New Project (1) 1 March 1994

- Epidemological modelling of PPRV and Rinderpest outbreaks -

This project will be carried out in collaboration with Prof. M. S. Shaila, ~~of~~ (Dept. of Microbiology and Cell Biology ~~Laboratory~~, Indian Institute of Science).

Preface: While the infection by the Rinderpest Virus (RV) has been ~~reported~~ known in India for both domestic as well as wild animals for last many decades, reports of outbreaks ~~of~~ due to the ~~the~~ Pestes-des-Petite-ruminant virus (PPRV) are of relatively recent origin. As implied by the name, ~~the~~ PPRV affects small ruminants, mainly goats and sheep, unlike ~~Rinderpest~~ RV, which has a much broader host range which includes cattle in addition to goats and sheep. Nevertheless, PPRV is also highly infectious, and ~~also~~ leads to high ~~levels~~ proportions of ~~mort~~ morbidity and mortality.

~~While~~ There have been several attempts to model the epidemiology of ~~Rinderpest~~ RV. However, there have been ~~no Sim~~ little or no work to model the outbreaks of PPRV, especially in India. The ~~migration~~ regular migration of nomadic communities which in turn lead to movement of sheep and goat herds over large distances, make the problem of modelling PPRV spread more challenging. The structure of the metapopulation of small ruminants, — population of a district subdivided into demes at a village level, with some amount of mixing brought about ~~by~~ due to the weekly markets where livestock of ~~adj~~ many adjoining villages is often bought and sold — is ~~also~~ likely to lead to complex patterns of the spread of PPRV epidemics.

The objective of the project is to investigate the effect of population sizes, mixing rates and migration patterns on the probabilities ~~of~~ ~~o~~ occurrence of PPRV outbreaks, and on their magnitudes. While deterministic models would lead to estimates of average effects, stochastic models would allow one to ~~estima~~ evaluate the reliability of these ~~pred~~ estimates.

1

New Project :

Epidemiologic Al Modelling of PPRV and Rindepest Outbreaks

This project is being carried out in collaboration with Prof. M.S. Shaila of the Department of Microbiology and Biology, Indian Institute of Science.

Preface :

Infection of domestic as well as wild animals by the Rinderpest Virus (RV) has been known in India since the last century. Reports of the outbreak of Peste des Petits Ruminants Virus (PPRV) are of a recent origin (Shaila et al 1989, Shaila et al 1990). As implied by the name, PPRV affects small ruminants like goats and sheep, unlike RV, which has a broader host-range, which includes cattle in addition to goats and sheep. Nevertheless, PPRV is highly infectious and leads to high levels of morbidity and mortality., and seems to be taking an increasingly heavy toll in Karnataka, Tamil Nadu, Andhra pradesh and Maharashtra (M.S. Shaila, unpublished results; also see ~~Dr~~ Ramachandran and Nejar, 1992)

There have been several attempts to model the epidemiology of RV (James and Rossiter 1989, Tille et al 1991). However, there has been little or no work to model the outbreaks of PPRV, especially in India. The regular migration of nomadic communities, which in turn leads to the movement of sheep and goats over large distances, make the problem of modelling PPRV more challenging. The structure of the metapopulation of small ruminants - population of a say district being subdivided into demes at a village level, with some amount of mixing brought about by the weekly markets where livestock of many adjoining villages are bought and sold; or the metapopulation of a village divided into demes corresponding to individual households, where mixing takes place

The PRINT.TST File

WordStar is designed to take the best advantage of your printer's features. This file (PRINT.TST) shows how the WordStar printing features work. Print the file to see how the features work on your default printer.

To print this file on a printer other than your default printer, press **^P?** while editing the file. You'll see a list of the printers you've installed. Choose the printer you want, then print the file again.

Print Enhancements

You can add the following print enhancements to your documents:

boldface	^PB	**double strike**	^PD
underline	^PS	~~strikeout~~	^PX
italics	^PY	overprint (for example, ô)	^PH

Customized Fonts

Choose fonts by name! Press **^P=** to see a menu of fonts customized for your default printer.

To see fonts for a different printer, press **^P?** to change the default printer for the document. Then press **^P=** to see a list of fonts for the new printer. Of course, you can print your document on any printer, and WordStar automatically chooses the closest available fonts.

Text Layout

You can center text between margins (^OC)

or align text at the right margin (^O]).

You can change the margins for a section of text . . . or for your entire document.

at the common grazing grounds - is likely to lead to complex patterns in the spread of PPRV epidemics.

It is known that animals immunized against RV are able to resist challenge by PPRV and vice versa. Against this backdrop, it would be interesting to investigate the competition between RV and PPRV in the arena of a rural livestock ecosystem - cattle, sheep, goats etc - both from an epidemiologic Al as well as an evolutionary point of view. It may be possible to extend these studies to include the interaction between domestic and wild animals (e.g. gaur) which occurs at the periphery of wildlife sanctuaries.

4 a

Objectives :

(i) To set up detailed deterministic models for the spread of PPRV in an isolated herd, and explore the range of parameters (permitted by the available data) such as duration of infection, contact rate, extent of production of infective particles, mortality rates etc. which would lead to outbreaks.

(ii) Modify the models to include stochastic variations, to obtain estimates of the reliability of the predictions made from the deterministic models.

(iii) Generalize the models to include spatial movements (and mixing) of the herds.

(iv) Investigate the effects of subjecting the populations to various degrees of vaccination.

(v) Explore the competition between PPRV and RV from epidemiologic Al as well as evolutionary perspectives.

Efforts at designing vaccines against RV and PPRV using the

Paragraph Styles

You can change a number of format settings at the same time by using paragraph styles. Each paragraph style contains a set of customized format instructions; for example, the paragraph style named "Title" chooses a larger font, turns boldface on, and centers the text. Another paragraph style, "Body Text," returns to the default font and the standard tabs and margins. Simply apply the paragraph style you want, and all the customized settings go into effect.

WordStar comes with some paragraph styles already set up, but you can create additional styles of your own. Paragraph styles can include margin and tab settings, fonts, print enhancements, such as boldface and underline, and format settings, such as justification, word wrap, and line spacing.

Columns

Using columns was never easier. You can print in two or more newspaper-style columns. When you reach the end of a column, text wraps automatically to the next column. This feature lets you create professional-looking newsletters and presentations.

Paragraph Indentation

Set a paragraph margin that is greater than the left margin to indent the first line of every paragraph automatically.

The first line of every paragraph indents to the paragraph margin, and the rest of the lines wrap to the left margin.

This indentation is useful for letters, newsletters, and other documents you want to print in paragraph style.

Hanging Indentation

Set a paragraph margin that is less than the left margin for hanging indentation. The first line of every paragraph extends to the left of the text. This is useful for:

- outlines, where you want the numbers to hang out in the left margin (especially convenient with automatic paragraph numbering).
- bulleted lists, such as this one.

recombinant DNA technology have already been underway at a few laboratories in India and the world, and preliminary results have been encouraging (M.S. Shaila, unpublished results). The mathematical models ~~described above~~ developed to describe PPRV epidemics may also be generalized to include the effects of vaccination. These would be helpful in devising optimal vaccination strategies so as to minimize the risks of the outbreaks of RV or PPRV epidemics in a cost-effective manner.

Bibliography

~~References~~ :

(i) James A.D. and Rossiter P.B. (1989)
Trop. Anim. Health Prod. 21: 59-68

(ii) Shaila M.S., Purushothamam V., Bhavsar D., Venugopal K. and Venkatesan R.A. (1989)
Vet. Rec. 125 : U602

(iii) Shaila M.S., Venugopal K., Purushothamam V. and Venkatesan R. A. (1990)
Indian Vet. J. 67 : 385-386

(iv) Tille A., Lefevre C.L., Pastoret P.P. and Thiry E. (1991)
Epidemio. Infect. 107: 441-452

(v) Ramachandran S and Nayak R (1992)
Current Science 63 : 55

Line Numbers

You can add line numbers to the page to make your document look like legal pleading paper. Notice the double-spaced line numbers in the left margin of this page. (Line numbers do not appear while you're editing, but if you have a graphics monitor, press **^OP** to preview them onscreen.)

Paragraph Numbers

Use the paragraph numbering feature to create numbered outlines or technical documents.

1 Each time you use the paragraph number command (^OZ), WordStar inserts the next consecutive number.

1.1 You can change the level of the paragraph number by using the arrow keys. For example, this paragraph number is one level deeper than the preceding paragraph number.

2 If you add or delete a paragraph number, all the subsequent numbers are automatically updated.

Colors

If your printer supports colors, press **^P-** to see a menu of colors.

Redlining and Double-underlining

To get shaded redlining or double-underlining, use the strikeout command (**^PX**). WordStar ordinarily uses a hyphen to strike out text, but you can change the strikeout character to any character your printer can print. To change the character used for strikeout, use the .xx command.

Redlining	Use **.xx** ░ (Alt-176: Shaded box)
Double underlining	Use **.xx** _ (Alt-95: Underline)
~~Any character~~	Use **.xx** ─ (Alt-196: Horizontal line)
~~Normal strikeout~~	Use **.xx** - (Alt-45: Hyphen)

Extended Character Sets

Many printers can print European, Greek, graphic, and math characters. If your printer can't produce the exact character you want, WordStar may print a close or composite character.

σ = β²(α+1)
Herman Sörget went to Mazatlán

```
╔═══╦═══╗
║   ║   ║
╠═══╬═══╣
║   ║   ║
╚═══╩═══╝
```

Here is a table of the extended characters on your printer. Keep in mind that different fonts may have different character sets.

128 Ç	144 É	160 á	176 ░	192 └	208 ╨	224 α	240 ≡
129 ü	145 æ	161 í	177 ▒	193 ┴	209 ╤	225 β	241 ±
130 é	146 Æ	162 ó	178 ▓	194 ┬	210 ╥	226 Γ	242 ≥
131 â	147 ô	163 ú	179 │	195 ├	211 ╙	227 π	243 ≤
132 ä	148 ö	164 ñ	180 ┤	196 ─	212 ╘	228 Σ	244 ⌠
133 à	149 ò	165 Ñ	181 ╡	197 ┼	213 ╒	229 σ	245 ⌡
134 å	150 û	166 ª	182 ╢	198 ╞	214 ╓	230 µ	246 ÷
135 ç	151 ù	167 º	183 ╖	199 ╟	215 ╫	231 τ	247 ≈
136 ê	152 ÿ	168 ¿	184 ╕	200 ╚	216 ╪	232 Φ	248 °
137 ë	153 Ö	169 ⌐	185 ╣	201 ╔	217 ┘	233 Θ	249 •
138 è	154 Ü	170 ¬	186 ║	202 ╩	218 ┌	234 Ω	250 ·
139 ï	155 ¢	171 ½	187 ╗	203 ╦	219 █	235 δ	251 √
140 î	156 £	172 ¼	188 ╝	204 ╠	220 ▄	236 ∞	252 ⁿ
141 ì	157 ¥	173 ¡	189 ╜	205 ═	221 ▌	237 ø	253 ²
142 Ä	158 ₧	174 «	190 ╛	206 ╬	222 ▐	238 ∈	254 ■
143 Å	159 ƒ	175 »	191 ┐	207 ╧	223 ▀	239 ∩	

To add an extended character to a document, select the font first, then hold down the **Alt** key and type the appropriate number on the numeric keypad.[1] On some printers, the character that appears onscreen may not match the printed character.

1. You can also choose extended characters from a menu. Press ^P0 to see a menu of extended characters. Then type the number of the character you want and press Enter.

1. Title : Epidemiological Modelling of PPRV and Rinderpest Outbreaks

2. Summary :

The deterministic mathematical model developed for modelling the propagation of PPRV epizootic in a nonreproducing herd of small ruminants of arbitrary size was extended to include three important effects : (A) using an open, instead of a closed population by replacing the dead animals by live, susceptible ones, (B) using a finite (instead of infinite) immunological memory and (C) combining these two effects.

Compared to the closed population model, the open population model (as expected) led to higher equilibrium proportions of susceptible and immune animals. A long term immunological memory led to an equilibrium population entirely of susceptible animals, while a short term memory led to the herd going extinct, exhibiting oscillatory dynamics. A combination of open population and long term memory led to sustained oscillations. Interestingly, open population with only a short term immunological memory led to a steady state involving non-zero values of susceptible, immune and infected animals, thus demonstrating endemic persistence.

3. Objectives :

The long-term objective of the project is to understand the dynamics of outbreaks of Peste Des Petit Ruminants virus (PPRV) and Rinderpest virus (RV) in the geographically structured, intermixing system of cattle-sheep-goat in Southern India. As a beginning, mathematical models of epidemics are being developed, using appropriate ranges of parameter values, to explore the range of behaviours (population extinction, episodic outbreaks, endemic persistence etc.) exhibited by this dynamical system.

In the present report, the objective was to investigate the effect of relaxing the assumption of a closed population (by allowing import of susceptible animals to replace dead ones) and the assumption of permanent immunity (by allowing the animal to become susceptible again after a prescribed lifetime interval). We also wished to examine the consequence of simultaneously relaxing both these assumptions.

the

4. Methodology :

The animals are divided into four categories - susceptible, infected but non-infective, infected and infective, and immune. Each infective animal is assumed to distribute 'c' number of contacts at random; any susceptible animal which receives a contact is assumed to become infected. The non-infective period is assumed to last for five days, followed by five days of infective period. The animal then either recovers (with a probability r), or else dies.

A deterministic model to simulate the day to day changes in the proportion of animals in each category had been developed earlier, as described in the report of 1994-95. In the modified model of open population, all the dead individuals were replaced by new, live, susceptible ones. To simulate loss of immunological memory, the animals who had recovered from the viral attack 'T' days ago were removed from the 'immune' category and replaced into the 'susceptible' category. The values of T were varied from 45 days (short term memory) to as long as 3 years (long term memory).

The computations were carried out using both single precision as well as double precision arithmetic, to guard against numerical artifacts influencing the outcomes; ~~the two approaches gave consistent results~~.

using FORTRAN, and double precision arithmetic,

on a 486 based personal computer

influences the fate of the epidemic, initiated with a small proportion of infected animals. For low 'c', for example, the infection peters off, whereas for high 'c', an epidemic gradually builds up to a peak, and then declines as the recovered, immune animals dominate the population. If the population is not wiped out, the infection disappears, and a stable equilibrium between the susceptible and the immune is obtained.

In an open population, where dead animals are instantly replaced by susceptible ones, the outcomes are qualitatively similar. The equilibrium proportions of both susceptible and immune animals are (as expected) greater than the corresponding ones in the closed population. Higher values of 'c' lead to lower equilibrium proportions of susceptibles, but lead to bigger epidemics (higher peak heights of infected animals) which peak earlier. A higher mortality rate (lower recovery rate) also leads to bigger epidemics, which peak later. Interestingly, higher mortality rates produce higher equilibrium proportions of susceptibles.

