The Value of Duck-embryo Vaccine and High-Egg-Passage Flury Vaccine in Experimental Rabies Infection in Guinea-pigs

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The authors have compared the value of multiple doses of duck-embryo and HEP Flury vaccine with that of pooled 5% sheep-brain vaccine in experimental rabies infection in guinea-pigs. They found that the duck-embryo vaccine given in a dosage corresponding to 14 ml of 10% vaccine (the dosage recommended for human treatment), either alone or with antirabies serum, gave no protection and that, even when administered in a dosage corresponding to 140 ml of 5% pooled vaccine, both the duck-embryo and the HEP Flury vaccines, whether alone or with serum, conferred little protection. Pooled phenolized vaccine under identical conditions gave good results. The immunogenicity of duck-embryo and HEP Flury vaccines, given before infection, was also inferior to that of pooled vaccine; and the duck-embryo vaccine was found to be a poorer antigen than the pooled vaccine in mouse potency tests.

The authors conclude that the dosage of duck-embryo vaccine recommended for human treatment is inadequate and that the HEP Flury vaccine in its present form is unsuitable for post-infection treatment.

Powell & Culbertson (1950) reported the successful cultivation of rabies fixed virus in embryonated duck's eggs. MacFarlane & Culbertson (1954) found the material derived from duck embryo to be substantially free from encephalomyelitic factors. The virus grown in duck embryo could be efficiently inactivated with β-propiolactone and the inactivated vaccine was found to be antigenic to mice in potency tests (Peck et al., 1956; Powell & Culbertson, 1959b). The killed vaccine enabled treated animals to withstand a subsequent challenge (Powell & Culbertson, 1959a; Powell et al., 1960). There have been numerous reports on the early appearance of serum antibodies and their persistence in treated animals and volunteers (Peck, 1959; Hectorne & Peck; Schnurrenberger et al.; Greenberg & Childress; Tierkel et al.; Anderson et al., 1960; Greenberg & Childress, 1960; Schnurrenberger et al., 1961; Tierkel, 1962).

The early appearance of serum antibodies, the reduced risk of neuroparalytic accident and conformity to the standards for potency and safety laid down by the US National Institutes of Health (NIH) have since led to the acceptance of the duck-embryo vaccine in human treatment in the USA.

As far as we are aware no studies have been reported on the value of duck-embryo vaccine in the post-infection treatment of experimental animals when given alone or with antirabies serum. Studies were therefore undertaken to determine its value in

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the pre- and post-infection treatment of guinea-pigs under standard conditions.

There has been considerable interest in the high-egg-passage (HEP) Flury live-virus vaccine developed by Koprowski et al. (1954). With a view to determining its suitability for human treatment, a large number of studies have been carried out to assess the serum antibody response elicited by the vaccine (Schwab et al., 1954; Fox, 1958; Schnurrenberger et al.; Ruegsegger et al.; Sharpless; Tierkel et al.; Ruegsegger et al., 1961; Schnurrenberger et al., 1961; Tierkel, 1962). We have reported earlier that a single dose of HEP Flury vaccine given with antirabies serum is not of much value in the post-infection treatment though, given alone 12 days before challenge, it could induce solid immunity in guinea-pigs (Veeraraghavan et al., 1957). In this study the value of giving multiple doses of HEP Flury vaccine before and after challenge was determined in the same way as for the duck-embryo vaccine.

A parallel series of groups given similar treatments with pooled phenolized vaccine served as controls. The results of these investigations are briefly summarized below.

MATERIALS AND METHODS

Animals

Healthy guinea-pigs, bred at the Pasteur Institute of Southern India and each weighing about 400 g, were used for all protection experiments. The mice employed for serum neutralization and vaccine potency tests were bred at the Institute from the Rockefeller Institute strain.

Challenge virus

The dog (D.266/56) strain of street virus was used in the street virus experiments. The material employed was the lyophilized submaxillary gland suspension of a dog infected in nature. The methods of administering the challenge and of determining the number of LD<sub>50</sub> used in each experiment were the same as those described by Veeraraghavan et al. (1957).

In the vaccine potency tests done according to Kaplan (1954), the CVS strain of fixed virus of mouse-brain origin was used for challenging the mice intracerebrally.

Antirabies serum

Lederle's antirabies serum L, lot No. 1648-1010B, and antirabies serum PIC raised in horses at the Pasteur Institute of Southern India were used.

Serum L, supplied in 2.5-ml amounts, each containing 1000 units, was diluted 1:1.6 to give 25 units in 0.1 ml and 1:8 to give 5 units in 0.1 ml.

