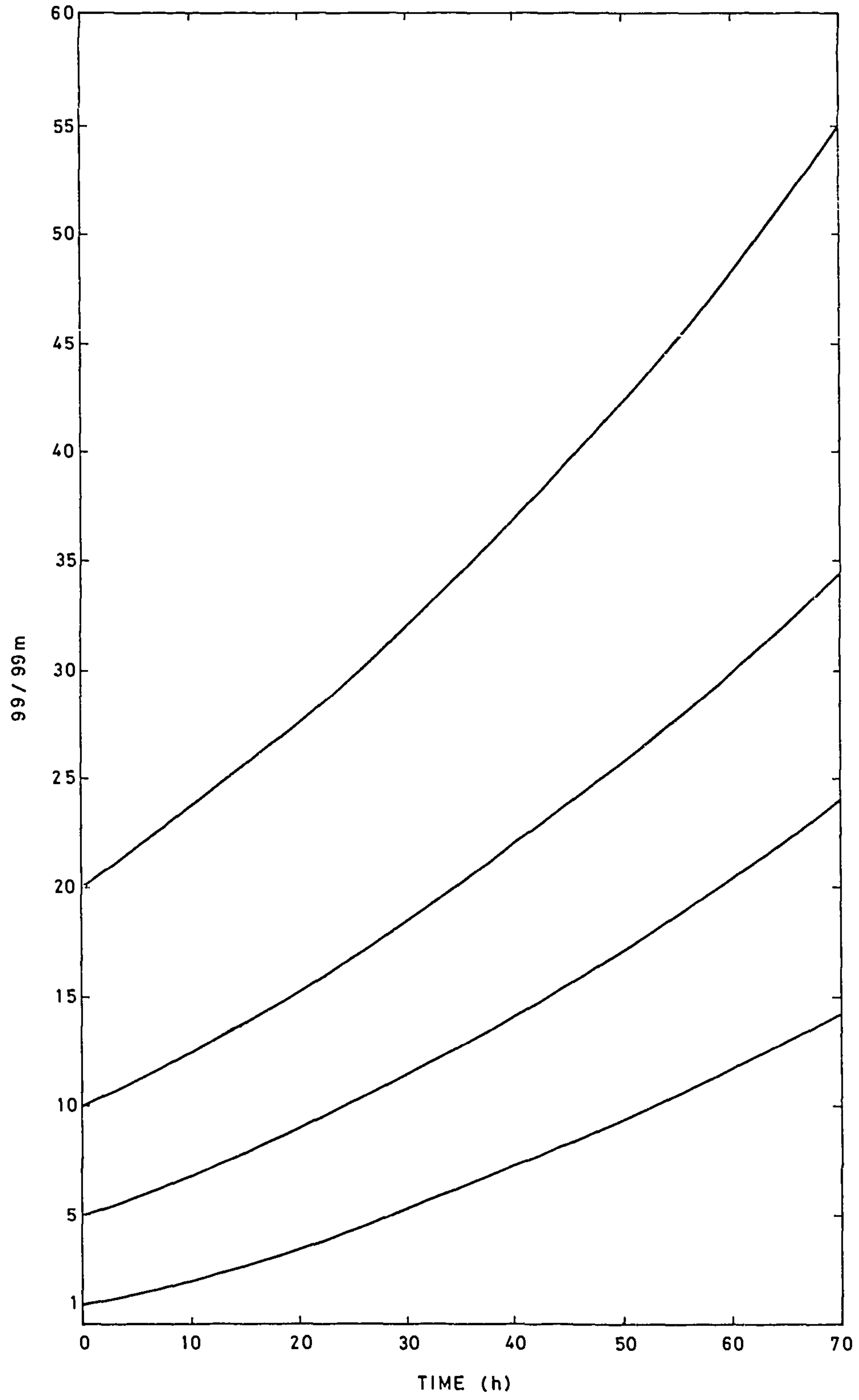


FIGURE 4. INCREASE IN 99/99m RATIO IN GENERATOR WITH TIME t'