In a closed population model, if the immunity is only of a short duration, the population is gradually wiped out in a series of epidemics of decreasing magnitudes. A long-term immunity, on the other hand, leads to a population almost exclusively of susceptibles. This is because first the infection disappears, unable to spread in a largely immune population, which subsequently reverts to a susceptible state.

A combination of open population and long term memory leads to a periodic occurrence of epidemics, interspersed with long stretches of time when there is no detectable level of infection. A short term immunological memory, on the other hand, leads to a steady state where the proportions of susceptible, infected and immune animals remain unchanged. In other words, for such a combination of parameters, the disease can be more appropriately described as an endemic, persistent disease.

6. Discussion :

Earlier models of population dynamics of rinderpest had, somewhat arbitrarily, assumed that persistence of infection in a population beyond 12 months as indicative of it being in a enzootic state. The present investigation has provided a combination of realistic assumptions and parameters such that a small but constant level of infection persists almost indefinitely. This seems to be a more satisfactory criterion for distinguishing between enzootics and epizootics.

A rather contrived feature of the present investigation is the instant (daily) replacement of dead animals. Secondly, it is assumed that all the replacements are susceptibles. A more realistic approach would involve a set of interacting populations, which exchange a few animals at weekly, fortnightly or monthly intervals. These and other refinements are in the process of being implemented.

7. Tables and Charts :

Four figures, with self explanatory titles, are enclosed.

8. Recommendations : Nil

9. Publications : Nil

10. Degrees awarded : Nil

EPIDEMIOLOGICAL MODELLING OF PPRV AND RINDERPEST OUTBREAKS

This project is being carried out in collaboration with Prof. M.S. Shaila of the Department of Microbiology and Cell Biology, Indian Institute of Science, Bangalore.

PART - II

1. Preface

Infection of domestic as well as wild animals by the Rinderpest Virus (RV) has been known in India since the last century. Reports of the outbreaks of Peste des Petits Ruminants Virus (PPRV) are, however, of a recent origin (Shaila et al 1989, Shaila et al 1990). As implied by the name, PPRV affects small ruminants like goats and sheep. Rinderpest virus primarily affects cattle, but has a broader host-range, which includes goats and sheep as well. Nevertheless, PPRV is highly infectious and leads to high levels of morbidity and mortality (Losos, 1981; Scott, 1990). Over the last few years, PPRV seems to be taking an increasingly heavy toll in Karnataka, Tamil Nadu, Andhra Pradesh and Maharashtra (Shaila et al, manuscript in preparation; see also Ramachandran and Nayak, 1992).

There have been several attempts to model the epidemiology of RV (James and Rossiter 1989, Tille et al 1991). However, there has been little or no work to model the outbreaks of PPRV, especially in India, where both the viruses cause separate cycles of infection in small ruminants. The regular migration of nomadic communities, which in turn leads to the movement of sheep and goats over large distances, makes the problem of modelling PPRV more challenging. The structure of the metapopulation of small ruminants

- population of a say district being subdivided into demes at the village level, with some amount of mixing brought about by the weekly markets where livestock of many adjoining villages are bought and sold; or the metapopulation of a village divided into demes corresponding to individual households, where mixing takes place at the common grazing grounds - is likely to lead to complex patterns of the spread of PPRV epidemics.

It is known that animals immunized against RV are able to resist challenge by PPRV and vice versa (Losos, 1981; Scott, 1990). Against this backdrop, it would be interesting to investigate the competition between RV and PPRV in the arena of a rural livestock ecosystem - cattle, sheep, goats etc. - both from an epidemiological as well as an evolutionary point of view. It may be possible to extend these studies to include the interaction between domestic and wild animals (e.g. gaur) which occurs at the periphery of wildlife sanctuaries.

The mathematical models developed to describe PPRV epidemics may also be generalized to include the effects of vaccination. These would be helpful in devising optimal vaccination strategies so as to minimize the risks of the outbreaks of RV or PPRV epidemics in a cost-effective manner.

2. Abstract of the project

A deterministic mathematical model has been developed to investigate the propagation of a PPRV epizootic in an isolated, non-reproducing herd of arbitrary size. The parameters corresponding to incubation period and virus excretion period were obtained from published literature. Since different strains of PPRV, different geographical areas and different breeds of hosts show considerable variations in the proportion of animals succumbing to the disease, the model was run for three different levels (high, medium and low, i.e., 0.9, 0.5 and 0.1) of

mortality rates. Since little or no information is available for the contact rate/transmission efficiency, this parameter was also varied over a wide range of values. For every combination of parameter values and for varying levels of the initial infection rate, the model simulated daily changes in the proportion of susceptible, infected, infectious, recovered/immune and dead animals, till they reached nearly constant values.

It is seen that more or less independently of the initial infection level, but with a sensitive dependence on the contact rate, the infection either peters off, or builds up into an epizootic with a large proportion of animals contacting the disease. A set of simulations was carried out to determine the dependence of onset, magnitude and duration of the epizootic on the virulence level and the contact rate/transmission efficiency of the PPR Virus.

3. Highlights of the findings achieved in the project

(i) A modified approach was developed for evaluating the probability of disease transmission, based on statistically more appropriate Poisson distribution, in contrast to the binomial distribution based investigations of the dynamics of rinderpest epizootics reported in veterinary literature.

(ii) In conformity with other epidemiological models, a threshold effect is observed for the contact rate / transmission efficiency such that for values even slightly lower than the threshold, the initial infection dwindles away, and for even slightly higher values, an epizootic sweeps through the herd. This emphasizes the need for developing more detailed, explicit and reliable theoretical as well as experimental techniques for determining the values of this crucial parameter for real-life situations.

(iii) Interestingly, the magnitude of the epizootic is higher for more virulent strains (higher mortality rates).

4. Detailed report of the work done on the project

a) Summary of the objectives

(i) To set up detailed deterministic models for the spread of PPRV in an isolated herd, and explore the range of parameters (permitted by the available data) such as duration of infection, contact rate, extent of production of infective particles, mortality rates etc. which would lead to outbreaks.

(ii) Modify the models to include stochastic variations, to obtain estimates of the reliability of the predictions made from the deterministic models.

(iii)Generalize the models to include spatial movements (and mixing) of the herds.

(iv) Investigate the effects of subjecting the populations to various degrees of vaccination.

(v) Explore the competition between PPRV and RV from epidemiological as well as evolutionary perspectives.

b) Methodology

An isolated, nonreproducing herd of arbitrary size is assumed to contain freely and randomly mixing individual animals. Four main categories into which the animals can be divided are :

* Susceptible, who have not yet contacted the disease,

* Infected animals, who have not yet become infective,

* Diseased animals, who excrete virus and are thus infective

* Recovered animals, who are immune against further infection, and

* Animals which have died due to the disease.

Initially (time T=0), the herd is assumed to contain only susceptible animals, except for a small proportion of introduced infected animals. The PPRV infection follows an approximately five day incubation period where the animals are not infective. In the next three to five days, the animals excrete virus (Losos, 1981; Taylor, 1984) and are therefore able to produce infections in other animals which come in contact with them. At the end of this period, a proportion 'd' of these infected animals die, and the remaining proportion '(1-d)'recover into an immune state. A single contact with an infected animal is assumed to be adequate for contacting the disease. Each infected animal is assumed to make an average of 'c' contacts with other animals (a value of c less than 1.0 can thus model a low transmission efficiency). If Ps, Pinf, Ptr and Pim denote the proportions of susceptible, infected (but not infective), infective (transmitting) and immune animals respectively at time 'T', the average number of contacts, 'Cav', received by an animal is given by

$$Cav = Ptr / (Ps + Pinf + Ptr + Pim)$$

The number of contacts received by the animals is assumed to follow a Poisson distribution. Hence, the probability of an animals receiving ZERO contacts is Exp (- Cav). The probability of contacting the disease, 'inf', is therefore the probability of receiving AT LEAST one contact, which is given by

$$inf = 1.0 - Exp(-Cav)$$

A proportion (Ps X inf) of the susceptible animals is thus seen to enter the infected state at time 'T+1'.

A FORTRAN program was developed to simulate the above situation for a given set of parameter values. The run was continued till the day to day changes in the proportion of animals in each of the above state were smaller than a prespecified value. In situations when an epizootic developed in the population, the program also recorded the magnitude (highest proportion of infected+infective animals reached) of the epizootic and the day on which the peak was attained.

In a modified version of the model, infective animals were assumed to have a constant daily mortality rate over the period 3-5 days from their becoming infective (8-10 days from the infection date). For a comparison of the results of the two models, the parameters were so chosen that the net mortality rate was identical in both the cases.

c) **Results**

The overall behaviour of the dynamics of the spread of PPR epizootic in a herd is similar to standard epidemiological models (Bailey, 1975; Anderson and May, 1982). The quantity which decides whether an epizootic will take off or not is the net 'reproductive rate' of the virus, which is equal to the average number of new infections produced by a single infected individual. This, in turn, is a function of the contact/transmission rate, and in many instances, of the mortality rate as well. When the net 'reproductive rate' is smaller than 1.0, a small initial infection gradually dwindles away (as seen in Fig.1, for contact rate of 0.10). On the other hand, for values of the reproductive rate greater than 1.0, an epizootic builds up (Fig.2 for contact rate 0.40). The proportion of infected individuals increases to a peak value, and then decreases since the infected individuals either recover into an immune state or die, and the number of susceptibles keeps on decreasing, so there are fewer individuals who can be infected.

One of the ways in which the epizootic can be quantified is the proportion of susceptible individuals remaining in the population after the epizootic has run its course. This value is depicted as a function of contact rate in Fig.3 for two different values of initial infection. The threshold-like property of the contact rate is clearly seen, with a sharper transition when the initial infection is low. Since in the first version of the model death can take place only on the 10th day, the proportion of susceptibles is independent of the mortality rate.

Three other descriptors of an epizootic are (a) magnitude of the peak , i.e., the maximum proportion of infected individuals reached during the course of the epizootic, (b) the time to reach the peak and (c) the duration of the epizootic i.e., the time at which there is little or no net change in proportions of the different categories of animals. The peak magnitude increases with increasing contact rate, once the threshold value is crossed (Fig.4). The initial level of infection seems to have little or no effect; the pairs of curves in Fig.4 are close together. The figure also shows that increasing rates of mortality lead to higher peak values. On the other hand, as seen from Fig. 5, a smaller initial infection implies longer time to attain the peak, as expected (top three curves vs bottom three curves). The mortality rate has an opposite effect, such that higher the mortality, slower is the peak reached (Fig.5). The variation in the duration of the epizootic with contact rate, with initial infection levels and with different mortality rates is given in Table I. For super-threshold contact rate, the duration increases with increasing contact rates, with increasing level of initial infection and decreases with increasing mortality rates.

A second version of the model permits death to take place on day 8, 9 or 10 from infection, while maintaining the net mortality at a prespecified value. As a result of this modification, animals are infective, on an average, for a relatively shorter duration. The net reproductive rate thus becomes a function of the mortality rate as well, and decreases with increasing mortality. This effect is clearly evident from Fig.6, where threshold values of the contact rate have shifted to the right for higher values of mortality rates.

d) Discussion and Analysis

An important detail in which this model differs from the previous models of rinderpest epizootics is the use of Poisson distribution for computing the range of contacts experienced by the animals, in contrast to the binomial distribution used earlier. Especially for large herd sizes, the Poisson model is statistically somewhat more appropriate. It is also more reasonable from a biological point of view, since a range of values of contacts 0,1,.... is permitted in this formulation, in contrast to the fixed number of contacts experienced by each animal in the earlier formulations. However, as far as the present simulation is concerned, the assumption of 'c' contacts from an infected animal is equivalent to the earlier assumption of fixed number of contacts, since in the present deterministic version (corresponding to an infinite population), it is only the **mean** number of contacts that governs the dynamics. The stochastic model, to be explored in future, would be sensitive to the variation in the number of contacts as well, and is therefore likely to differ from the earlier stochastic models in a significant manner. It is also relatively straightforward to extend this formalism to simulate the more realistic clumped distributions, and this would be taken up in the next phase where the spatial dimension may be explicitly introduced.

One of the interesting patterns seen from the present model is the effect of mortality rate on the peak value of the epizootic, and on the time needed to reach it. Higher levels of mortality lead to higher peak values, but at a relatively later time. This may possibly be due to the assumption of a fixed, nonreproducing herd. Higher mortality rates reduce the population faster, and a lower number of immune animals leads to an effectively higher number of contacts per animal and hence a faster transmission. A lower mortality rate on the other hand converts animals from susceptible to immune state with a higher efficiency, and there being no new susceptible animals, a higher proportion of infected animals cannot be obtained. A more realistic model to be developed in the next phase would include reproduction as well as influx of new animals by immigration. It would be desirable to see if the present pattern of mortality dependence is still retained.

If c is the contact rate, then in the first model, since an infected individual is infective for 5 days, it will on an average infect 5c individuals before it dies or recovers. Thus, the threshold will be reached when 5c is greater than 1.0, or when c is greater than 0.2. This is clearly borne out by Fig. 3. On the other hand, in the second model, if m is the mortality rate per day, an individual will be infective for 3 days with probability m, for 4 days with probability m(1-m), and for 5 days with probability (1-2m+m*m). The net reproductive rate will then be given by

$$c\,(\,5 - 3m + m*m\,)$$

This is less than 5c for all the values of m, and in fact monotonically decreases from 5c to 3c as m increases from 0 to 1. The threshold thus increases from 0.2 for m=0 to 0.33 for m=1. This difference in thresholds is clearly seen in Fig.6 especially for the two mortality rates of 0.10 and 0.90.

One of the objectives of this project is to evaluate the effect of different vaccination strategies. Preliminary simulations indicate that vaccinating a certain proportion of individuals brings down the peak infection by a corresponding amount. This in turn implies that vaccination on a large scale may be needed to ward off epizootics, and this does not seem prima facie a very cost-effective approach.

A question of considerable biological as well as practical interest would be to determine the factors/parameters which lead to persistence (enzootic) of PPRV in the population, without either dying out or leading to epizootics. The current 'closed population' model is clearly unsuitable for this purpose. Earlier workers had somewhat arbitrarily equated persistence beyond 12 months as indicative of enzootic state. A geographically structured population with some episodes of mixing, to be investigated in the next phase, may lead to a better criterion for defining the enzootic state.

e) <u>Tables; Charts</u>

Table I. Duration of the epizootic

The table gives the duration (in days) for which the epizootic lasted, having begun on day 0 with a small proportion of infected animals. Two different values of initial infection level, and three different values of mortality rates were used in the simulation. The epizootic was considered to have completed its course by the somewhat arbitrary criterion of the net day-to-day change (added over all the categories) was less than 0.00001.