In the case of serum PIC, 0.1 ml of a 1:10 dilution was employed, as this dose had given the best results in our earlier experiments. On subsequent titration it was found that the dose of serum administered contained about 10 units.

All sera were diluted with 2% deactivated guinea-pig serum in physiological saline.

Serum was always given intramuscularly.

The method of determination of the neutralizing antibody content of the serum against the particular challenge was the same as that described by Veeraraghavan et al. (1957).

Duck-embryo vaccine

Duck-embryo vaccine, lot No. AX-29245-A 2130-740654-FR manufactured by Eli Lilly & Co., USA, was used in the first experiment. The vaccine used in the second experiment was lot No. AX-29245-A 0016-790403-pH.

The content of each vial was rehydrated with 1.1 ml of sterile distilled water, and material from the different vials was pooled and diluted to 5% tissue concentration with an equal volume of sterile distilled water. Reconstitution was done each day, enough vials being used to meet the day's requirement. The vaccine was used within an hour of rehydration.

A schedule of 14 daily doses of 0.015 ml of 5% vaccine was selected for the first experiment on the basis of the manufacturer's recommendation that for an adult human being the complete treatment consists of one subcutaneous dose daily for fourteen days, each dose being 1 ml of 10% vaccine. The value of higher doses could not be studied as the amount of vaccine available was limited. Subsequently, a sufficient amount of the vaccine was procured and in the second experiment it was used in 14 daily doses of 0.075 ml, bringing the total...
amount given to the same level as in the case of phenolized vaccine.

The duck-embryo vaccine was always given subcutaneously.

**HEP Flury vaccine**

Lederle's high-egg-passage chicken-embryo-adapted rabies vaccine, lots No. 7-1173-218B and No. 7-1173-229A, were used in the first and second experiments respectively.

The vaccine was reconstituted with 2.4 ml of physiological saline to give a 35% suspension, withdrawn from the vials and diluted to 5% tissue concentration, kept in ice and used within an hour. Two dosage schedules, $14 \times 0.015$ ml and $14 \times 0.075$ ml, were employed, the former corresponding to the recommended dosage of duck-embryo vaccine and the latter to that of phenolized vaccine.

The HEP Flury vaccine was always given subcutaneously.

**Pooled phenolized vaccine**

Vaccine obtained by mixing 12 batches of 5% Semple vaccine prepared from 12 infected sheep brains according to the method described by Veeraraghavan (1959) was used. On the basis of our earlier work, the vaccine was administered subcutaneously in 14 daily doses of 0.075 ml.

**Period of observation**

Guinea-pigs were observed for a minimum period of 6 months and mice for 30 days after challenge.

**Diagnosis**

For each death, a diagnosis was established by approved methods, including fluorescence microscopy and animal inoculation test, wherever indicated.

**RESULTS**

In the first two experiments reported here, an attempt has been made to determine if the avian embryo vaccines compare favourably with pooled vaccine when given (a) before infection and (b) after infection, alone or with different doses of serum. In the third experiment, a comparison is made between the potencies of duck-embryo and phenolized vaccine in a test done according to Kaplan (1954).

**Experiment 1**

The value of administering 14 doses of 0.015 ml of either duck-embryo vaccine or HEP Flury vaccine alone or with 5 or 25 units of serum L, or 10 units of serum PIC, in the post-infection treatment of guinea-pigs was studied. The effect of administering 14 doses of 0.075 ml of phenolized vaccine under similar conditions was also investigated. The value of a higher dosage of duck-embryo vaccine could not be determined as sufficient material was not available. The effect of increasing the dosage of HEP Flury vaccine was studied by giving $14 \times 0.075$ ml alone or with 10 units of serum PIC. The challenge employed proved to be 42.7 LD$_{50}$.

The results are summarized in Table 1.