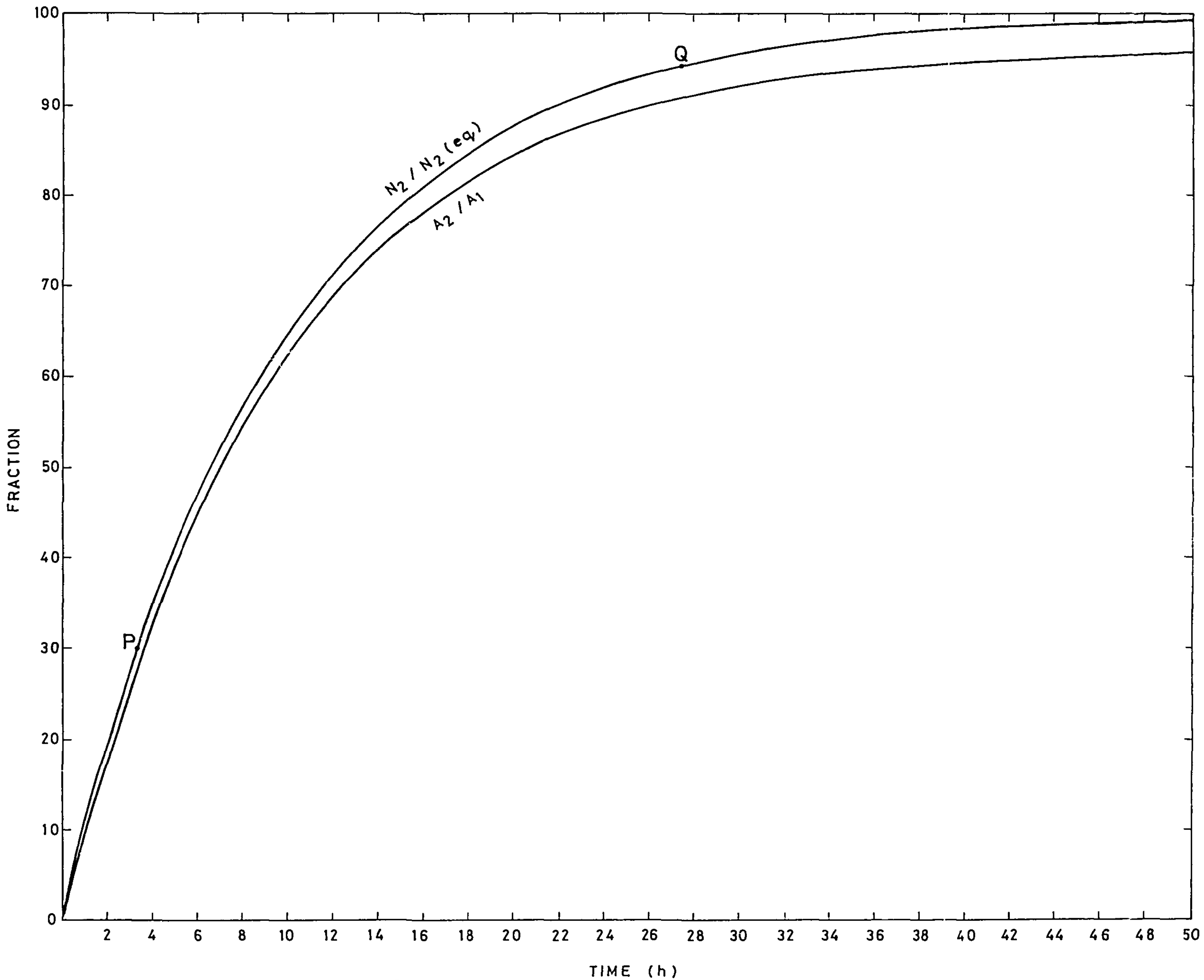


FIGURE 5. GROWTH OF $^{99m}$Tc EXPRESSED AS FRACTION OF EQUILIBRIUM VALUE

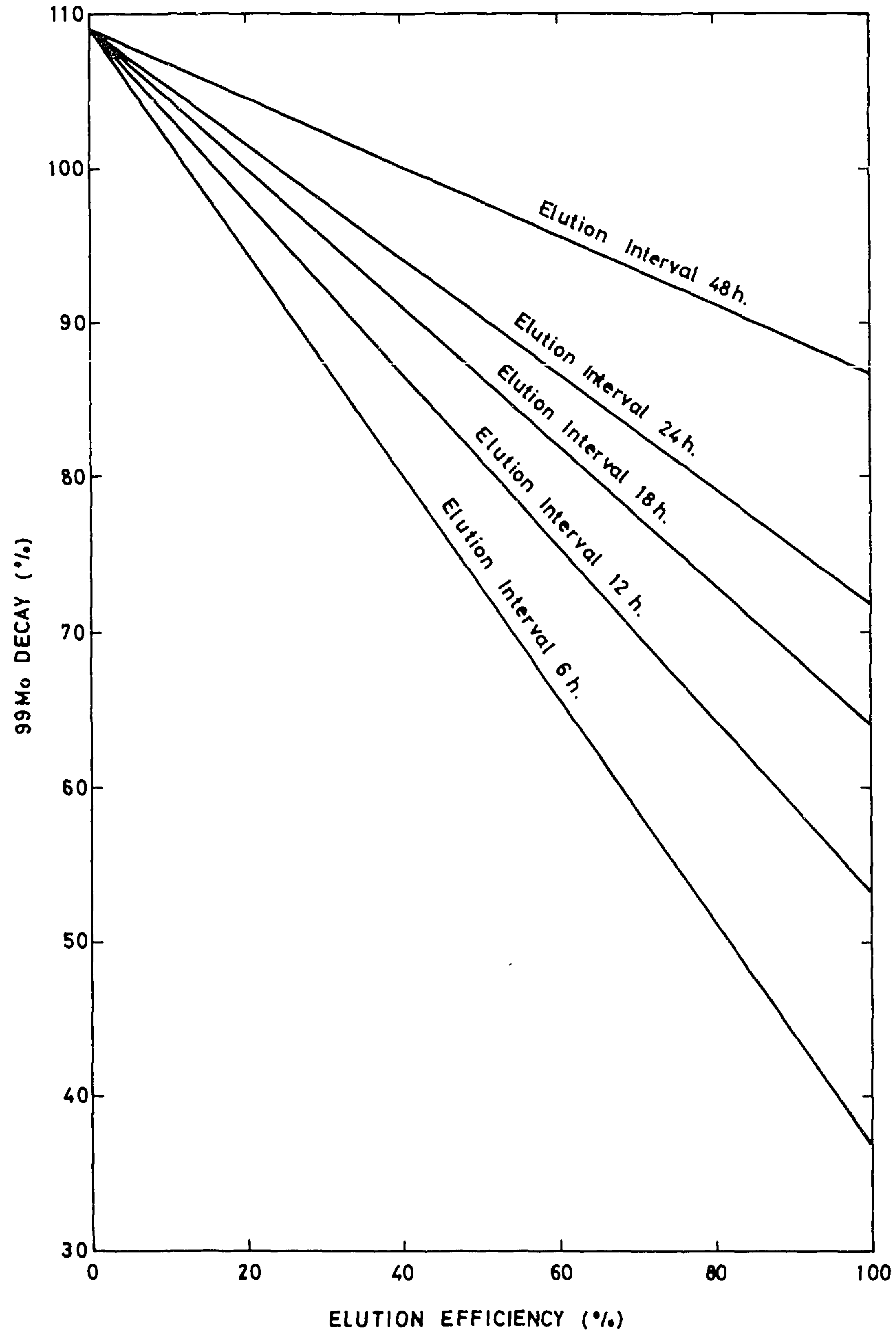


FIGURE 6. $^{99}$Tc FORMED BETWEEN ELUTIONS EXPRESSED AS A FRACTION OF Tc FORMED BY DECAY OF $^{99}$Mo DURING SAME PERIOD