	InitialInfection 0.001			InitialInfection 0.01		
	Mortality			Mortality		
Contact Rate	0.1	0.5	0.9	0.1	0.5	0.9
0.05	30	30	30	43	43	44
0.10	47	47	47	73	73	74
0.15	99	100	100	150	150	161
0.20	862	1114	2452	405	528	1070
0.25	422	432	410	311	330	323
0.30	268	264	238	216	214	192
0.35	205	198	177	169	164	144
0.40	169	162	145	142	135	119
0.45	147	140	126	123	117	103
0.50	131	125	112	110	104	92

f) Figures

The six figures (Fig.1 to Fig.6) referred to in the 'Results' section as well as in the 'Discussion and analysis' section have been appended at the end of the report. Each figure is suitably titled, labeled and provided with legend to make it self-explanatory.

g) Likely impact of the work on the scientific potential of our country

The modelling work described above is at a preliminary stage. Moreover, detailed data on the population structure, mortality rates, movement patterns etc. from the locations where PPRV outbreaks have occurred is not yet available. It would therefore be premature to evaluate the impact of the work carried out so far on the scientific potential of our country.

h) Bibliography

1. Shaila M.S., Purushothaman V., Bhavsar D., Venugopal K. and Venkatesan R.A. (1989). *Vet. Rec.* 125 : U602.

2. Shaila M.S., Venugopal K., Purushothaman V. and Venkatesan R. A. (1990). *Indian Vet. J.* 67 : 385-386.

3. Losos, G.J. (1981). 'Infectious tropical diseases of domestic animals' (Longmans)

4. Scott, G.R. (1990). in 'Virus infections of Vertebrates vol. 3 : Virus infections of ruminants', eds. Dinter, Z. and Morein, B. (Elsevier)

5. Ramachandran, S. and Nayak, R. (1992). *Curr. Sci.* 63 : 55

6. James A.D. and Rossiter P.B. (1989). *Trop. Anim. Health Prod.* 21 : 59-68.

7. Tille A., Lefevre C.L., Pastoret P.P. and Thiry E. (1991). *Epidemio. Infect.* 107 : 441-452.

8. Taylor, W.P. (1984). *Prev. Vet. Med.* 2 : 157-166

9. Bailey, N.T.J. (1975). 'The mathematical theory of infectious diseases and its applications'

(Charles Griffin)

10. Anderson, R.M. and May, R. M. (1982). 'The population biology of infectious diseases' (Springer Verlag)

11. Anderson, Roy M. (1982). 'Population dynamics of infectious diseases' (Chapman and Hall)

PART - III

1. **Recommendations including remedial measures relevant to the environmental problems studied under the scheme :**

   The investigations envisioned in this project are yet to reach a stage when recommendations can be made.

2. **List of research papers published/accepted in the research work done under the scheme :**

   Nil

3. **Whether any research fellow associated with the scheme has been awarded Ph.D. etc. :**

   Not applicable.

Fig. 1: Sub-threshold contact rate 0.10

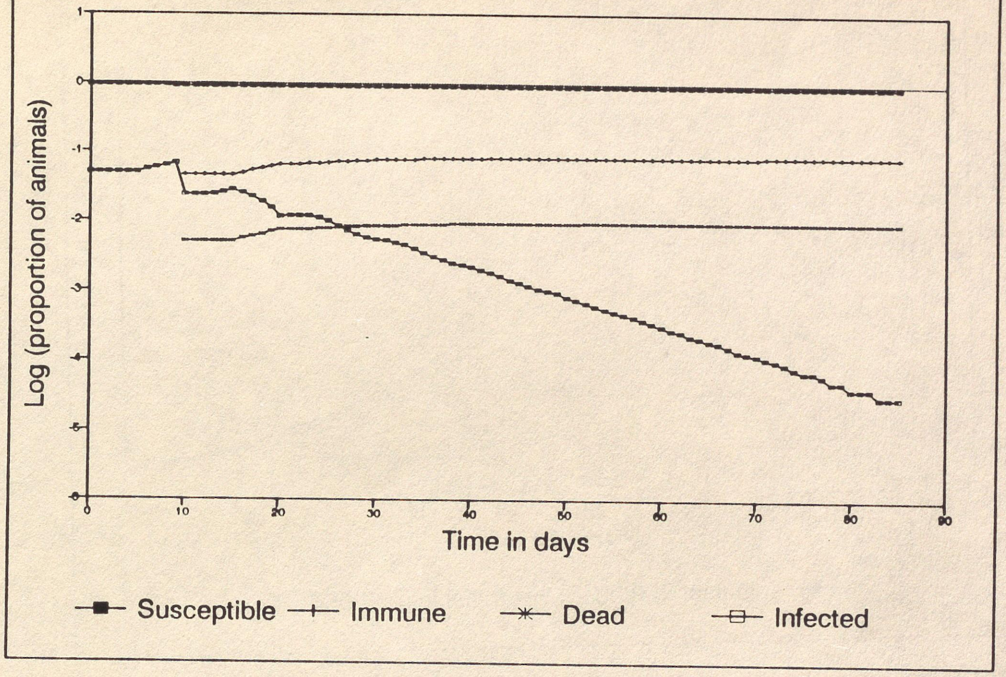


Fig.2: Super-threshold contact rate 0.40

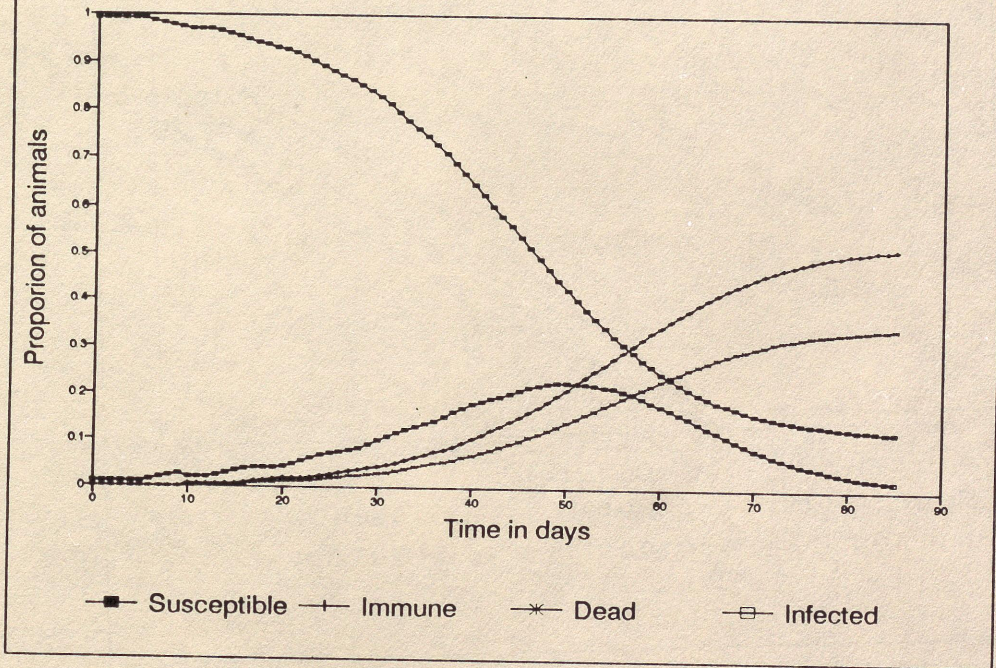


Fig.3: Effect of Contact Rate

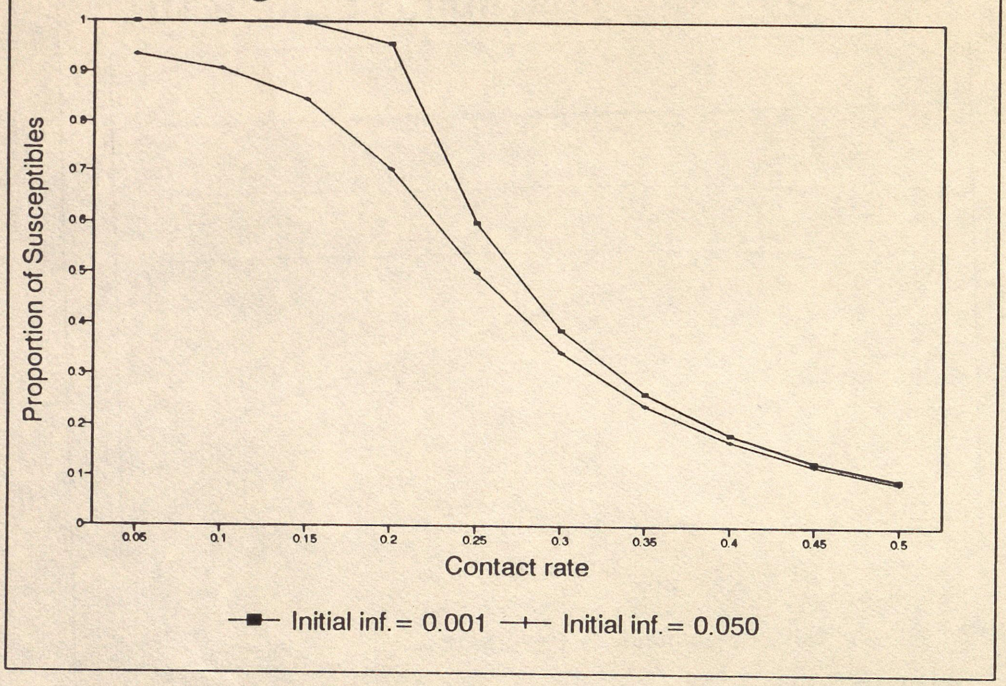


Fig.4: Peak proportion of infection

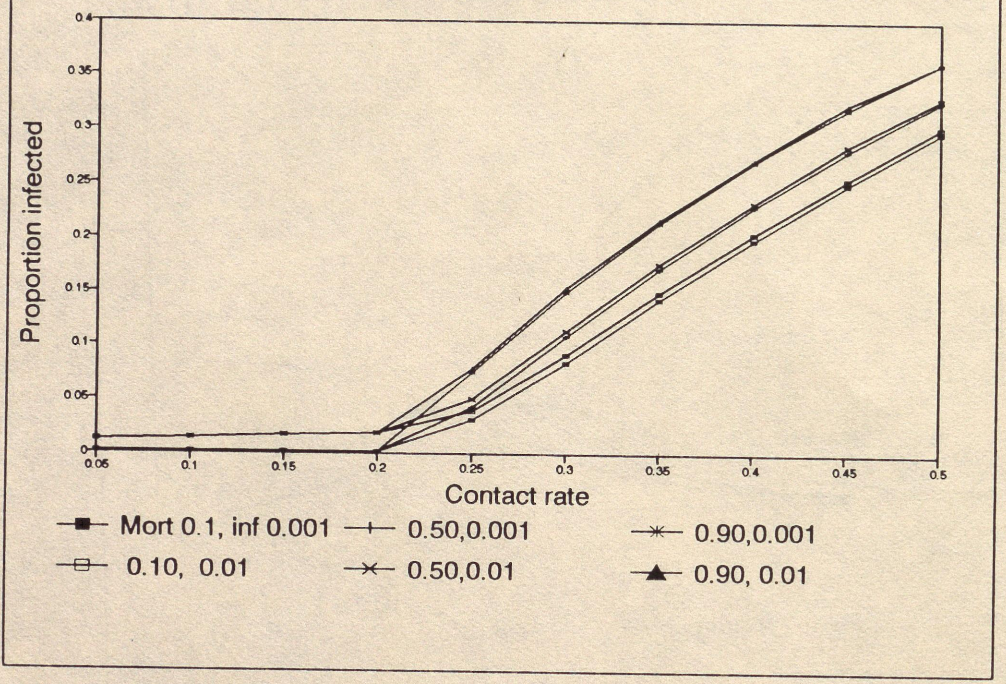


Fig. 5: Time to reach peak of epizootic

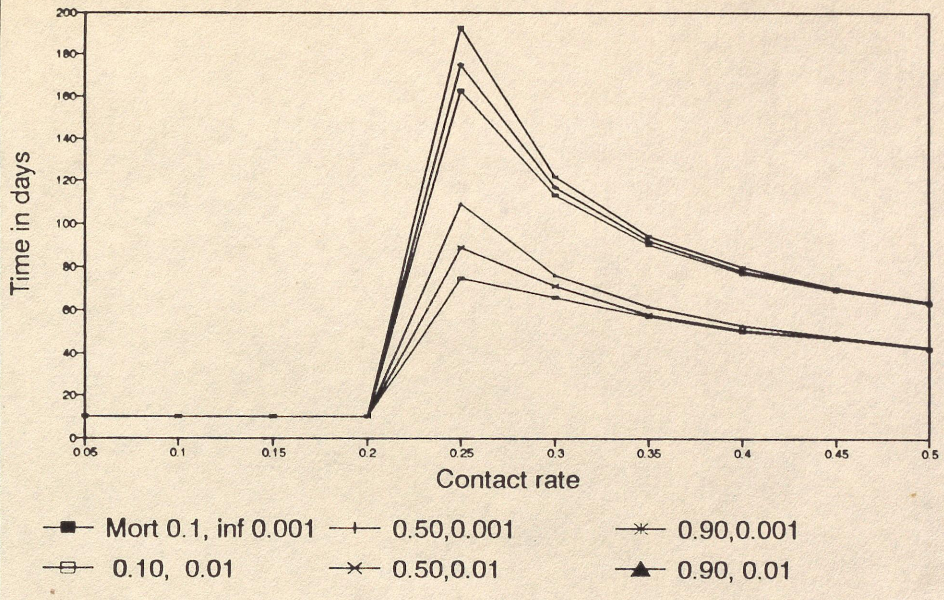
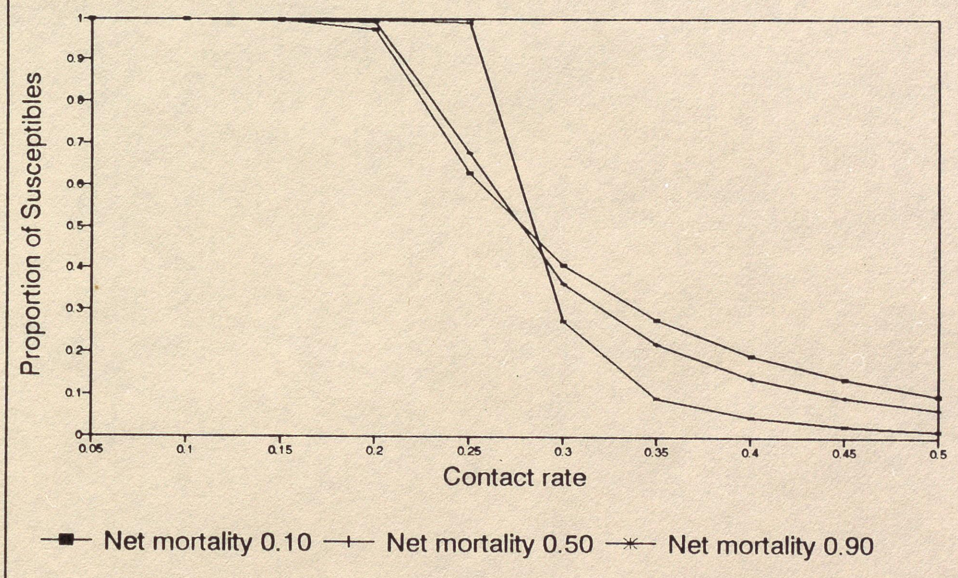


Fig.6: Effect of Contact rate & Mortality Death on days 8,9 and 10



0. The subdirectory PROJ11 contains all files.
1. File is RP103, in WS4. 16 March 95

A final printout is needed for the annual report. (This is Project 11).