<table>
<thead>
<tr>
<th>Vaccine $^b$</th>
<th>Dosage</th>
<th>Serum L, 5 units $^c$ (Serum ND $^d$ = 125)</th>
<th>Serum L, 25 units $^c$ (Serum ND $^d$ = 625)</th>
<th>Serum PIC, 10 units $^c$ (Serum ND $^d$ = 302)</th>
<th>No serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duck-embryo</td>
<td>$14 \times 0.015$ ml</td>
<td>23/23</td>
<td>24/25</td>
<td>24/25</td>
<td>24/24</td>
</tr>
<tr>
<td>HEP Flury</td>
<td>$14 \times 0.015$ ml</td>
<td>24/24</td>
<td>22/24</td>
<td>21/23</td>
<td>23/23</td>
</tr>
<tr>
<td></td>
<td>$14 \times 0.075$ ml</td>
<td>---</td>
<td>---</td>
<td>20/25</td>
<td>24/24</td>
</tr>
<tr>
<td>Pooled phenolized</td>
<td>$14 \times 0.075$ ml</td>
<td>13/21</td>
<td>18/21</td>
<td>12/22</td>
<td>14/24</td>
</tr>
<tr>
<td>No vaccine</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>24/24</td>
</tr>
</tbody>
</table>

$a$ Results expressed as the number of guinea-pigs dying over the number tested.

$b$ Started 1 hour after challenge and immediately after serum, if serum was given.

$c$ Given 1 hour after challenge.

$d$ ND = neutralizing doses against challenge virus.
It was found that $14 \times 0.015$ ml of duck-embryo vaccine failed to give significant protection whether given alone or with the different doses of serum. The mortality was 100% when the vaccine was given alone or with 5 units of serum L.

With $14 \times 0.015$ ml of HEP Flury vaccine, the protection was equally poor whether the vaccine was given alone or with different doses of serum. The higher dose ($14 \times 0.075$ ml) of HEP Flury vaccine failed to save any animal when given alone, but the mortality was only 80% when the vaccine was administered with 10 units of serum PIC.

In contrast, combined therapy with pooled phenolized vaccine and 5 units of serum L or 10 units of serum PIC conferred significant protection. The vaccine, administered alone, also saved a significant proportion of the animals. The best results, however, were obtained when $14 \times 0.075$ ml of pooled vaccine were given with 10 units of serum PIC.

The results indicate that in the doses administered, duck-embryo vaccine and HEP Flury vaccine were found to be poorer antigens than phenolized vaccine, whether given alone or with different doses of serum. The mortality was 100% when the embryo vaccines were given alone compared with 42% survival in the group treated with phenolized vaccine alone.

**Experiment 2**

It was considered necessary to determine whether the superiority of the pooled vaccine over the duck-embryo vaccine could be explained on the basis of the smaller dose of duck-embryo vaccine used. An attempt was therefore made to compare the three vaccines given in identical doses of $14 \times 0.075$ ml, alone or with the three different doses of serum. The effect of administering seven doses of 0.3 ml of each vaccine daily for seven days before challenge was also determined. Two additional control groups were incorporated in the experiment, one receiving 25 units of serum L and the other 10 units of serum PIC alone. The challenge employed proved to be 73 LD$_{50}$.

The results are summarized in Table 2.

When given in seven doses of 0.3 ml, all the three vaccines afforded significant protection against a challenge given on the eighth day. However, treatment with $7 \times 0.3$ ml of pooled vaccine was significantly superior to that with the same dose of duck-embryo or Flury vaccine, the latter two not differing between each other in the protection conferred.

Post-infection treatment with duck-embryo vaccine failed to bestow significant protection when given alone or with either dose of serum L. But, when administered with 10 units of serum PIC it afforded significant protection.

<table>
<thead>
<tr>
<th>Vaccine used</th>
<th>Time started</th>
<th>Dosage</th>
<th>Serum L, 5 units $^b$ (Serum ND $^c=73.6$)</th>
<th>Serum L, 25 units $^b$ (Serum ND $^c=368$)</th>
<th>Serum PIC, 10 units $^b$ (Serum ND $^c=177.8$)</th>
<th>No serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duck-embryo</td>
<td>7 days before challenge</td>
<td>7 x 0.3 ml</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>12/20</td>
</tr>
<tr>
<td></td>
<td>1 hour after challenge</td>
<td>14 x 0.075 ml</td>
<td>18/19</td>
<td>18/19</td>
<td>10/19</td>
<td>17/20</td>
</tr>
<tr>
<td>HEP Flury</td>
<td>7 days before challenge</td>
<td>7 x 0.3 ml</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>11/19</td>
</tr>
<tr>
<td></td>
<td>1 hour after challenge</td>
<td>14 x 0.075 ml</td>
<td>16/20</td>
<td>17/20</td>
<td>16/20</td>
<td>20/20</td>
</tr>
<tr>
<td>Pooled phenolized</td>
<td>7 days before challenge</td>
<td>7 x 0.3 ml</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>1/20</td>
</tr>
<tr>
<td></td>
<td>1 hour after challenge</td>
<td>14 x 0.075 ml</td>
<td>12/20</td>
<td>10/20</td>
<td>7/19</td>
<td>14/20</td>
</tr>
<tr>
<td>No vaccine</td>
<td>--</td>
<td>--</td>
<td>20/20</td>
<td>19/20</td>
<td>20/20</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Results expressed as the number of guinea-pigs dying over the number tested.