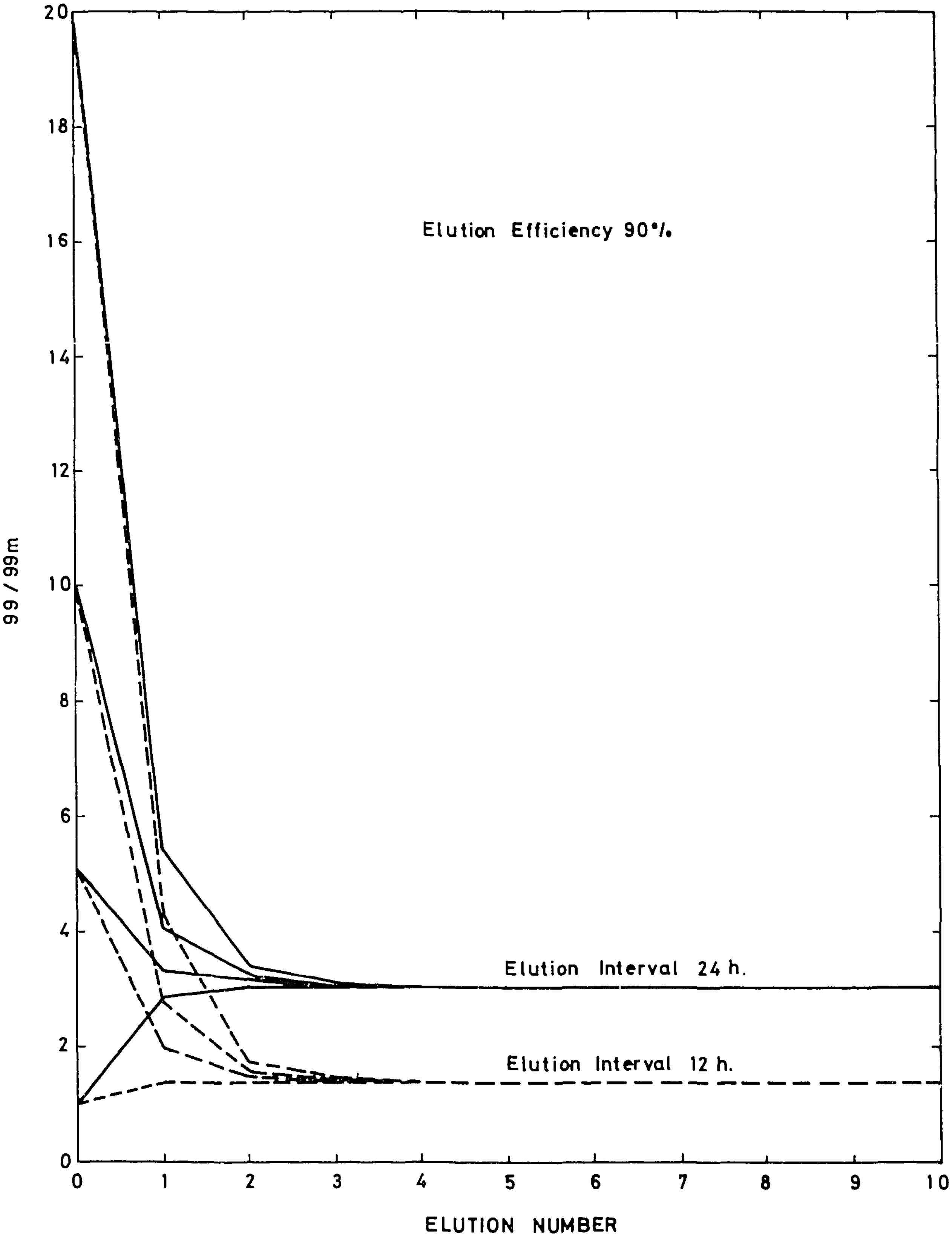


FIGURE 7. CHANGE IN 99/99m RATIO IN SUCCESSIVE ELUTIONS FOR SELECTED RATIOS AT WASH TIME AND ELUTION EFFICIENCY OF 90%

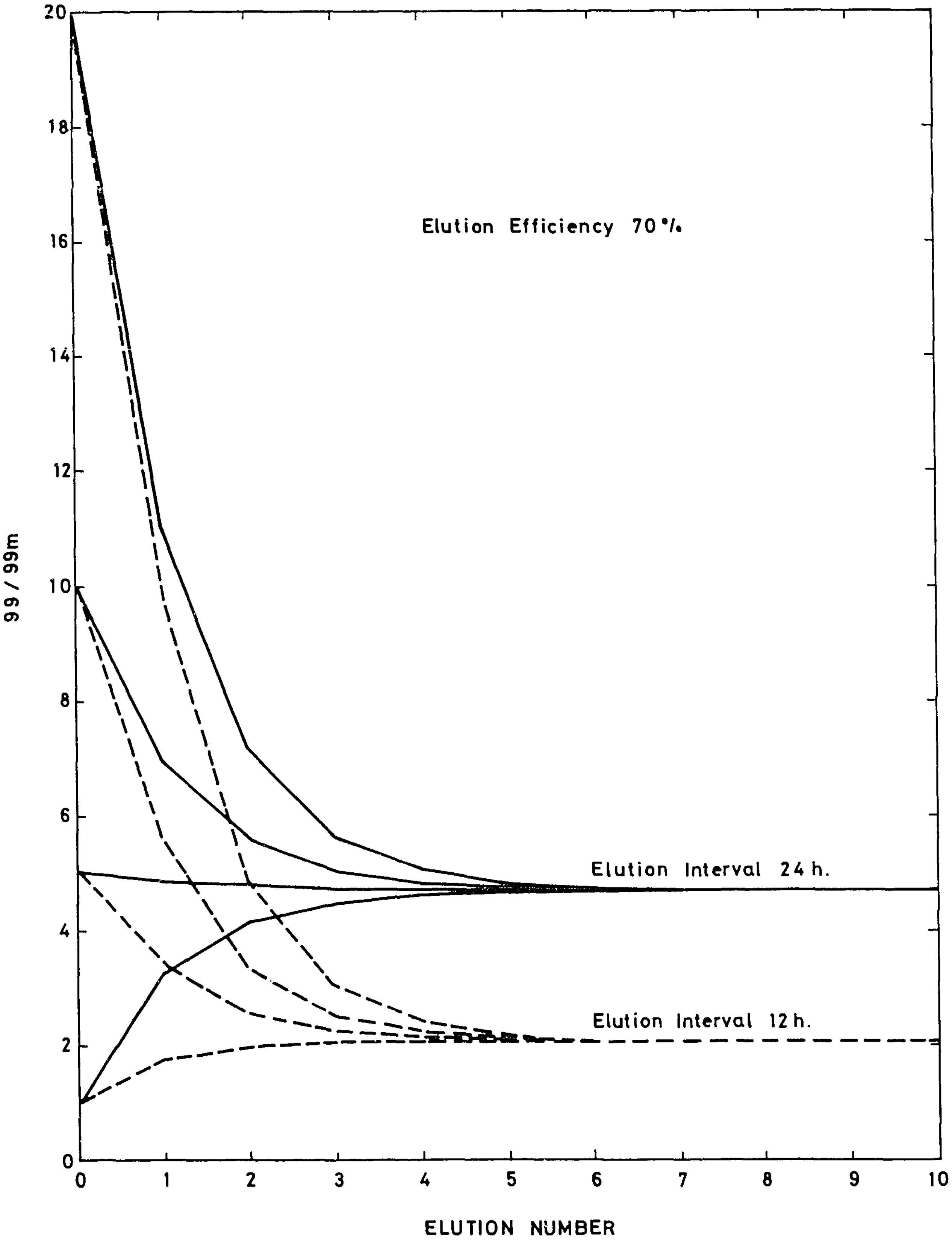


FIGURE 8. CHANGE IN 99/99m RATIO IN SUCCESSIVE ELUTIONS FOR SELECTED RATIOS AT WASH TIME AND ELUTION EFFICIENCY OF 70%

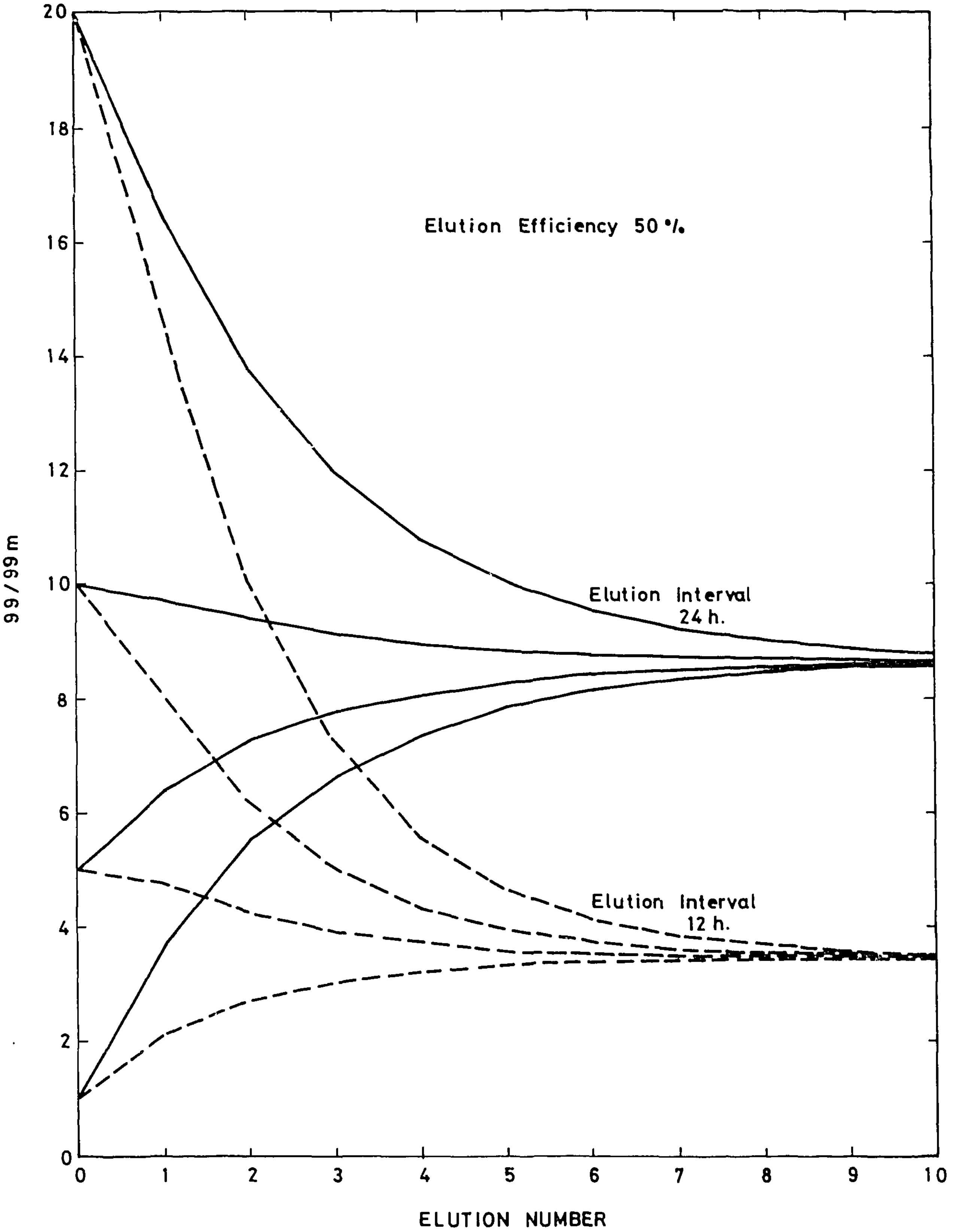


FIGURE 9. CHANGE IN 99/99m RATIO IN SUCCESSIVE ELUTIONS FOR SELECTED RATIOS AT WASH TIME AND ELUTION EFFICIENCY OF 50%

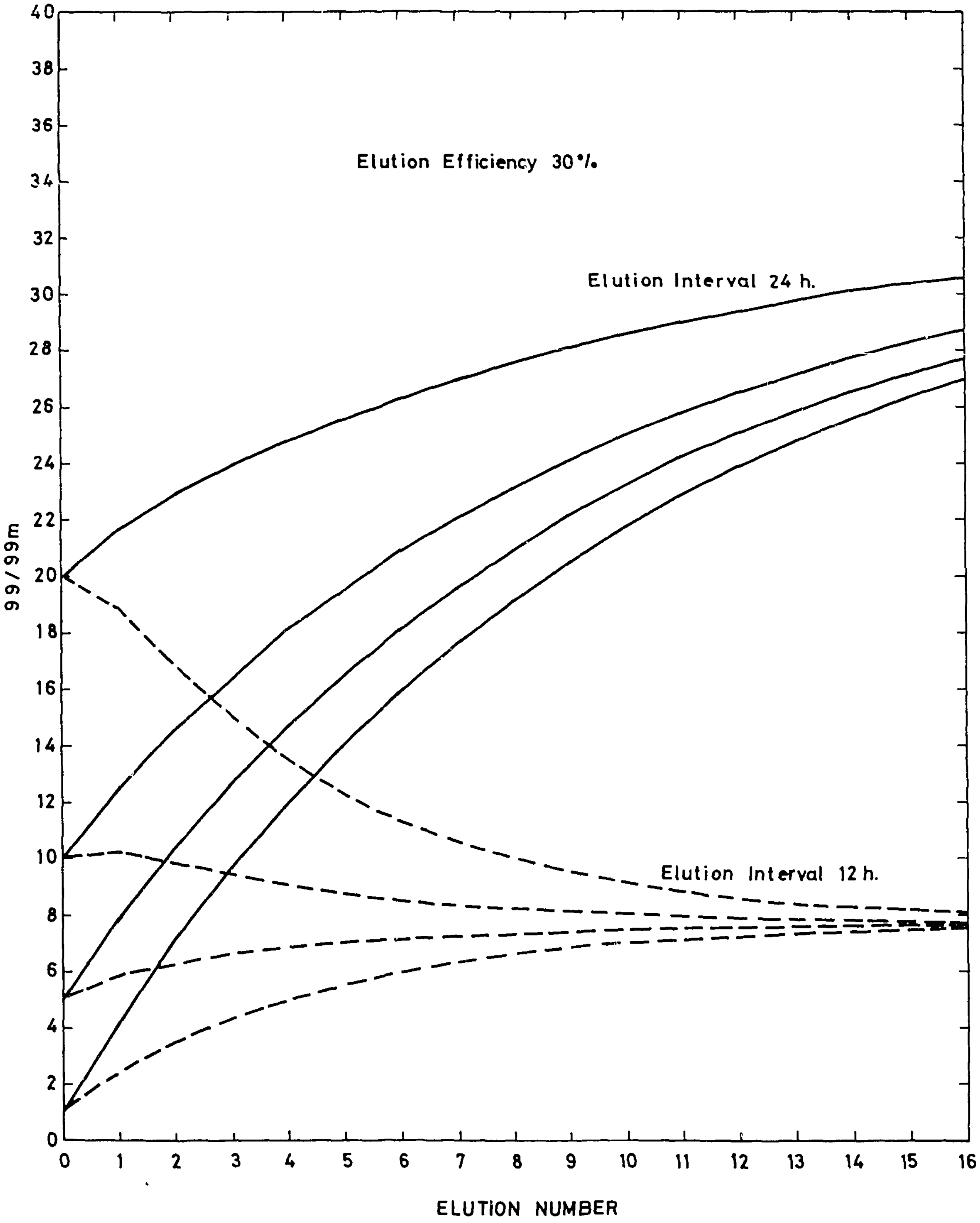


FIGURE 10. CHANGE IN 99/99m RATIO IN SUCCESSIVE ELUTIONS FOR SELECTED RATIOS AT WASH TIME AND ELUTION EFFICIENCY OF 30%

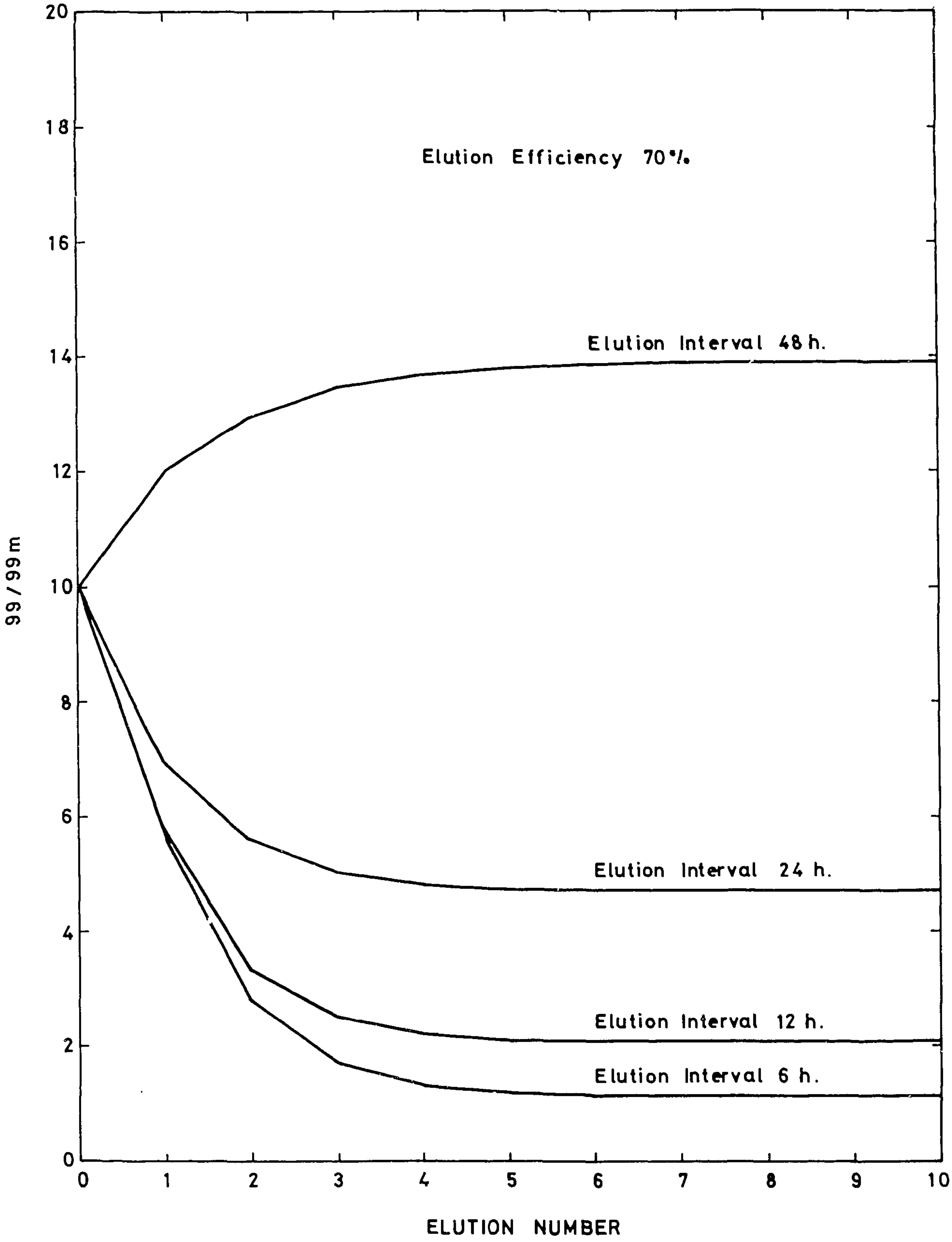


FIGURE 11. CHANGE IN 99/99m RATIO IN SUCCESSIVE ELUTIONS WITH ELUTION INTERVAL

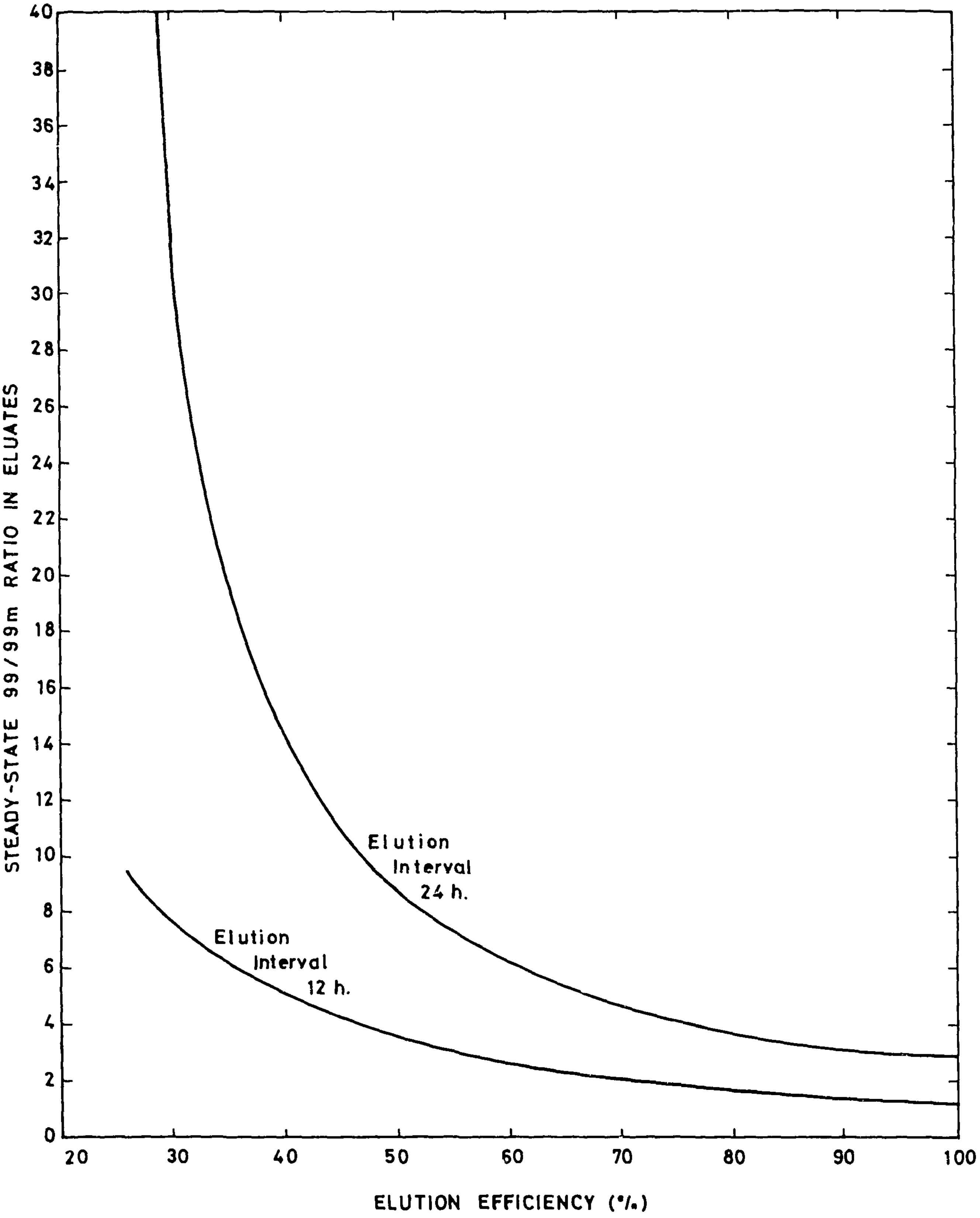


FIGURE 12. CHANGE IN STEADY-STATE 99/99m RATIO WITH ELUTION EFFICIENCY

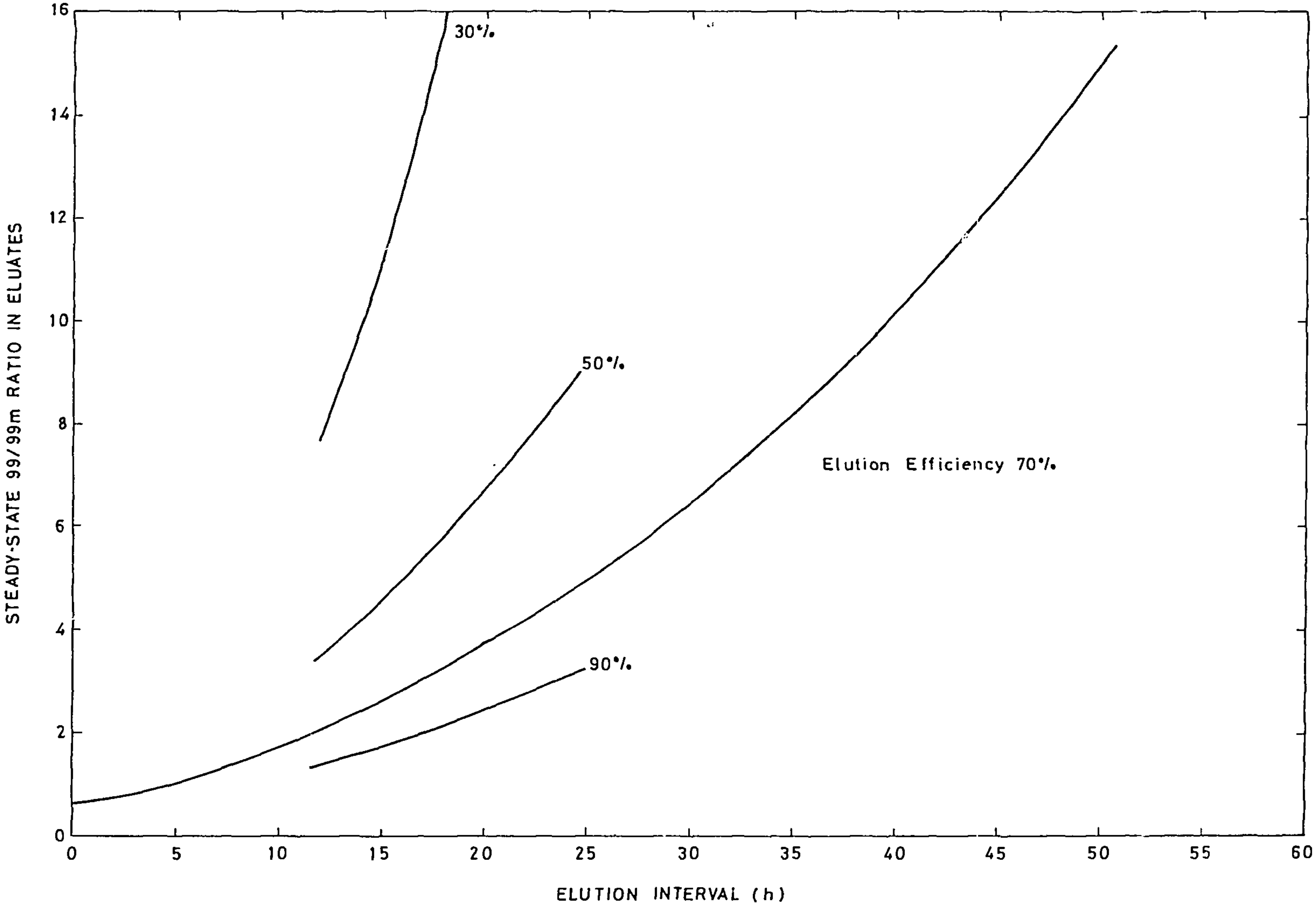


FIGURE 13. CHANGE IN STEADY-STATE 99/99m RATIO WITH ELUTION INTERVAL

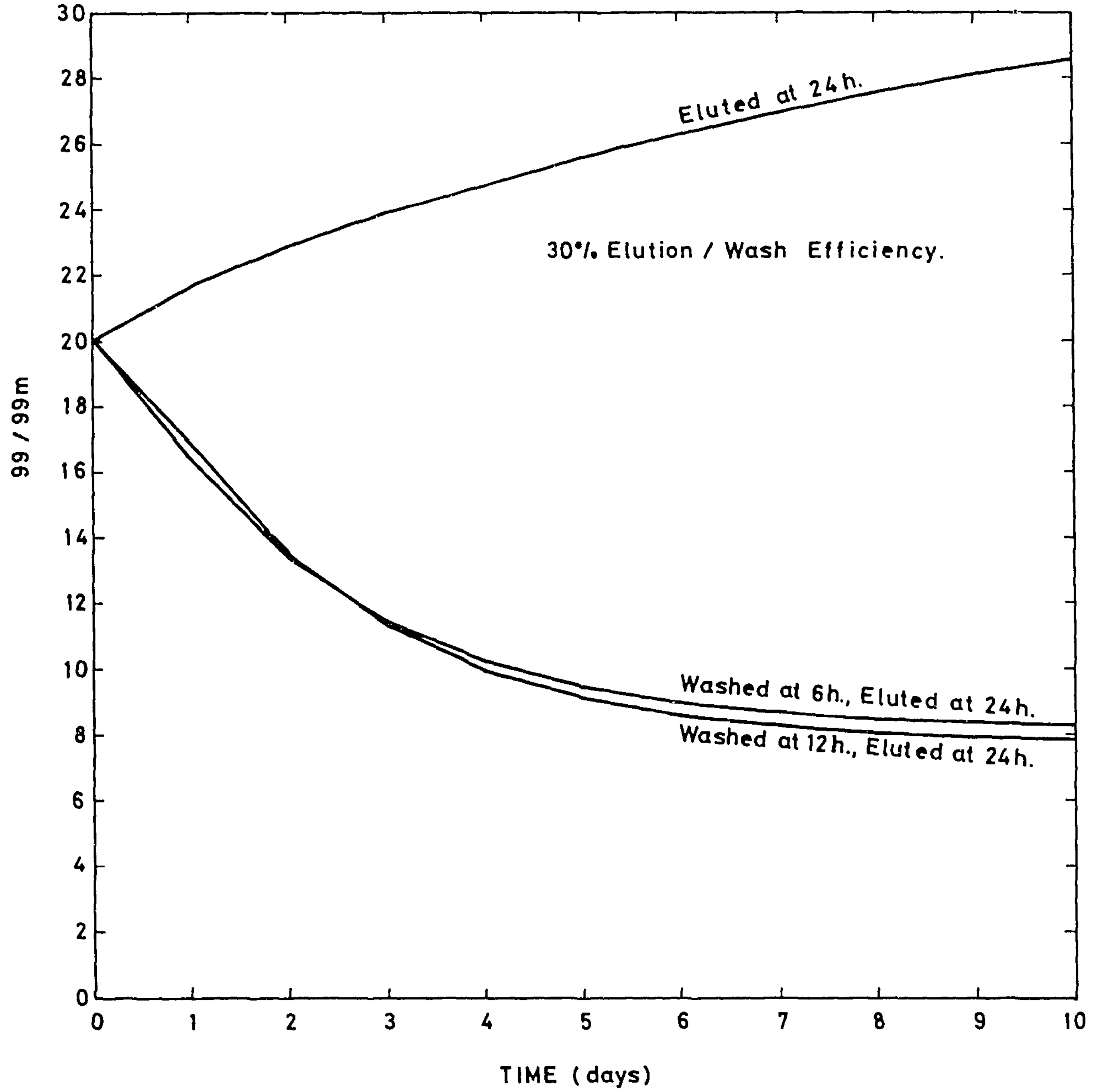


FIGURE 14. CHANGE IN 99/99m RATIO IN SUCCESSIVE ELUTIONS FOR THREE VARIATIONS OF THE 24 HOUR ELUTION CYCLE

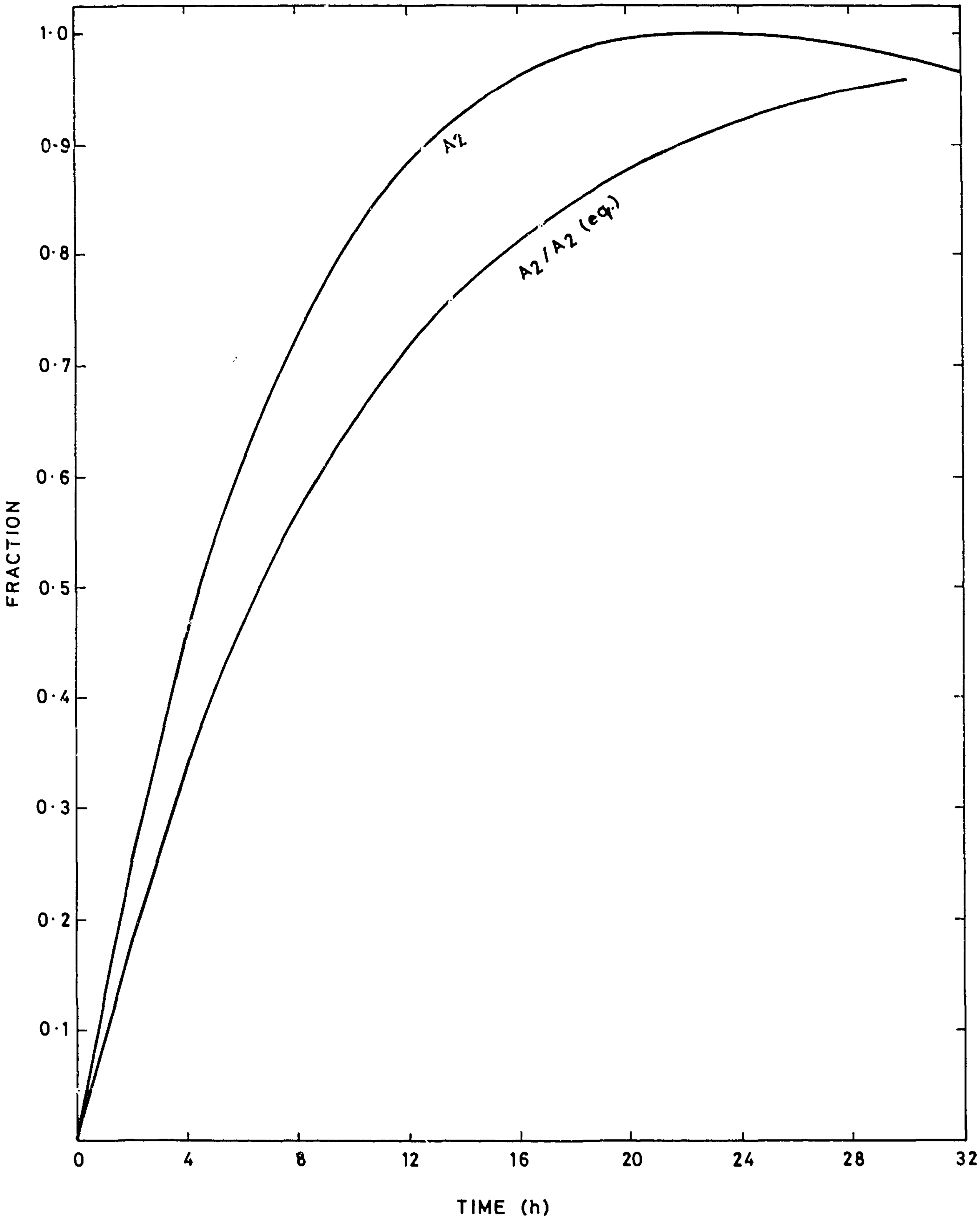


FIGURE 15. GROWTH OF $^{99m}$Tc ACTIVITY BETWEEN ELUTIONS EXPRESSED IN TWO DIFFERENT WAYS

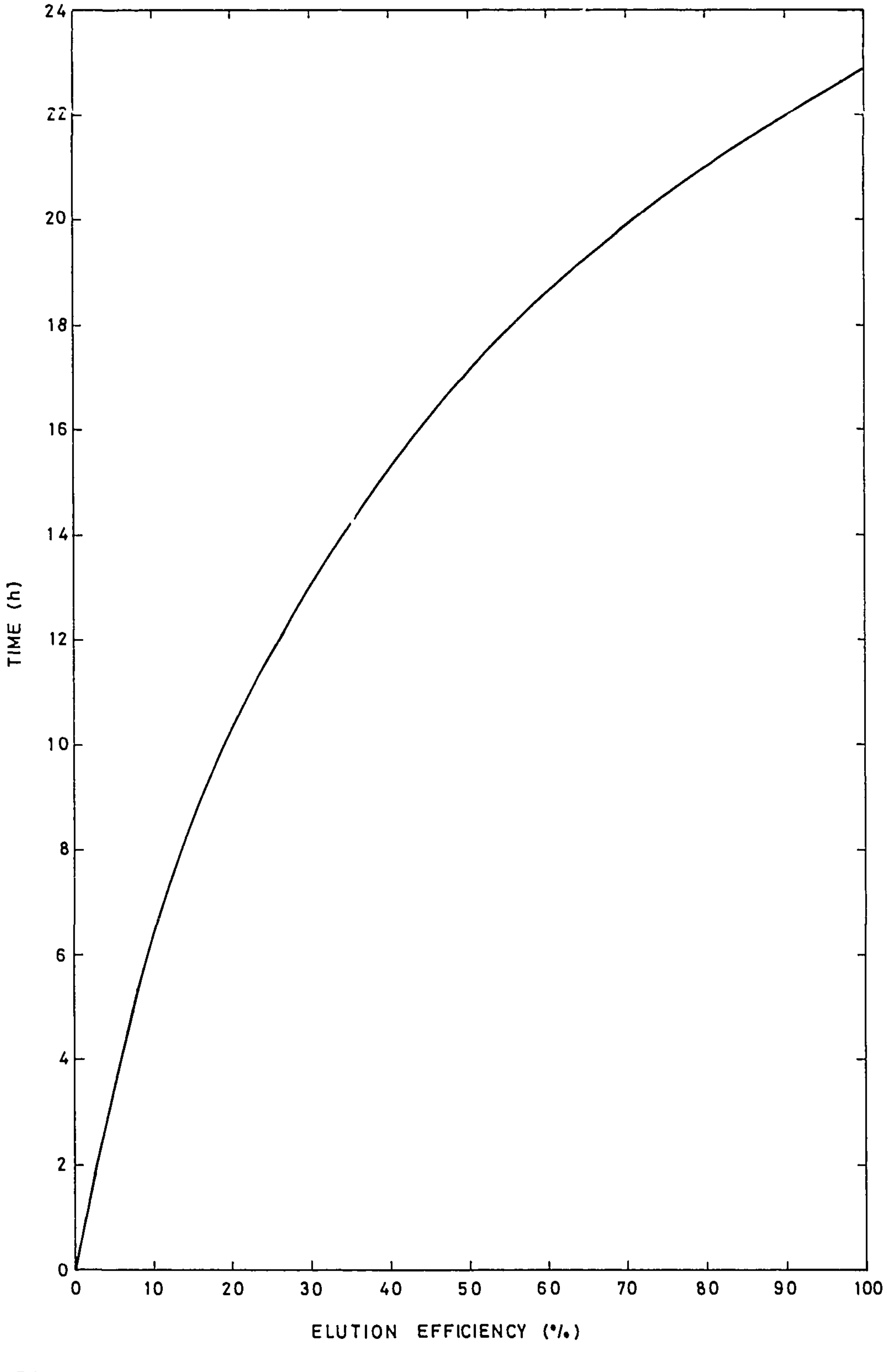