You can edit the file to change the format (e.g. double space etc., whatever is done for Dr. NMR's reports). ~~I~~

I've made all the connections marked on this copy, so no changes need to be made.

2. The figures are in FIG1.WK1 to FIG6.WK1. Small alterations may be needed, as marked. Figure number (i.e. FIG.1) etc. have to be added. It would be nice if two can fit in one page.
3. If you wish, you can take a draft printout. Else please take a final printout (+2 copies for me).

Thanks.

Project II
C:\ANURPT95\EPIMODRV\RPT\RPT03

EPIDEMIOLOGICAL MODELLING OF PPRV AND RINDERPEST OUTBREAKS

This project is being carried out in collaboration with Prof. M.S. Shaila of the Department of Microbiology and Cell Biology, Indian Institute of Science, Bangalore.

PART - II

1. Preface

Infection of domestic as well as wild animals by the Rinderpest Virus (RV) has been known in India since the last century. Reports of the outbreaks of Peste des Petits Ruminants Virus (PPRV) are, however, of a recent origin (Shaila et al 1989, Shaila et al 1990). As implied by the name, PPRV affects small ruminants like goats and sheep, unlike RV, which has a broader host-range, which includes cattle in addition to goats and sheep. Nevertheless, PPRV is highly infectious and leads to high levels of morbidity and mortality (Losos, 1981; Scott, 1990). Over the last few years, PPRV seems to be taking an increasingly heavy toll in Karnataka, Tamil Nadu, Andhra Pradesh and Maharashtra (Shaila et al, manuscript in preparation; see also Ramachandran and Nayak, 1992).

There have been several attempts to model the epidemiology of RV (James and Rossiter 1989, Tille et al 1991). However, there has been little or no work to model the outbreaks of PPRV, especially in India.* The regular migration of nomadic communities, which in turn leads to the movement of sheep and goats over large distances, makes the problem of modelling PPRV more challenging. The structure of the metapopulation of small ruminants - population of a say district being subdivided into demes at the village level, with some amount of mixing brought about by the weekly markets where livestock of many adjoining villages are bought and sold; or the metapopulation of a village divided into demes corresponding to individual households, where mixing takes place at the common grazing grounds - is likely to lead to complex patterns of the spread of PPRV epidemics.

* where both viruses cause separate cycles infections in small ruminants

It is known that animals immunized against RV are able to resist challenge by PPRV and vice versa (Losos, 1981; Scott, 1990). Against this backdrop, it would be interesting to investigate the competition between RV and PPRV in the arena of a rural livestock ecosystem - cattle, sheep, goats etc. - both from an epidemiological as well as an evolutionary point of view. It may be possible to extend these studies to include the interaction between domestic and wild animals (e.g. gaur) which occurs at the periphery of wildlife sanctuaries.

is this necessary?

Efforts at designing vaccines against RV and PPRV using the recombinant DNA technology have already been under way at a few laboratories in India and the world, and preliminary results have been encouraging (M.S. Shaila, unpublished results). The mathematical models developed to describe PPRV epidemics may also be generalized to include the effects of vaccination. These would be helpful in devising optimal vaccination strategies so as to minimize the risks of the outbreaks of RV or PPRV epidemics in a cost-effective manner.

2. Abstract of the project

A deterministic mathematical model has been developed to investigate the propogation of a PPRV epizootic in an isolated, non-reproucing herd of arbitrary size. The parameters corresponding to incubation period and virus excretion period were obtained from published literature. Since different strains of PPRV, different geographical areas and different breeds of hosts show considerable variations in the proportion of animals succumbing to the disease, the model was run for three different levels (high, medium and low, i.e., 0.9, 0.5 and 0.1) of mortality rates. Since little or no information is available for the contact rate/transmission efficiency, this parameter was also varied over a wide range of values. For every combination of parameter values and for varying levels of the initial infection rate, the model simulated daily changes in the proportion of susceptible, infected, infectious, recovered/immune and dead animals, till they reached nearly constant values.

It is seen that more or less independently of the initial infection level, but with a sensitive dependence on the contact rate, the infection either peters off, or builds up into an epizootic with a large proportion of animals contacting the disease. A set of simulations was carried out to determine the dependence of onset, magnitude and duration of the epizootic on the virulence level and the contact rate/transmission efficiency of the PPR Virus.

3. Highlights of the findings achieved in the project

(i) A modified approach was developed for evaluating the probability of disease transmission, based on statistically more appropriate Poisson distribution, in contrast to the binomial distribution based investigations of the dynamics of rinderpest epizootics reported in veterinary literature.
(ii) In conformity with other epidemiological models, a threshold effect is observed for the contact rate / transmission efficiency such that for values even slightly lower than the threshold, the initial infection dwindles away, and for even slightly higher values, an epizootic sweeps through the herd. This emphasizes the need for developing more detailed, explicit and reliable theoretical as well as experimental techniques for determining the values of this crucial parameter for real-life situations.
(iii) Interestingly, the magnitude of the epizootic is higher for more virulent strains (higher mortality rates).

4. Detailed report of the work done on the project

4.a) Summary of the objectives

(i) To set up detailed deterministic models for the spread of PPRV in an isolated herd, and explore the range of parameters (permitted by the available data) such as duration of infection, contact rate, extent of production of infective particles, mortality rates etc. which would lead to outbreaks.

(ii) Modify the models to include stochastic variations, to obtain estimates of the reliability of the predictions made from the deterministic models.

(iii)Generalize the models to include spatial movements (and mixing) of the herds.

(iv) Investigate the effects of subjecting the populations to various degrees of vaccination.

(v) Explore the competition between PPRV and RV from epidemiologcal as well as evolutionary perspectives.

4.b) Methodology

An isolated, nonreproducing herd of arbitrary size is assumed to contain freely and randomly mixing individual animals. Four main categories into which the animals can be divided are :

* Susceptible, who have not yet contacted the disease,
* Infected animals, who have not yet become infective,
* Diseased animals, who excrete virus and are thus infective
* Recoverd animals, who are immune against further infection, and
* Animals which have died due to the disease.

Initially (time T=0), the herd is assumed to contain only susceptible animals, except for a small proportion of introduced infected animals. The PPRV infection follows an approximately five day incubation period where the animals are not infective. In the next three to five days, the animals excrete virus (Losos, 1981; Taylor, 1984) and are therefore able to produce infections in other animals which come in contact with them. At the end of this period, a proportion 'd' of these infected animals die, and the remaining proportion '(1-d)'recover into an immune state. A single contact with an infected animal is assumed to be adequate for contacting the disease. Each infected animal is assumed to make an average of 'c' contacts with other animals (a value of c less than 1.0 can thus model a low transmission efficiency). If Ps, Pinf, Ptr and Pim denote the proportions of susceptible, infected (but not infective), infective (transmitting) and immune animals respectively at time 'T', the average number of contacts, 'Cav', recieved by an animal is given by

$$Cav = Ptr / (Ps + Pinf + Ptr + Pim)$$

The number of contacts recieved by the animals is assumed to follow a Poisson distribution. Hence, the probability of an animals recieving ZERO contacts is Exp (- Cav). The probability of contacting the disease, 'inf', is therefore the probability of recieving AT LEAST one contact, which is given by

$$inf = 1.0 - Exp (- Cav)$$

A proportion (Ps X inf) of the susceptible animals is thus seen to enter the infected state at time 'T+1'.

A FORTRAN program was developed to simulate the above situation for a given set of parameter values. The run was continued till the day to day changes in the proportion of animals in each of the above state were smaller than a prespecified value. In situations when an epizootic developed in the population, the program also recorded the magnitude (highest proportion of infected+infective animals reached) of the epizootic and the day on which the peak was attained.

In a modified version of the model, infective animals were assumed to have a constant daily mortality rate over the period 3-5 days from their becoming infective (8-10 days from the infection date). For a comparison of the results of the two models, the parameters were so chosen that the net mortality rate was identical in both the cases.

4.c) Results

The overall behaviour of the dynamics of the spread of PPR epizootic in a herd is similar to standard epidemiological models (Bailey, 1975; Anderson and May, 1982). The quantity which decides whether an epizootic will take off or not is the net 'reproductive rate' of the virus, which is equla to the average number of new infections produced by a single infected individual. This, in turn, is a function of the contact/transmission rate, and in many instances, of the mortality rate as well. When the net 'reproductive rate' is smaller than 1.0, a small initial infection gradually dwindles away (as seen in Fig.1, for contact rate of 0.10). On the other hand, for values of the reproductive rate greater than 1.0, an epizootic builds up (Fig.2 for contact rate 0.40). The proportion of infected individuals increases to a peak value, and then decreases since the infected individuals either recover into an immune state or die, and the number of susceptibles keeps on decreasing, so there are fewer individuals who can be infected.

One of the ways in which the epizootic can be quantified is the proportion of susceptible individuals remaining in the population after the epizootic has run its course. This value is depicted as a function of contact rate in Fig.3 for two different values of initial infection. The threshold-like property of the contact rate is clearly seen, with a sharper transition when the initial infection is low. Since in the first version of the model death can take place only on the 10th day, the proportion of susceptibles is independent of the mortality rate.

Three other descriptors of an epizootic are (a) magnitude of the peak , i.e., the maximum proportion of infected individuals reached during the course of the epizootic, (b) the time to reach the peak and (c) the duration of the epizootic i.e., the time at which there is little or no net change in proportions of the different categories of animals. The peak magnitude increases with increasing contact rate, once the threshold value is crossed (Fig.4). The initial level of infection seems to have little or no effect; the pairs of curves in Fig.4 are close together. The figure also shows that increasing rates of mortality lead to higher peak values. On the other hand, as seen from Fig. 5, a smaller initial infection implies longer time to attain the peak, as expected (top three curves vs bottom three curves). The mortality rate has an opposite effect, such that higher the mortality, slower is the peak reached (Fig.5). The variation in the duration of the epizootic with contact rate, with initial infection levels and with different mortality rates is given in Table I. For super-threshold contact rate, the duration increases with increasing contact rates, with increasing level of initial infection and decreases with increasing mortality rates.

A second version of the model permits death to take place on day 8, 9 or 10 from infection, while maintaining the net mortality at a prespecified value. As a result of this modification, animals are infective, on an average, for a relatively shorter duration. The net reproductive rate thus becomes a function of the mortality rate as well, and decreases with increasing mortality. This effect is clearly evident from Fig.6, where threshold values of the contact rate have shifted to the right for higher values of mortality rates.

4.d) <u>Discussion and Analysis</u>

An important detail in which this model differs from the previous models of rinderpest epizootics is the use of Poisson distribution for computing the range of contacts experienced by the animals, in contrast to the binomial distribution used earlier. Especially for large herd sizes, the Poisson model is statistically somewhat more appropriate. It is also more reasonable from a biological point of view, since a range of values of contacts 0,1,.... is permitted in this formulation, in contrast to the fixed number of contacts experienced by each animal in the earlier formulations. It is also relatively straightforward to extend this formalism to simulate the more realistic clumped distributions, and this would be taken up in the next phase where the spatial dimension may be explicitely introduced.

One of the interesting patterns seen from the present model is the effect of mortality rate on the peak value of the epizootic, and on the time needed to reach it. Higher levels of mortality lead to higher peak values, but at a relatively later time. This may possibly be due to the assumption of a fixed, nonreproducing herd. Higher mortality rates reduce the population faster, and a lower number of immune animals leads to an effectively higher number of contacts per animal and hence a faster transmission. A lower mortality rate on the other hand converts animals from susceptible to immune state with a higher efficiency, and there being no new susceptible animals, a higher proportion of infected animals cannot be obtained. A more realistic model to be developed in the next phase would include reproduction as well as influx of new animals by immigration. It would be desirable to see if the present pattern of mortality dependence is still retained.

If c is the contact rate, then in the first model, since an infected individual is infective for 5 days, it will on an average infect 5c individuals before it dies or recovers. Thus, the threshold will be reached when 5c is greater than 1.0, or when c is greater than 0.2. This is clearly borne out by Fig. 3. On the other hand, in the second model, if m is the mortality rate per day, an individual will be infective for 3 days with probability m, for 4 days with probability m(1-m), and for 5 days with probability (1-2m+m*m). The net reproductive rate will then be given by

$$c (5 - 3m + m*m)$$

This is less than 5c for all the values of m, and in fact monotonically decreases from 5c to 3c as m increases from 0 to 1. The threshold thus increases from 0.2 for m=0 to 0.33 for m=1. This differnce in thresholds is clearly seen in Fig.6 especially for the two mortality rates of 0.10 and 0.90.

One of the objectives of this project is to evaluate the effect of different vaccination strategies. Preliminary simulations indicate that vaccinating a certain proportion of individuals brings down the peak infection by a corresponding ammount. This in turn implies that vaccination on a large scale may be needed to ward off epizootics, and this does not seem prima facie a very cost-effective approach.

A question of considerable biological as well as practical interest would be to determine the factors/parameters which lead to persistence (enzootic) of PPRV in the population, without either dying out or leading to epizootics. The current 'closed population' model is clearly unsuitable for this purpose. Earlier workers had somewhat arbitrarily equated persistence beyond 12 months as indicative of enzootic state. A geographically structured population with some episodes of mixing, to be investigated in the next phase, may lead to a better criterion for defining the enzootic state.

4.e) <u>Tables; Charts</u>

Table I. Duration of the epizootic

The table gives the duration (in days) for which the epizootic lasted, having begun on day 0 with a small proportion of infected animals. Two different values of initial infection level, and three different values of mortality rates were used in the simulation. The epizootic was considered to have completed its course by the somewhat arbitrary criterion of the net day-to-day change (added over all the categories) was less than 0.00001.