$^b$ Given 1 hour after challenge.

$^c$ ND = neutralizing doses against challenge virus.
HEP Flury vaccine, given after infection, did not save a significant proportion of animals, whether given alone or with the different doses of serum.

Combined therapy with pooled vaccine and 5 or 25 units of serum L or 10 units of serum PIC conferred significant protection. Treatment with pooled vaccine and 5 or 25 units of serum L was significantly superior to that with the same dose of serum and duck-embryo vaccine. But, when serum PIC was used the difference was not marked, although pooled vaccine gave better survival rates. As in Experiment 1, the best results were obtained with 10 units of serum PIC and 14×0.075 ml of pooled vaccine. The protection afforded by 14×0.075 ml of pooled vaccine alone was also significant, while the mortality rates in the case of duck-embryo and HEP Flury vaccines were 85% and 100% respectively.

Serum alone (25 units of serum L or 10 units of serum PIC) failed to protect animals, confirming our earlier observations.

The results indicate that even when given in identical doses, pooled phenolized vaccine was superior to the other two vaccines, whether given before or after infection, alone or with different doses of serum. The dose of duck-embryo vaccine used in this experiment corresponded to five times that recommended for human treatment.

Experiment 3

An attempt was made to determine whether potency tests in mice would reflect the superiority of pooled vaccine over the duck-embryo vaccine that was evident in protection experiments. The ED₅₀ of the two batches of duck-embryo vaccine and pooled vaccine used in this study and their antigenic value with respect to the former NIH reference vaccine 164 were determined.

The results are presented in Table 3.

It was found that in both the potency tests, the duck-embryo vaccines proved to be poorer antigens than the pooled phenolized vaccines. They, however, passed the minimum requirements of potency with reference to former reference vaccine 164, which had dropped considerably in potency and had been withdrawn.

**DISCUSSION**

The studies of several workers indicate that the duck-embryo vaccine is free from encephalomyelitic factors and that antibodies appear early in treated animals and volunteers and persist for long periods. But the only protection experiments reported with the vaccine are those of Powell & Culbertson (1959a) and Powell et al. (1960). They determined the immune status of rabbits and guinea-pigs by treating them with the vaccine and challenging them subsequently with street virus and concluded that the vaccine conferred demonstrable immunity.

Their work suffers from the following drawbacks. (1) Large doses of vaccine, which have no relation to the doses recommended for human treatment, were given to the rabbits and guinea-pigs. For instance, 36 ml of 2% vaccine were given over 24 days to rabbits weighing 4-5 pounds (1.8-2.2 kg). Although the method closely parallels the one employed originally by Semple (1911), it would appear that the long period over which the vaccine is given, together with a further delay of a week in challenging the animals, might enable even a marginally potent vaccine to pass the test. In the case of guinea-pigs, the first group received 14 daily doses of 0.1 ml of 10% vaccine, while the second received 10 daily doses of 0.1 ml of 10% vaccine. Neither of these bears any relation to the recommendation of 14 doses of 1 ml for an adult human being. The very large doses of vaccine employed and the

### TABLE 3

**COMPARISON OF THE ANTIGENICITY OF DUCK-EMBRYO AND POOLED PHENOLIZED VACCINES**

<table>
<thead>
<tr>
<th>Potency test</th>
<th>Challenge CVS LD₅₀</th>
<th>Former reference vaccine 164</th>
<th>Duck-embryo vaccine (1)</th>
<th>Pooled vaccine (1)</th>
<th>Duck-embryo vaccine (2)</th>
<th>Pooled vaccine (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ED₅₀ (mg)</td>
<td>Antigenic value a</td>
<td>ED₅₀ (mg)</td>
<td>Antigenic value a</td>
<td>ED₅₀ (mg)</td>
<td>Antigenic value a</td>
</tr>
<tr>
<td>1</td>
<td>0.56</td>
<td>2.57</td>
<td>0.518</td>
<td>5.0</td>
<td>&lt;0.4</td>
<td>&gt;6.4</td>
</tr>
<tr>
<td>2</td>
<td>1.00</td>
<td>5.57</td>
<td></td>
<td></td>
<td>1.23</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.538</td>
<td>10.4</td>
</tr>
</tbody>
</table>