FIGURE 16. TIME REQUIRED FOR GENERATORS TO REACH MAXIMUM ACTIVITY FOLLOWING ELUTION WITH STATED EFFICIENCY

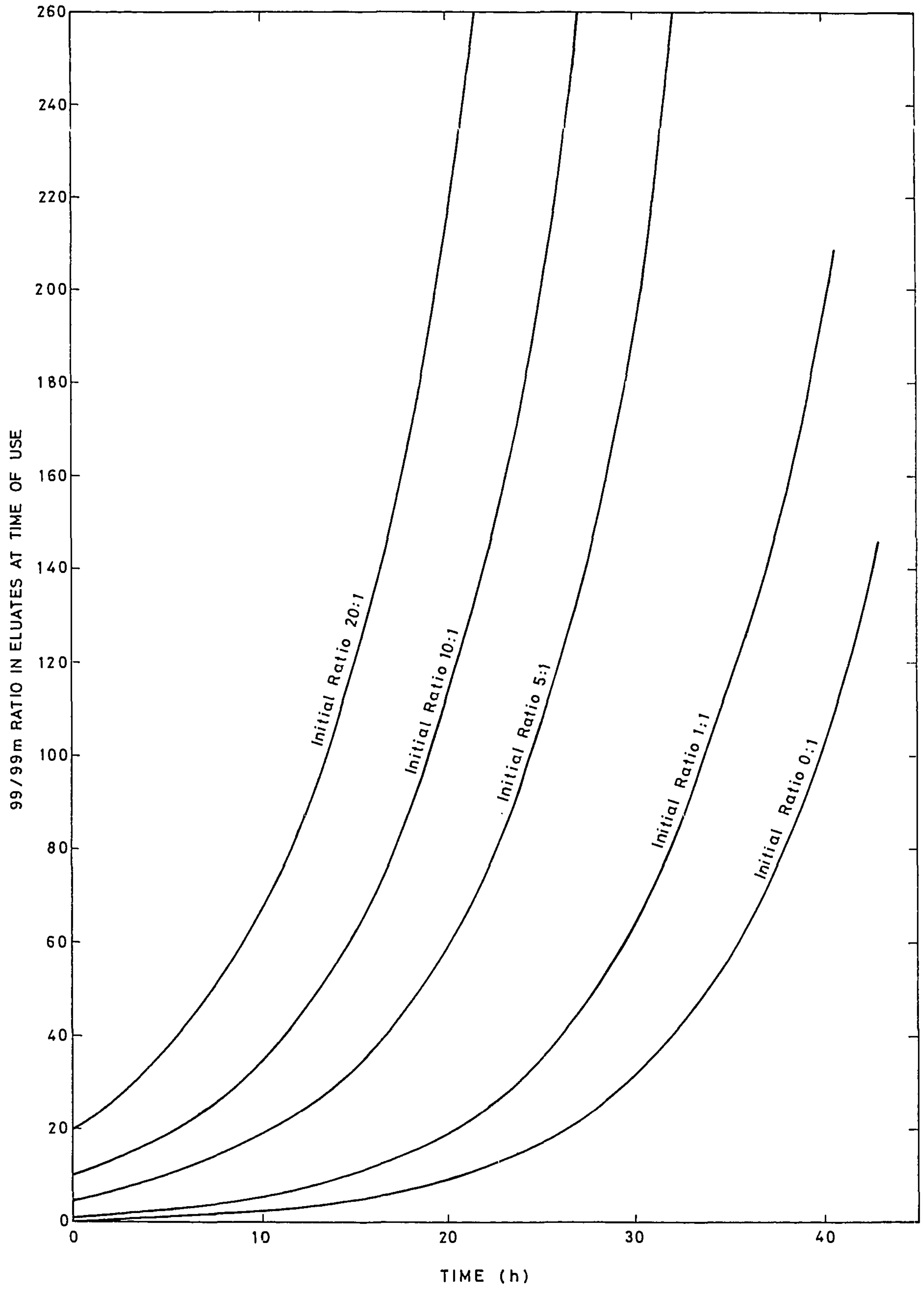


FIGURE 17. INCREASE IN 99/99m RATIO WITH TIME AFTER ELUTION

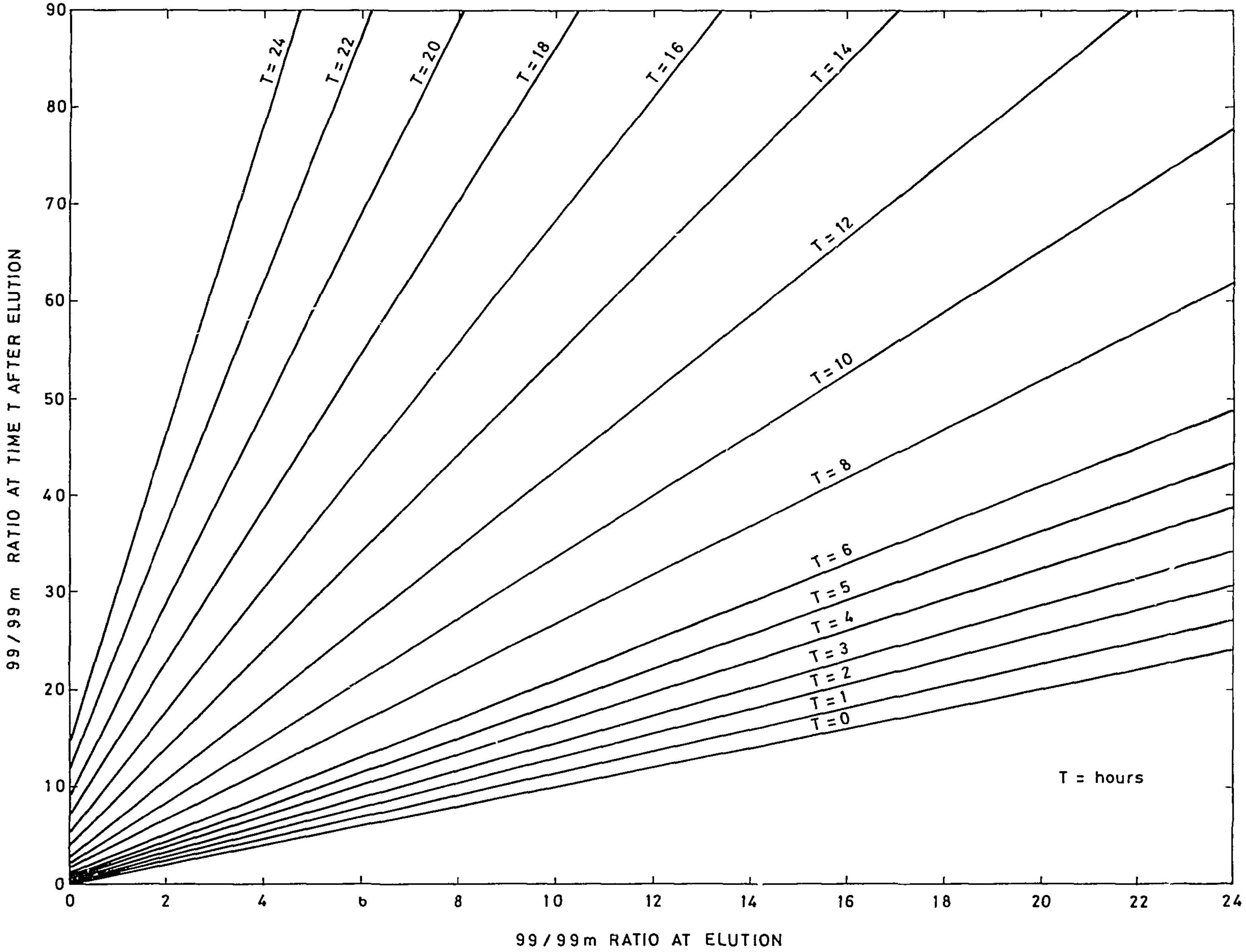


FIGURE 18. 99/99m RATIO AT TIME t AFTER ELUTION AS A FUNCTION OF THE 99/99m RATIO AT ELUTION

# APPENDIX A

## DETERMINATION OF 99/99m RATIOS UNDER SPECIFIC PRODUCTION CONDITIONS

### A1. THE SOLVENT EXTRACTION METHOD FOR THE PRODUCTION OF READY-TO-INJECT $TcO_4^-$ SOLUTIONS

### A1.1 Poor Production Conditions

| | |
|---|---|
| Irradiation | 7 days |
| Cooling/transport/processing | 36 hours (longer if $^{99}$Mo is imported) |
| Wash efficiency | 30% |
| Extraction efficiency | 30% |
| Extraction interval | 24 hours |
| Time between extraction and use | 27 hours (extracted at 9 a.m. for use next day at noon (interstate delivery) |

| | 99/99m ratio |
|---|---|
| At end of irradiation | 13.5:1 |
| At wash time | 25.5:1* |
| First extraction at extraction time | 26.5:1* |
| First extraction at time of use | 619:1* |
| Fifth extraction at extraction time | 29.0:1* |
| Fifth extraction at time of use | 669:1* |

*Could be much higher if $TcO_4^-$ supply is supplemented by the extraction of earlier batches of molybdate.

### A1.2 Average Production Conditions

| | |
|---|---|