	Initial Infection 0.001			Initial Infection 0.01		
Contact	Mortality			Mortality		
Rate	0.1	0.5	0.9	0.1	0.5	0.9
0.05	30	30	30	43	43	44
0.10	47	47	47	73	73	74
0.15	99	100	100	150	155	161
0.20	862	1140	2452	405	528	1070
0.25	422	432	410	311	330	323
0.30	268	264	238	216	214	192
0.35	205	198	177	169	164	144
0.40	169	162	145	142	135	119
0.45	147	140	126	123	117	103
0.50	131	125	112	110	104	92

4.f) Figures

The six figures (Fig.1 to Fig.6) referred to in the 'Results' section as well as in the 'Discussion and analysis' section have been appended at the end of the report. Each figure is suitably titled, labelled and provided with legend to make it self-explanatory.

4.g) Likely impact of the work on the scientific potential of our country

The modelling work described above is at a preliminary stage. Moreover, detailed data on the population structure, mortality rates, movement patterns etc. from the locations where PPRV outbreaks have occurred is not yet available. It would therefore be premature to evaluate the impact of the work carried out so far on the scientific potential of our country.

4.h) Bibliography

1. Shaila M.S., Purushothamam n V., Bhavsar D., Venugopal K. and Venkatesan R.A. (1989). *Vet. Rec.* 125 : U602.

2. Shaila M.S., Venugopal K., Purushothamam V. and Venkatesan R. A. (1990). *Indian Vet. J.* 67 : 385-386.

3. Losos, G.J. (1981). 'Infectious tropical diseases of domestic animals' (Longmans)

4. Scott, G.R. (1990). in 'Virus infections of Vertebrates vol. 3 : Virus infections of ruminants', eds. Dinter, Z. and Morein, B. (Elsevier)

5. Ramachandran, S. and Nayak, R. (1992). *Curr. Sci.* 63 : 55

6. James A.D. and Rossiter P.B. (1989). *Trop. Anim. Health Prod.* 21 : 59-68.

7. Tille A., Lefevre C.L., Pastoret P.P. and Thiry E. (1991). *Epidemio. Infect.* 107 : 441-452.

8. Taylor, W.P. (1984). *Prev. Vet. Med.* 2 : 157-166

9. Bailey, N.T.J. (1975). 'The mathematical theory of infectious diseases and its applications' (Charles Griffin)

10. Anderson, R.M. and May, R. M. (1982). 'The population biology of infectious diseases' (Springer Verlag)

11. Anderson, Roy M. (1982). 'Population dynamics of infectious diseases' (Chapman and Hall)

PART - III

1. **Recommendations including remedial measures relevant to the environmental problems studied under the scheme :**

The investigations envisioned in this project are yet to reach a stage when recommendations can be made.

2. **List of research papers published/accepted in the research work done under the scheme :**

Nil

3. **Whether any research fellow associated with the scheme has been awarded Ph.D. etc :**

Not applicable.

FIG. 1

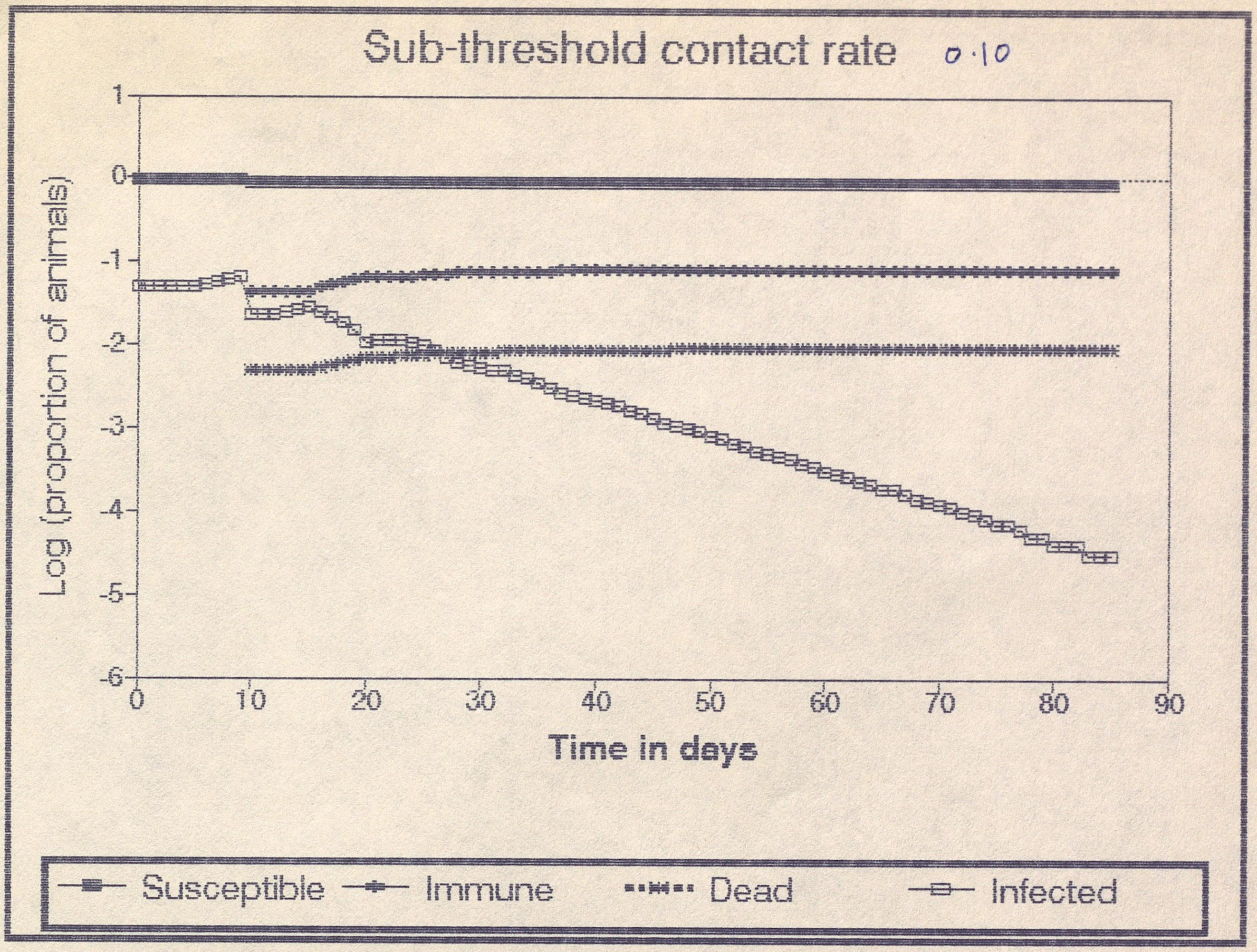

Sub-threshold contact rate 0·10
Log (proportion of animals)
1
0
-1
-2
-3
-4
-5
-6
0
10
20
30
40
50
60
70
80
90
Time in days
Susceptible
Immune
Dead
Infected

FIG. 2

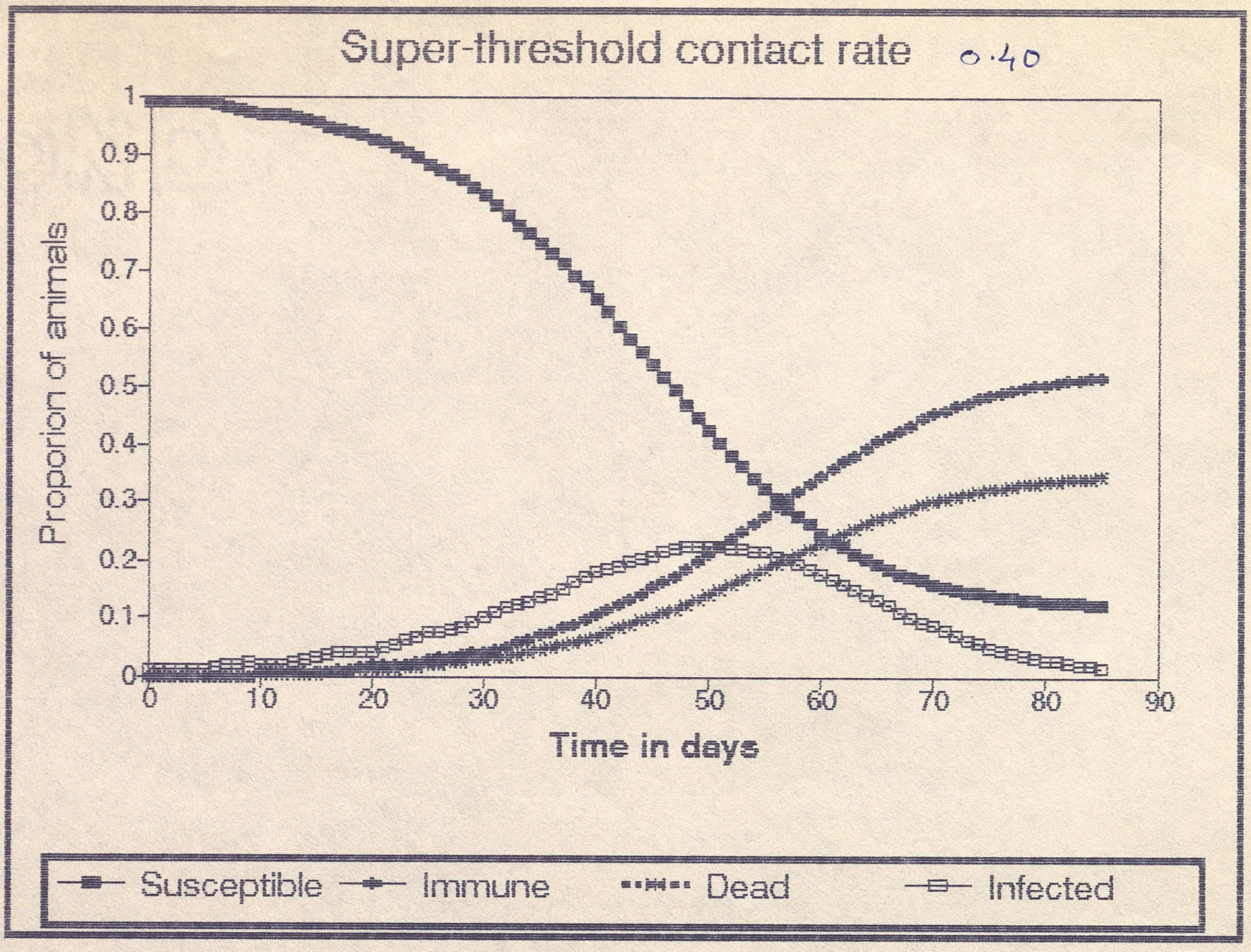

Super-threshold contact rate 0.40
Proporion of animals
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
10
20
30
40
50
60
70
80
90
Time in days
Susceptible
Immune
Dead
Infected

FIG. 3

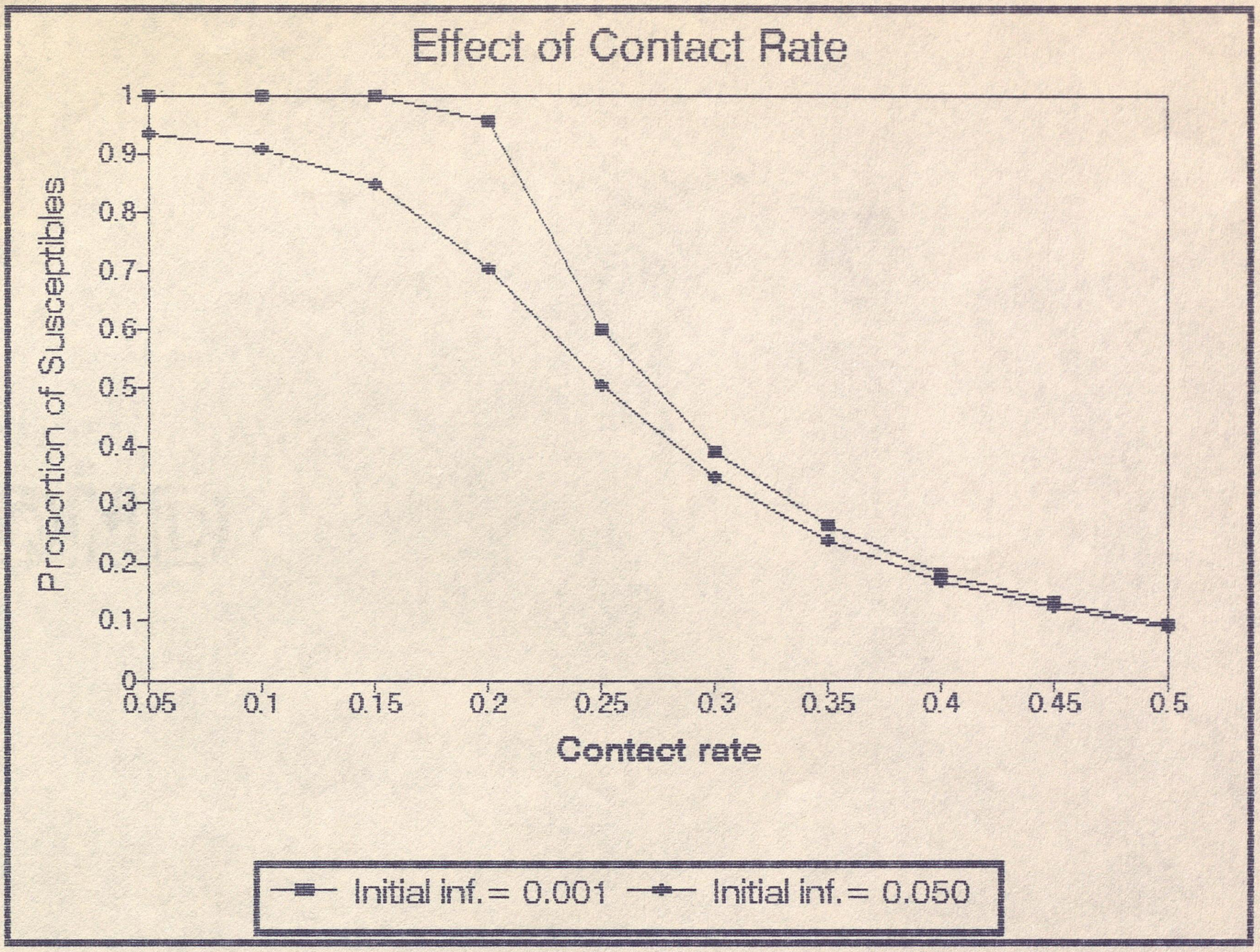

Effect of Contact Rate
Proportion of Susceptibles
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
0.5
Contact rate
Initial inf. = 0.001
Initial inf. = 0.050