a Antigenic value with respect to former reference vaccine 164.
delaying of the challenge up to 21 days after the first dose of vaccine could explain the excellent results in the first experiment. When the dosage of vaccine was reduced to $10 \times 0.1$ ml and the challenge was administered on the tenth day in the second experiment, the results were poorer, the mortality being 7/23 compared with 0/23 in the first experiment. (2) The challenge was given seven days after the completion of treatment in the case of rabbits and the first group of guinea-pigs, and on the last day of treatment in the case of the second group of guinea-pigs. (3) The challenge was given intracerebrally in rabbits. The experience of the senior author of the present paper has been that the results of intracerebral challenge of rabbits with street virus are irregular and are not always reproducible. (4) The number of animals used for each dilution of the virus was only two or three. (5) The observation period of 30 days in rabbits and 52 days in guinea-pigs was admittedly inadequate in street virus work, especially when the animals have received massive doses of vaccine. (6) The $LD_{50}$ of the challenge used was not known in each experiment. The erratic kill among the untreated controls even at very low dilutions suggests that the challenges should have been very mild.

As the authors themselves admit, more information could have been derived by challenging immunized and control groups with a single challenge, though the range of 5-10 $LD_{50}$ suggested by them may be too low to bring out the differences between the vaccines.

In the experiments reported in this paper the following steps have been taken to overcome the drawbacks listed above. (1) The challenges have been kept at about 50 $LD_{50}$. These are not low enough to enable vaccines of marginal potency to pass and not too high to mask minor differences in antigenicity among them. The challenge level was chosen on the basis of our earlier results that $14 \times 0.075$ ml of phenolized vaccine given alone after infection can confer significant protection (Veeraraghavan, 1959; Veeraraghavan & Subrahmanyan, 1960). (2) The dosage of vaccines used is proportional to that recommended for human treatment. The dosage of $14 \times 0.075$ ml of phenolized vaccine represents the proportionate dose for a guinea-pig weighing about a pound calculated on the basis of $14 \times 10$ ml for a person weighing 140 pounds. In the case of duck-embryo vaccine, 14 doses of 1 ml of 10% vaccine are recommended for human treatment and the proportionate dosage for a guinea-pig would work out to be $14 \times 0.015$ ml of 5% vaccine. In the absence of any recommendation for HEP Flury vaccine, it was given at both levels. (3) The $LD_{50}$ of the virus used in each experiment and the number of neutralizing doses contained in the serum against the challenge have been determined in each case. (4) The animals have been observed for a minimum period of 6 months.

In addition, the value of serum alone and as an adjunct to the different vaccines has been studied.

The results clearly show that the duck-embryo vaccine failed to protect the animals to a significant degree, whether it was given alone or in combination with serum, when administered in a dose recommended by the manufacturers for human treatment in the leaflet 00251 PA 1664AMP (revised 14 June 1960) accompanying the vials. In the second experiment, duck-embryo vaccine was administered in a dose equal to that of pooled vaccine on the basis of tissue concentration, which was five times the dose employed earlier. The failure of the vaccine despite this is an indication of its poor antigenicity. An interesting finding was that duck-embryo vaccine in five times the recommended dose and with serum PIC conferred significant protection.

In general, the duck-embryo vaccines have fared very poorly against both the challenges compared with pooled vaccines, which have afforded significant immunity. Even when seven doses of 0.3 ml of duck-embryo vaccine were started seven days before challenge, the protection conferred was significantly inferior to that obtained with the same dose of pooled vaccine. It is possible that the poor results obtained with the duck-embryo vaccines are due to their lower virus titres. Powell & Culbertson (1950) reported titres of $10^{-2}$ to $10^{-4}$ in intracerebral titrations in mice. In a later paper (1958), they have mentioned a titre of $10^{-6.94}$. These titres are lower than the minimum titre of $10^{-6}$ we regularly obtain in the brains of infected sheep used in the manufacture of pooled vaccine.

The recently revised recommendation that the dosage of duck-embryo vaccine should be increased to a total of 21 ml of 10% vaccine ($7 \times 2$ ml for the first seven days, followed by $7 \times 1$ ml for the next seven days) in the case of wild animal bites is also not likely to be adequate, as the dosage used in our second experiment is nearly 3.5 times the total amount of vaccine corresponding to this recommendation. The poor results even with doses corresponding to $14 \times 10$ ml would suggest that very large doses would be required for persons at genuine
risk. In the light of these findings it is possible that the failure of duck-embryo vaccine given with serum in a case of infection with a proved rabid bat (Humphrey et al., 1960; Lennette et al., 1960) was due to inadequate vaccine therapy.