| Irradiation | 7 days |
| Cooling/transport/processing | 12 hours |
| Wash efficiency | 70% (two clearing runs) |
| Extraction efficiency | 60% |
| Extraction interval | 24 hours |
| Time between extraction and use | 10 hours (extracted at midnight for use next day at 10 a.m. (Sydney/Melbourne delivery)) |

| | 99/99m ratio |
|---|---|
| At end of irradiation | 13.5:1 |
| At wash time | 17.0:1 |
| First extraction at extraction time | 10.0:1 |
| First extraction at time of use | 33.0:1 |
| Fifth extraction at extraction time | 6.5:1 |
| Fifth extraction at time of use | 22.5:1 |

### A1.3 Ideal Production Conditions

| | |
|---|---|
| Irradiation | 7 days |
| Cooling/transport/processing | 9 hours |
| Wash efficiency | 90% (two clearing runs three hours apart) |
| Extraction efficiency | 80% |
| Extraction interval | 12 hours |
| Time between extraction and use | 4 hours (extracted at 5 a.m. for use at 9 a.m. (Sydney delivery only)) |

| | 99/99m ratio |
|---|---|
| At end of irradiation | 13.5:1 |
| At wash time | 16.0:1 |
| First extraction at extraction time | 4.0:1 |
| First extraction at time of use | 6.5:1 |
| Fifth extraction at extraction time | 2.0:1 |
| Fifth extraction at time of use | 3.5:1 |

## A2. JUMBO GEL GENERATOR FOR PRODUCTION OF READY-TO-INJECT $TcO_4^-$ SOLUTIONS

### A2.1 Poor Production Conditions

| | |