FIG. 4

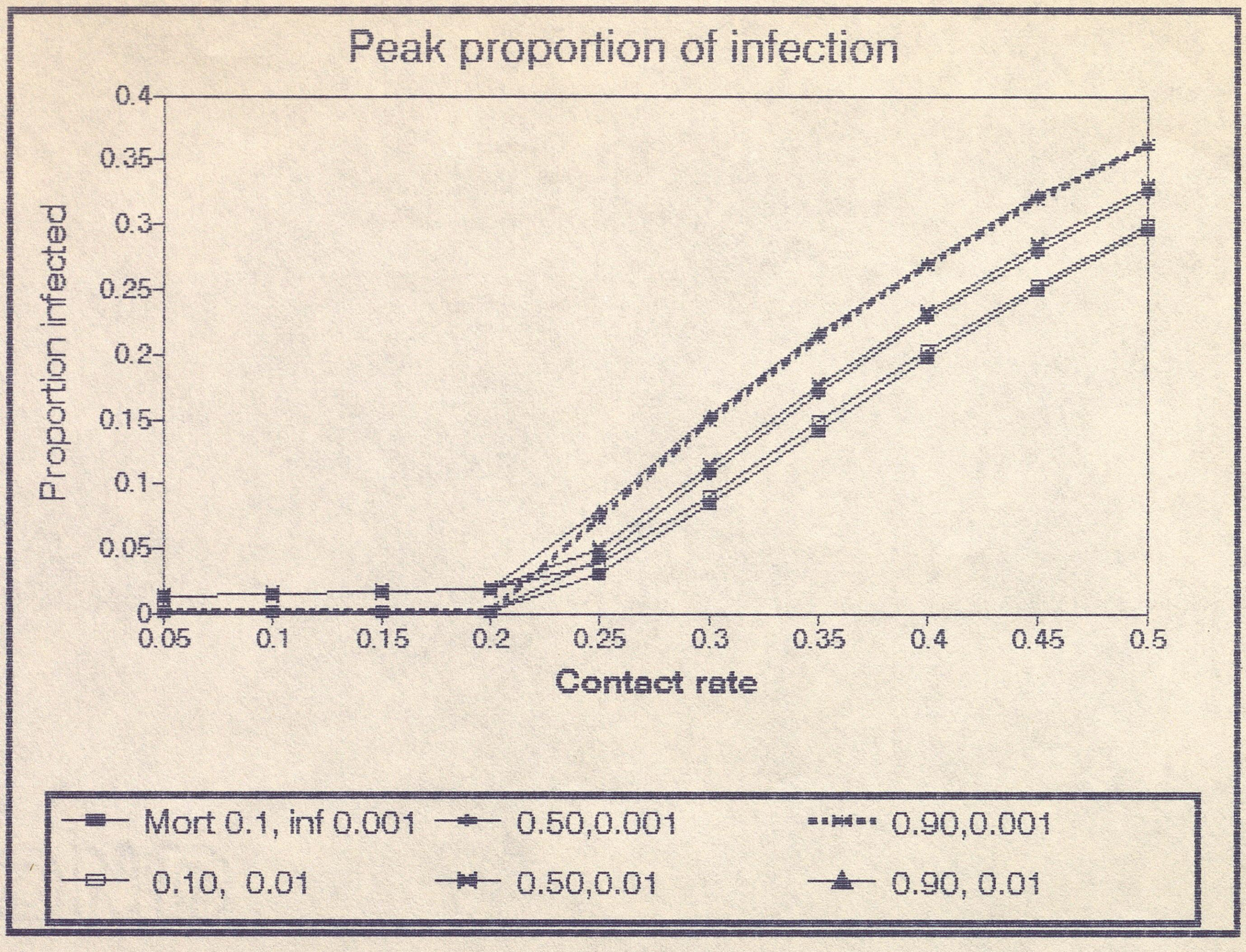
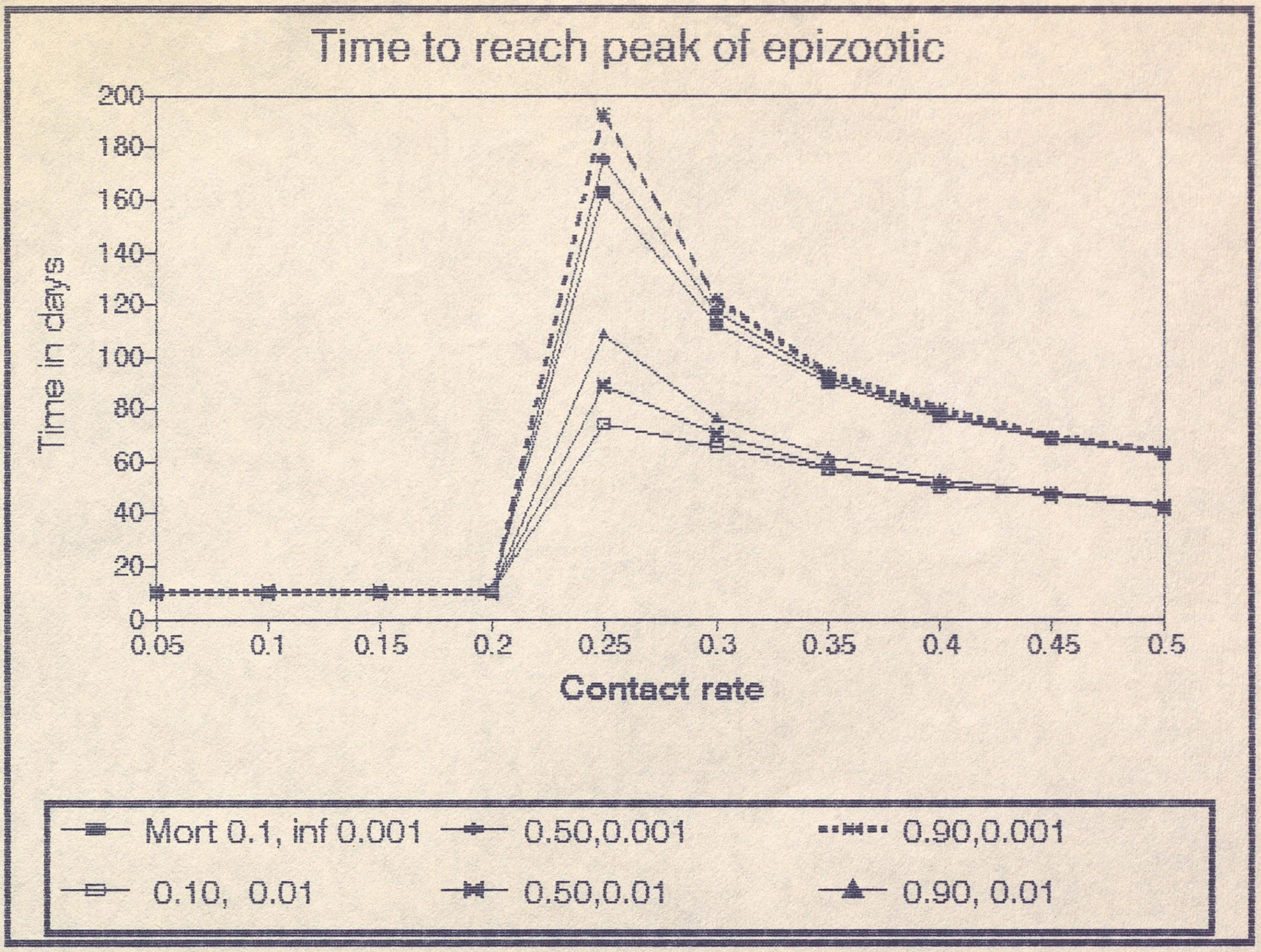
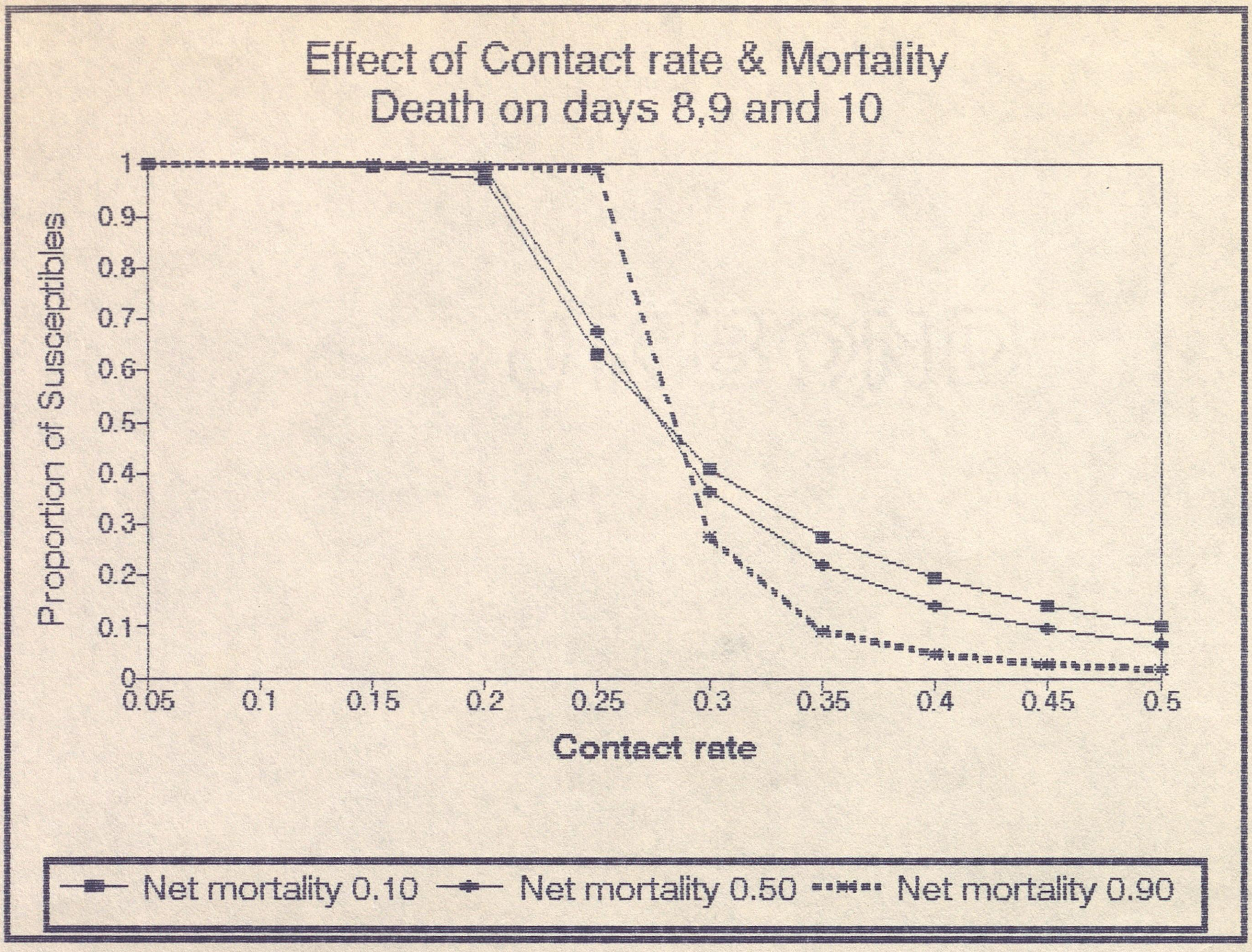

Peak proportion of infection
Proportion infected
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
0.5
Contact rate
Mort 0.1, inf 0.001
0.50,0.001
0.90,0.001
0.10, 0.01
0.50,0.01
0.90, 0.01

FIG. 5



Time to reach peak of epizootic
Time in days
0
20
40
60
80
100
120
140
160
180
200
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
0.5
Contact rate
Mort 0.1, inf 0.001
0.50,0.001
0.90,0.001
0.10, 0.01
0.50,0.01
0.90, 0.01

FIG. 6



Effect of Contact rate & Mortality
Death on days 8,9 and 10
Proportion of Susceptibles
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
0.5
Contact rate
Net mortality 0.10
Net mortality 0.50
Net mortality 0.90

EPIDEMIOLOGICAL MODELLING OF PPRV AND RINDERPEST OUTBREAKS

This project is being carried out in collaboration with Prof. M.S. Shaila of the Department of Microbiology and Biology, Indian Institute of Science.

PART - II

Cell

1. Preface

Infection of domestic as well as wild animals by the Rinderpest Virus (RV) has been known in India since the last century. Reports of the outbreaks of Peste des Petits Ruminants Virus (PPRV) are, however, of a recent origin (Shaila et al 1989, Shaila et al 1990). As implied by the name, PPRV affects small ruminants like goats and sheep, unlike RV, which has a broader host-range, which includes cattle in addition to goats and sheep. Nevertheless, PPRV is highly infectious and leads to high levels of morbidity and mortality (Losos, 1981; Scott, 1990). Over the last few years, PPRV seems to be taking an increasingly heavy toll in Karnataka, Tamil Nadu, Andhra Pradesh and Maharashtra (Shaila et al, manuscript in preparation; see also Ramachandran and Nayak, 1992).

There have been several attempts to model the epidemiology of RV (James and Rossiter 1989, Tille et al 1991). However, there has been little or no work to model the outbreaks of PPRV, especially in India. The regular migration of nomadic communities, which in turn leads to the movement of sheep and goats over large distances, makes the problem of modelling PPRV more challenging. The structure of the metapopulation of small ruminants - population of a say district being subdivided into demes at the village level, with some amount of mixing brought about by the weekly markets where livestock of many adjoining villages are bought and sold; or the metapopulation of a village divided into demes corresponding to individual households, where mixing takes place at the common grazing grounds - is likely to lead to complex patterns of the spread of PPRV epidemics.

Ref Losos, 1981; Scott, 1990

It is known that animals immunized against RV are able to resist challenge by PPRV and vice versa. Against this backdrop, it would be interesting to investigate the competition between RV and PPRV in the arena of a rural livestock ecosystem - cattle, sheep, goats etc. - both from an epidemiological as well as an evolutionary point of view. It may be possible to extend these studies to include the interaction between domestic and wild animals (e.g. gaur) which occurs at the periphery of wildlife sanctuaries.

Efforts at designing vaccines against RV and PPRV using the recombinant DNA technology have already been under way at a few laboratories in India and the world, and preliminary results have been encouraging (M.S. Shaila, unpublished results). The mathematical models developed to describe PPRV epidemics may also be generalized to include the effects of vaccination. These would be helpful in devising optimal vaccination strategies so as to minimize the risks of the outbreaks of RV or PPRV epidemics in a cost-effective manner.