On the basis of these results, it would appear that if the duck-embryo vaccine has to be employed it has to be given in doses larger than that of phenolized vaccine, i.e., 70 ml of 10% vaccine. This would obviously be beyond the means of countries such as India, in view of the fact that the cost of the vaccine is US $1.09 per ml.

The poorer antigenic value of duck-embryo vaccine in mouse potency tests supports the conclusion drawn from the protection experiments. It is possible that the duck-embryo vaccine passed the minimum requirement because (a) the challenge was with a homologous virus (namely, the CVS strain) which is used in the vaccine production (Anderson et al., 1960) and (b) the former NIH reference vaccine 164 used for comparison has shown a considerable drop in potency. Our findings on the poor antigenicity of the duck-embryo vaccine are also in agreement with the results reported recently by Dean & Sherman (1962). They found that while all the seven lots of Semple type nervous tissue vaccines of rabbit origin passed the Habel test, 13 (72.2%) of 18 lots of duck-embryo vaccine did not meet minimum requirements, while others passed marginally. Six lots of duck-embryo vaccine evaluated for potency by the NIH method failed to satisfy minimum requirements when compared with a potent standard. They also found that the potency of this type of vaccine could be markedly improved by increasing the tissue concentration. This finding parallels our results in protection experiments, according to which a much higher dose of vaccine would be indicated for post-infection treatment.

HEP Flury vaccine has been reported to induce satisfactory serum antibody response, but it has not been recommended for post-infection treatment. Its performance in the protection experiments, whether given alone or with serum, has been too poor to warrant its use in the post-infection treatment of rabies.

The results of treatment with pooled phenolized vaccine are in agreement with our earlier work. Given alone or with different doses of serum, pooled vaccine gave good results.

It is obvious from this study that any attempt to replace vaccines of nervous tissue origin by other vaccines should be done only after very carefully controlled studies.

CONCLUSIONS

1. Post-infection treatment of guinea-pigs with duck-embryo vaccine in a dose corresponding to that recommended for human treatment gave very poor results whether the vaccine was given alone or with serum. HEP Flury vaccine in a dose equal to that of duck-embryo vaccine also gave poor results.

2. Even when the dosage of duck-embryo vaccine and HEP Flury vaccine was raised to the same level as that recommended for pooled vaccine, the results with either vaccine given alone or with different doses of serum were inferior to those obtained with pooled vaccine given under identical conditions.

3. In groups given the vaccine before infection, all the vaccines afforded significant protection, but pooled vaccine gave results significantly superior to those given by the others.

4. Potency tests also demonstrated the better antigenicity of pooled vaccine compared to that of duck-embryo vaccine.

5. The results indicate that the dosage of duck-embryo vaccine recommended for human treatment is inadequate and that the HEP Flury vaccine, in the present form, is unsuitable for post-infection treatment.

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RÉSUMÉ

L'efficacité de doses multiples de vaccin antirabique préparé sur embryon de canard et celle du vaccin Flury HEP ont été comparées à celle d'un vaccin phénolé à base de cerveau de mouton à 5% dans le traitement de la rage expérimentale du cobaye. L'on a vu que le vaccin préparé sur embryon de canard, administré à une dose correspondant à 14 ml de vaccin à 10% recommandée pour le traitement de la rage humaine ne pouvait, aussi bien seul qu'en association avec du sérum antirabique, sauver les animaux. Même administrés à une dose correspondant à 140 ml d'un mélange de vaccin à 5%, ni le vaccin préparé sur embryon de canard ni le vaccin Flury HEP n'ont, injectés isolément ou en association avec du sérum, exercé une bonne protection. Dans les mêmes conditions d'expérience le mélange de vaccin phénolé a donné de bons résultats. Le pouvoir immunisant du vaccin préparé sur embryon de canard et celui du vaccin Flury HEP, administrés avant l'infection, est également inférieur à celui du mélange de vaccin phénolé. Le vaccin préparé sur embryon de canard présente dans le test de séro-neutralisation chez la souris un pouvoir antigénique inférieur à celui du mélange de vaccin phénolé.

Les résultats montrent que le dosage de vaccin préparé sur embryon de canard recommandé pour le traitement de la rage chez l'homme ne donne pas satisfaction et que le vaccin Flury HEP ne peut, sous sa forme actuelle, être efficacement utilisé après morsure.

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