|---|---|
| Irradiation | 7 days |
| Cooling/transport/processing | 36 hours (longer if $^{99}$Mo is imported) |
| Wash efficiency | 70% |
| Elution efficiency | 50% |
| Elution interval | 24 hours |
| Time between elution and use | 27 hours (eluted at 9 a.m. for use next day at midday (interstate delivery)) |

| | 99/99m ratio |
|---|---|
| At end of irradiation | 13.5:1 |
| At wash time | 25.5:1 |
| First elution at elution time | 13.0:1 |
| First elution at time of use | 318:1 |
| Fifth elution at elution time | 9.5:1 |
| Fifth elution at time of use | 233:1 |

### A2.2 Average Production Conditions

| | |
|---|---|
| Irradiation | 7 days |
| Cooling/transport/processing | 15 hours (longer if $^{99}$Mo is imported) |
| Wash efficiency | 90% |
| Elution efficiency | 80% |
| Elution interval | 24 hours |
| Time between elution and use | 10 hours (eluted at midnight for use next day at 10 a.m. (interstate delivery)) |

| | 99/99m ratio |
|---|---|
| At end of irradiation | 13.5:1 |
| At wash time | 18.0:1 |
| First elution at elution time | 5.0:1 |
| First elution at time of use | 18.5:1 |

| | |
|---|---|
| Fifth elution at elution time | 3.5:1 |
| Fifth elution at time of use | 14.0:1 |

## A2.3 Ideal Production Conditions

| | |
|---|---|
| Irradiation | 7 days |
| Cooling/transport/processing | 12 hours |
| Wash efficiency | 98% |