DEE-PEE COMPUTER FORMS PVT LTD DEHRADUN

2. Abstract of the project

A deterministic mathematical model has been developed to investigate the propogation of a PPRV epizootic in an isolated, non-reproucing herd of arbitrary size. The parameters corresponding to incubation period and virus excretion period were obtained from published literature. Since different strains of PPRV, different geographical areas and different breeds of hosts show considerable variations in the proportion of animals succumbing to the disease, the model was run for three different levels (high, medium and low, i.e., 0.9, 0.5 and 0.1) of mortality rates. As The contact rate/transmission efficiency, this parameter was also varied over a wide range of values ~~due to lack of~~ published information. For every combination of parameter values and ~~for varying~~ levels of the initial infection rate, the model simulated daily changes in the proportion of susceptible, infected, infectious, recovered/immune and dead animals, till they reached nearly constant values.

since little or no is available for ~~this~~ quantity.

It is seen that more or less independently of the initial infection level, but with a sensitive dependence on the contact rate, the infection either peters off, or builds up into an epizootic with a large proportion of animals contacting the disease. A set of simulations was carried out to determine the dependence of onset, magnitude and duration of the epizootic on the virulence level and the contact rate/transmission efficiency of the PPR Virus.

3. Highlights of the findings achieved in the project

(i) A modified approach was developed for evaluating the probability of disease transmission, based on statistically more appropriate Poisson distribution, in contrast to the binomial distribution based investigations of the dynamics of rinderpest epizootics reported in veterinary literature.
(ii) In conformity with other epidemiological models, a threshold effect is observed for the contact rate / transmission efficiency such that for values even slightly lower than the threshold, the initial infection dwindles away, and for even slightly higher values, an epizootic sweeps through the herd. This emphasizes the need for developing more detailed, explicit and reliable theoretical as well as experimental techniques for determining the values of this crucial parameter for real-life situations.
(iii) Interestingly, the magnitude of the epizootic is higher for more virulent strains (higher mortality rates).

4. Detailed report of the work done on the project

a) Summary of the objectives

(i) To set up detailed deterministic models for the spread of PPRV in an isolated herd, and explore the range of parameters (permitted by the available data) such as duration of infection, contact rate, extent of production of infective particles, mortality rates etc. which would lead to outbreaks.

(ii) Modify the models to include stochastic variations, to obtain estimates of the reliability of the predictions made from the deterministic models.

(iii)Generalize the models to include spatial movements (and mixing) of the herds.

(iv) Investigate the effects of subjecting the populations to various

DEE PEE COMPUTER FORMS PVT LTD DEHRADUN

degrees of vaccination.

(v) Explore the competition between PPRV and RV from epidemiologcal as well as evolutionary perspectives.

b) <u>Methodology</u>

An isolated, nonreproducing herd of arbitrary size is assumed to contain ~~N~~ freely and randomly mixing individual animals. ~~Four~~ Five main categories into which the animals can be divided are :

* Susceptible, who have not yet contacted the disease,
* Infected animals, who have not yet become infective,
* Diseased animals, who excrete virus and are thus infective
* Recoverd animals, who are immune against further infection, and
* Animals which have died due to the disease.

T=0

Initially (time=0), the herd is assumed to contain only susceptible animals, except for a small proportion of introduced infected animals. The PPRV infection follows an approximately five day incubation period where the animals are not infective. In the next three to five days, the animals excrete virus (Losos, 1981; Taylor, 1984) and are therefore able to produce infections in other animals which come in contact with them. At the end of this period, a proportion 'd' of these infected animals die, and the remaining proportion '(1-d)' recover into an immune state. A single contact with an infected animal is assumed to be adequate for contacting the disease. Each infected animal is assumed to make an average of 'c' contacts with other animals (a value of c less than 1.0 can thus model a low transmission efficiency). If Ps, Pinf, Ptr and Pim denote the proportions of susceptible, infected (but not infective), infective (transmitting) and immune animals respectively at time 'T', the average number of contacts, 'Cav', recieved by an animal is given by

$$Cav = Ptr / (Ps + Pinf + Ptr + Pim)$$

The number of contacts recieved by the animals is assumed to follow a Poisson distribution. Hence, the probability of an animals recieving ZERO contacts is Exp (- Cav). The probability of contacting the disease, 'inf', is therefore the probability of recieving AT LEAST one contact, which is given by

$$inf = 1.0 - Exp (- Cav)$$

A proportion (Ps X inf) of the susceptible animals is thus seen to enter the infected state at time 'T+1'.

A FORTRAN program was developed to simulate the above situation for a given set of parameter values. The run was continued till the day to day changes in the proportion of animals in each of the above state were smaller than a prespecified value. In situations when an epizootic developed in the population, the program also recorded the magnitude (highest proportion of infected+infective animals reached) of the epizootic and the day on which the peak was attained.

In a modified version of the model, infective animals were assumed to have a constant daily mortality rate over the period 3-5 days from their becoming infective (8-10 days from the infection date). For a comparison of the results of the two models, the parameters were so chosen that the net mortality rate was identical in both the cases.

g) Likely impact of the work on the scientific potential of our country

The modelling work described above is at a preliminary stage. Moreover, detailed data etc. on the population structure, mortality rates, movement patterns etc. from the locations where PPRV outbreaks have occurred is not yet available. It would therefore be premature to evaluate the impact of the work carried out so far on the scientific potential of our country.

h) Bibliography

1. Shaila M.S., Purushothamam V., Bhavsar D., Venugopal K. and Venkatesan R.A. (1989). *Vet. Rec.* 125 : U602.

2. Shaila M.S., Venugopal K., Purushothamam V. and Venkatesan R. A. (1990). *Indian Vet. J.* 67 : 385-386.

3. Losos, G.J. (1981). 'Infectious tropical diseases of domestic animals' (Longmans)

4. Scott, G.R. (1990). in 'Virus infections of Vertebrates'*, eds. Dinter, Z. and Morein, B. (Elsevier)
* vol. 23 : virus infections of Ruminants

5. Ramachandran, S. and Nayak, R. (1992). *Curr. Sci.* 63 : 55

6. James A.D. and Rossiter P.B. (1989). *Trop. Anim. Health Prod.* 21 : 59-68.

7. Tille A., Lefevre C.L., Pastoret P.P. and Thiry E. (1991). *Epidemio. Infect.* 107 : 441-452.

8. Taylor, W.P. (1984). *Prev. Vet. Med.* 2 : 157-166

9. Baily NTJ, Math. Theo of inf Dis

10. Anderson & May —

PART - III

1. Recommendations including remedial measures relevant to the environmental problems studied under the scheme :

The investigations envisioned in this project are yet to reach a stage when recommendations can be made.

2. List of research papers published/accepted in the research work done under the scheme :

Nil

3. Whether any research fellow associated with the scheme has been awarded Ph.D. etc :

Not applicable.

RESULTS

The overall behaviour of the dynamics of the spread of PPR epizootic in a herd is similar to standard epidemiological models (Bailey, 1975; Anderson and May, ~~1979~~ 1982). The quantity which decides whether an epizootic will take off or not is the net 'reproductive rate' of the virus, ~~in terms of~~ which is equal to the average number of new infections produced by a single infected individual. This, in turn, is a function of the contact/transmission rate, and in many instances, of the mortality rate as well. When the net 'reproductive rate' is smaller than 1.0, a small initial infection gradually dwindles away (as seen in Fig.1, for contact rate of 0.10). On the other hand, for values of the reproductive rate greater than 1.0, an epizootic builds up (Fig.2 for contact rate 0.40). The proportion of infected individuals increases to a peak value, and then decreases since the infected individuals either recover into an immune state or die, and the number of susceptibles keeps on decreasing, so there are fewer individuals who can be infected.

One of the ways in which the epizootic can be quantified is the proportion of susceptible individuals remaining in the population after the epizootic has run its course. This value is depicted as a function of contact rate in Fig.3 for two different values of initial infection. The threshold-like property of the contact rate is clearly seen, with a sharper transition when the initial infection is low. Since in the first version of the model death can take place only on the 10th day after infection, ~~there is no dependence of the number~~ the proportion of susceptibles ~~individuals on~~ is independent of the mortality rate.

Three other descriptors of an epizootic are (a) magnitude of the peak , i.e., the maximum proportion of infected individuals reached during the course of the epizootic, (b) the time to reach the peak and (c) the duration of the epizootic i.e., the time at which there is little or no net change in proportions of the different categories of animals. The peak magnitude increases with increasing contact rate, once the threshold value is crossed (Fig.4). The initial level of infection seems to have little or no effect; ~~as~~ the pairs of curves in Fig.4 are close together. The figure also shows that increasing rates of mortality lead to lower peak values. On the other hand, as seen from Fig. 5, a smaller initial infection implies longer time to attain the peak, as expected (top three curves vs bottom three curves). The mortality rate has an opposite effect, such that higher the mortality, faster is the peak reached (Fig.5). The variation in the duration of the epizootic with contact rate, with initial infection levels and with different mortality rates is given in Table I. For super-threshold contact rate, the duration increases with increasing contact rates, with increasing level of initial infection and decreases with increasing mortality rates.

A second version of the model permits death to take place on day 8, 9 or 10 from infection, while maintaining the net mortality at a prespecified value. As a result of this modification, animals are infective, on an average, for a relatively shorter duration. The net reproductive rate thus becomes a function of the mortality rate as well, and decreases with increasing mortality. This effect is clearly ~~seen~~ ~~in~~ evident from Fig.6, where the threshold values of contact rates has ~~shifted to a higher value~~ for higher values of mortality rates. ~~increased~~ are seen ~~to have~~ shifted to the right

Discussion and Analysis

An important detail in which this model differs from the previous models of rinderpest epizootics is the use of Poisson distribution for computing the range of contacts experienced by the animals, in contrast to the binomial distribution used earlier. Especially for large herd sizes, the Poisson model is statistically somewhat more appropriate. It is also more reasonable from a biological point of view, since a range of values of contacts 0,1,.... is permitted in this formulation, in contrast to the fixed number of contacts experienced by each animal in the earlier formulations. It is also relatively straightforward to extend this formalism to simulate the more realistic clumped distributions, and this would be taken up in the next phase where the spatial dimension may be explicitely introduced.

One of the interesting patterns seen from the present model is the effect of mortality rate on the peak value of the epizootic, and on the time needed to reach it. Higher levels of mortality lead to higher peak values, but at a relatively later time. This may possibly be due to the assumption of a fixed, nonreproducing herd. Higher mortality rates reduce the population faster, and a lower number of immune animals leads to an effectively higher number of contacts per animal and hence a faster transmission. A lower mortality rate on the other hand converts animals from susceptible to immune state with a higher efficiency, and there being no new susceptible animals, a higher proportion of infected animals cannot be obtained. A more realistic model to be developed in the next phase would include reproduction as well as influx of new animals by immigration. It would be desirable to see if ~~this~~ the present pattern of mortality dependence is still retained.

If c is the contact rate, then in the first model, since an infected individual is infective for 5 days, it will on an average infect 5 ~~X~~ c individuals before it dies or recovers. Thus, the threshold will be reached when 5 X c is greater than 1.0, or when c is greater than 0.2. This is clearly borne out by Fig. 3. On the other hand, in the second model, if m is the mortality rate per day, an individual will be infective for 3 days with probability m, for 4 days with probability m X (1-m), and for 5 days with probability (1-2m+m*m). The net reproductive rate will then be given by

c ~~X~~ (5 - 3m + m*m)

This is less than 5 ~~X~~ c for all the values of m, and in fact monotonically decreases from 5c to 3c as m increases from 0 to 1. The threshold thus increases from 0.2 for m=0 to 0.33 for m=1. This differnce in thresholds is clearly seen in Fig.6 especially for the two mortality rates of 0.10 and 0.90.

One of the objectives of this project is to evaluate the effect of different vaccination strategies. Preliminary simulations indicate that vaccinating a certain proportion of individuals brings down the peak infection by a corresponding ammount. This in turn implies that vaccination on a large scale may be needed to ward off epizootics, and this does not seem prima facie a very cost-effective approach.

A question of considerable biological as well as practical interest would be to determine the factors/parameters which lead to persistence (enzootic) of PPRV in the population, without either dying out or leading to epizootics. The current 'closed population' model is clearly unsuitable for this purpose. Earlier workers had somewhat arbitrarily equated persistence beyond 12 months as indicative of enzootic state. A geographically structured population with some episodes of mixing, to be investigated in the next phase, may lead to a better criterion for defining the enzootic state.