| Elution efficiency | 90% |
| Elution interval | 12 hours (or 6 hour/18 hour alternating) |
| Time between elution and use | 4 hours (eluted at 5 a.m. for use at 9 a.m. (Sydney delivery only)) |

| | 99/99m ratio |
|---|---|
| At end of irradiation | 13.5:1 |
| At wash time | 17.0:1 |
| First elution at elution time | 1.5:1 |
| First elution at time of use | 3.5:1 |
| Fifth elution at elution time | 1.5:1 |
| Fifth elution at time of use | 3.0:1 |

## A3. FISSION PRODUCT $^{99}$Mo GENERATOR FOR HOSPITAL USE (CHROMATOGRAPHIC GENERATOR)

### A3.1 Poor Production Conditions

| | |
|---|---|
| Irradiation | 7 days |
| Cooling/transport/processing | 72 hours (longer if $^{99}$Mo is imported) |
| Wash efficiency | 70% |
| Time between wash and first elution | 90 hours (final wash 2 p.m. Thursday for elution 8 a.m. Monday) |
| Elution efficiency | 50% |
| Elution interval | 24 hours |
| Time between elution and use | 5 hours (eluted at 8 a.m.; could be used as late as 1 p.m.) |

| | 99/99m ratio |
|---|---|
| At end of irradiation | 13.5:1 |
| At wash time | 42.5:1 |
| First elution at elution time | 50.5:1 |
| First elution at time of use | 90.5:1 |
| Fifth elution at elution time | 16.0:1 |
| Fifth elution at time of use | 29.5:1 |

### A3.2 Average Production Conditions

| | |
|---|---|
| Irradiation | 7 days |
| Cooling/transport/processing | 44 hours (unloaded 7 a.m. Tuesday, processing complete 3 a.m. Thursday) |
| Wash efficiency | 90% |
| Time between wash and first elution | 66 hours (final wash 2 p.m. Friday for elution 8 a.m. Monday) |
| Elution efficiency | 70% |
| Elution interval | 24 hours |
| Time between elution and use | 2 hours (eluted at 8 a.m. for use at 10 a.m.) |

| | 99/99m ratio |
|---|---|
| At end of irradiation | 13.5:1 |
| At wash time | 28.5:1 |
| First elution at elution time | 16.5:1 |
| First elution at time of use | 21.0:1 |
| Fifth elution at elution time | 5.0:1 |
| Fifth elution at time of use | 6.5:1 |

## A3.3 Ideal Production Conditions

| | |
|---|---|
| Irradiation | 7 days |
| Cooling/transport/processing | 26 hours (minimum processing time) |
| Wash efficiency | 95% |
| Time between wash and first elution | 42 hours (final wash 2 p.m. Saturday for elution 8 a.m. Monday) |
| Elution efficiency | 90% |
| Elution interval | 12 hours (or 6 hour/18 hour alternating) |
| Time between elution and use | 1 hour (eluted at 8 a.m. for use at 9 a.m.) |

| | 99/99m ratio |
|---|---|
| At end of irradiation | 13.5:1 |
| At wash time | 21.5:1 |
| First elution at elution time | 7.0:1 |
| First elution at time of use | 8.0:1 |
| Fifth elution at elution time | 1.5:1 |
| Fifth elution at time of use | 1.5:1 |