DEE PEE COMPUTER FORMS PVT LTD DEHRADUN

Fig. 1

Sub-threshold contact rate

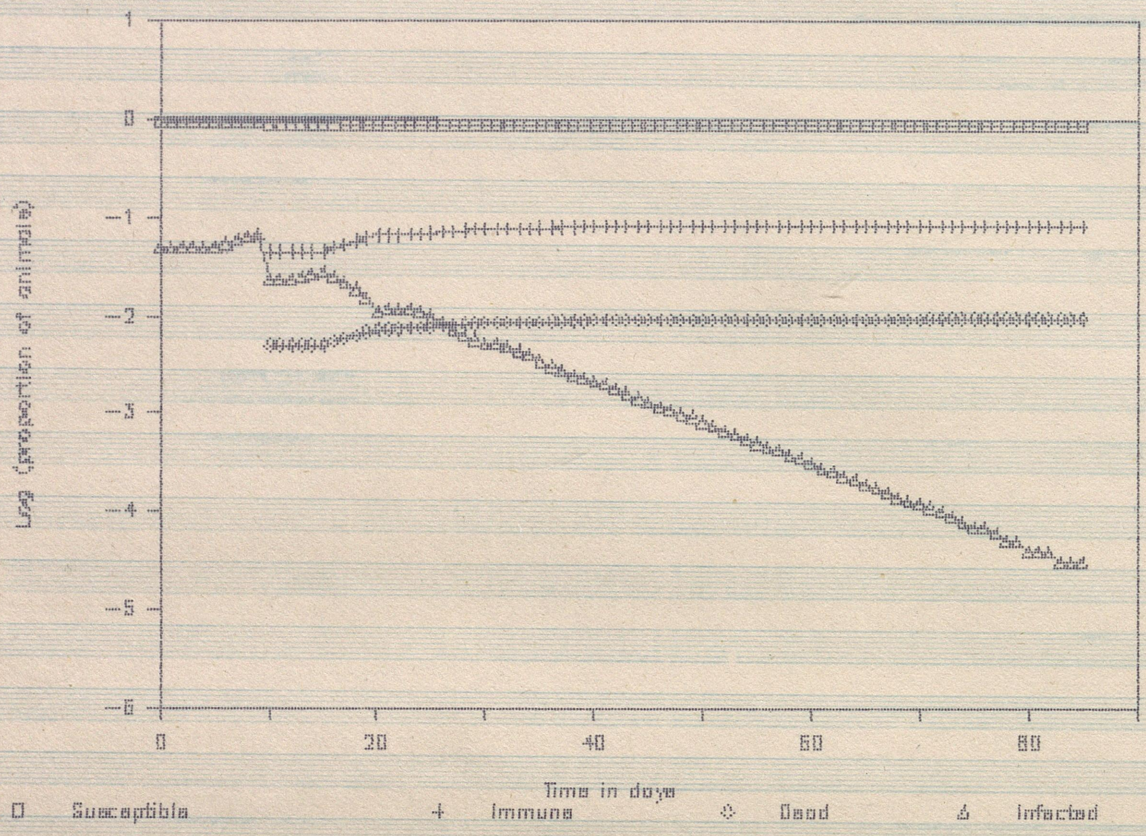
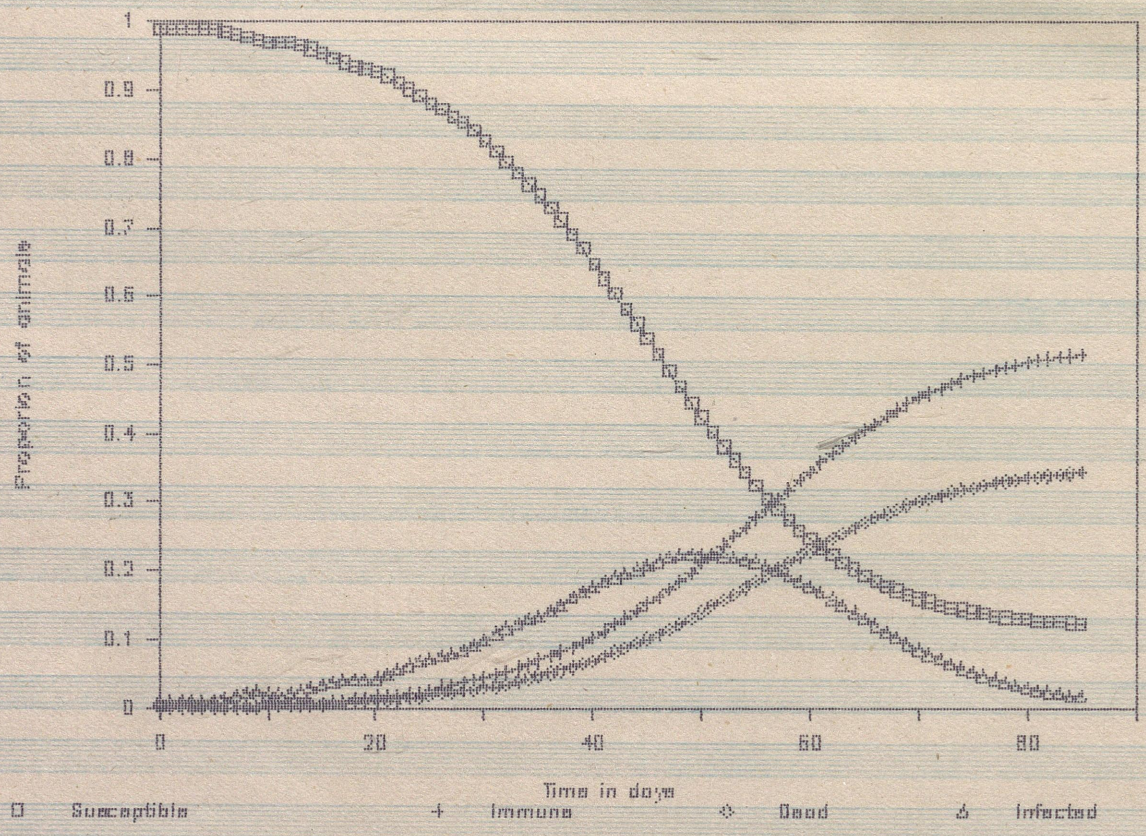


Fig. 2

Super-threshold contact rate



DEE PEE COMPUTER FORMS PVT. LTD. DEHRADUN

Fig. 3

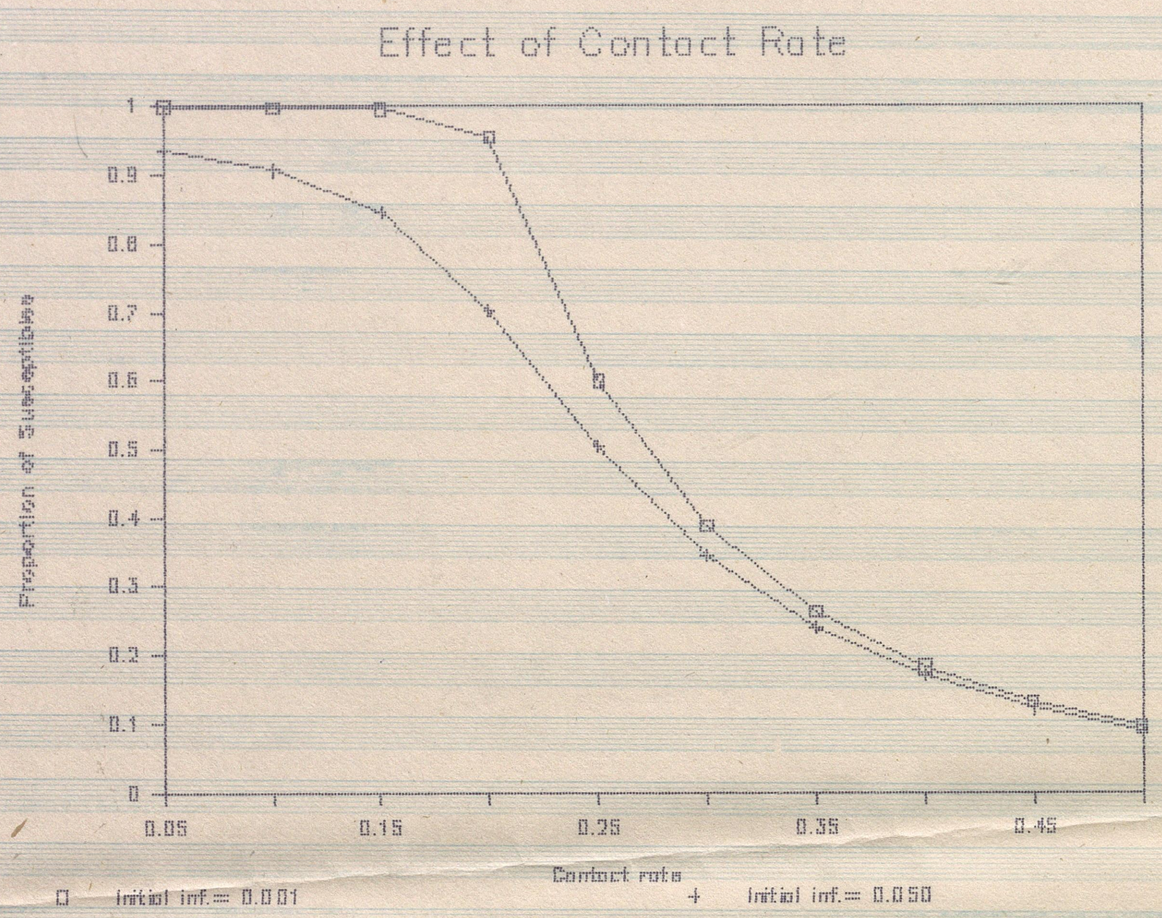
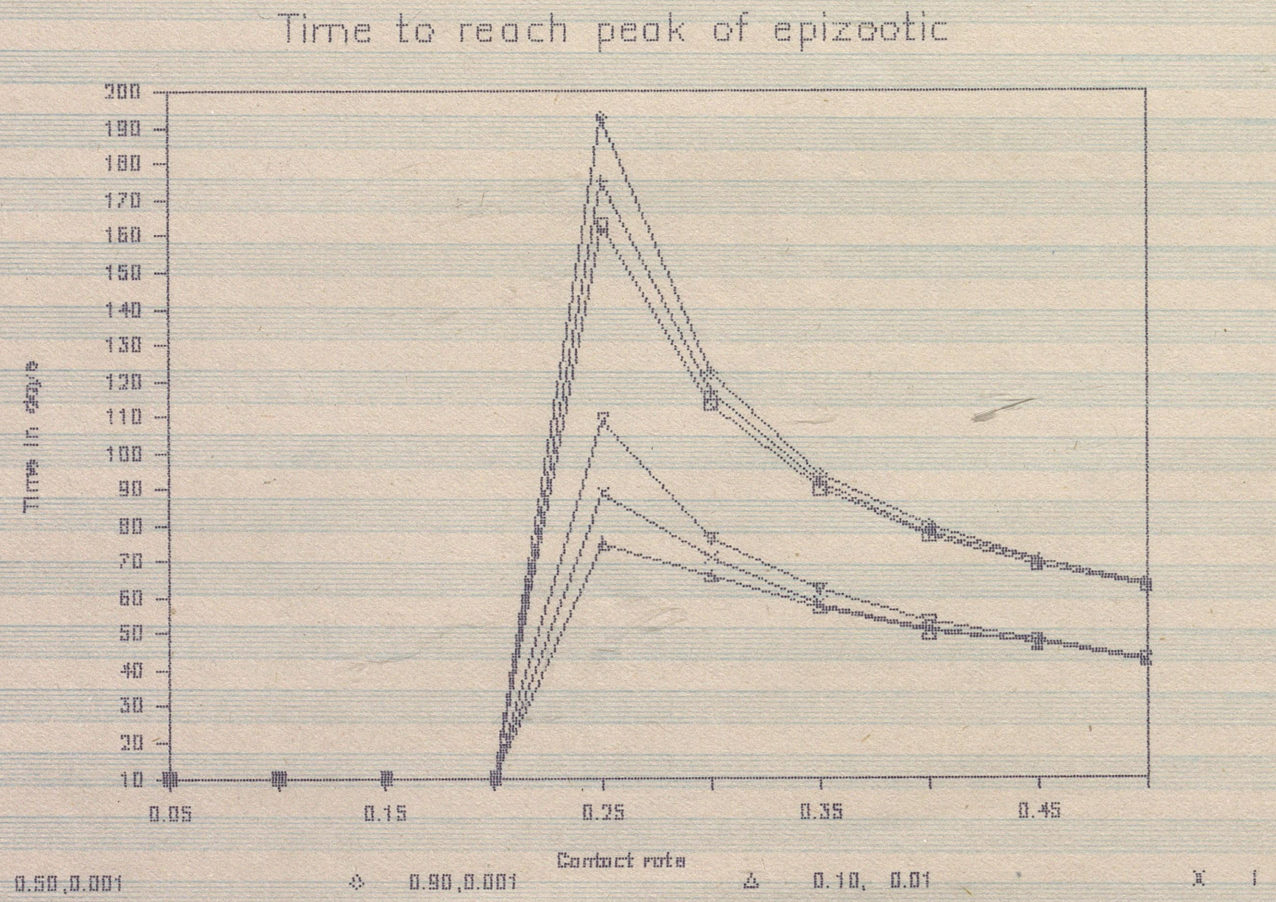


Fig. 5



DEE PEE COMPUTER FORMS PVT LTD DEHRADUN

Fig 4
Fig 5

Peak proportion of infection

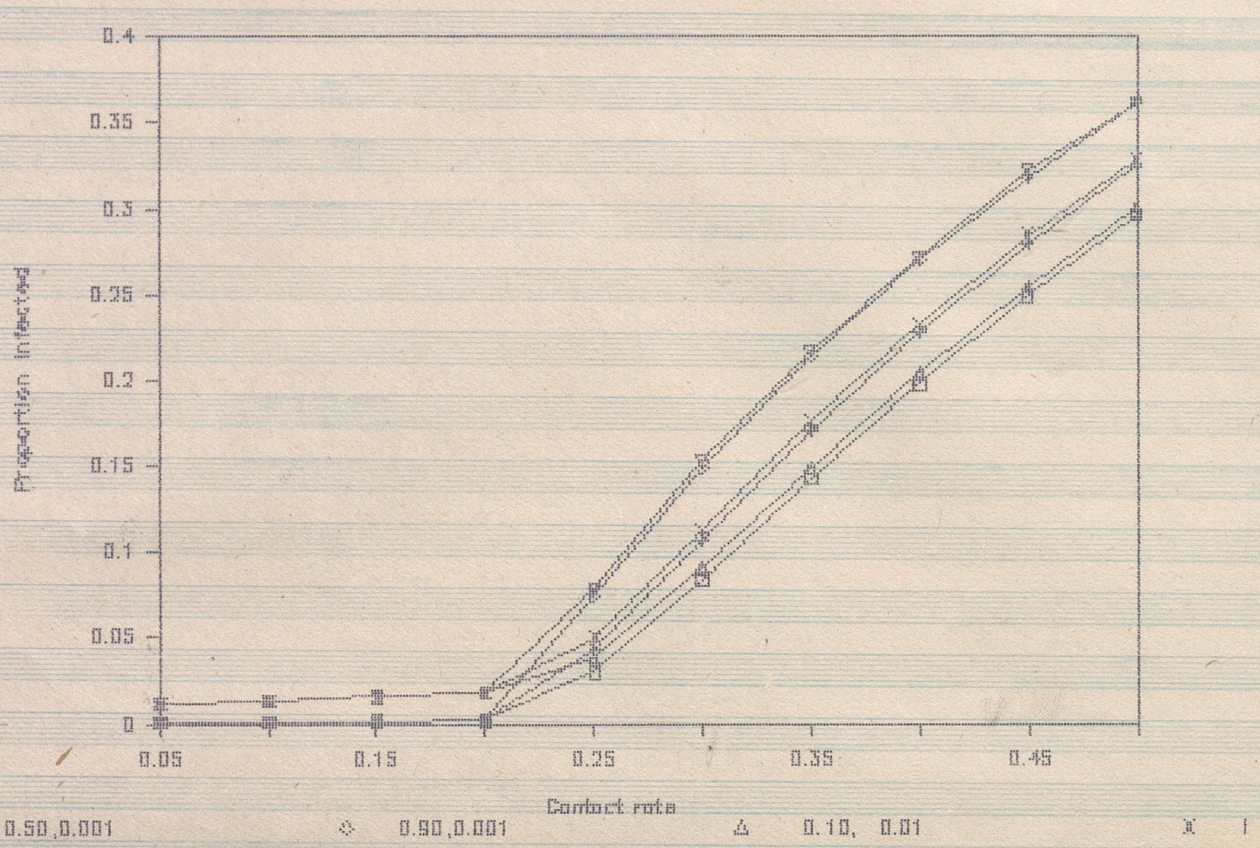
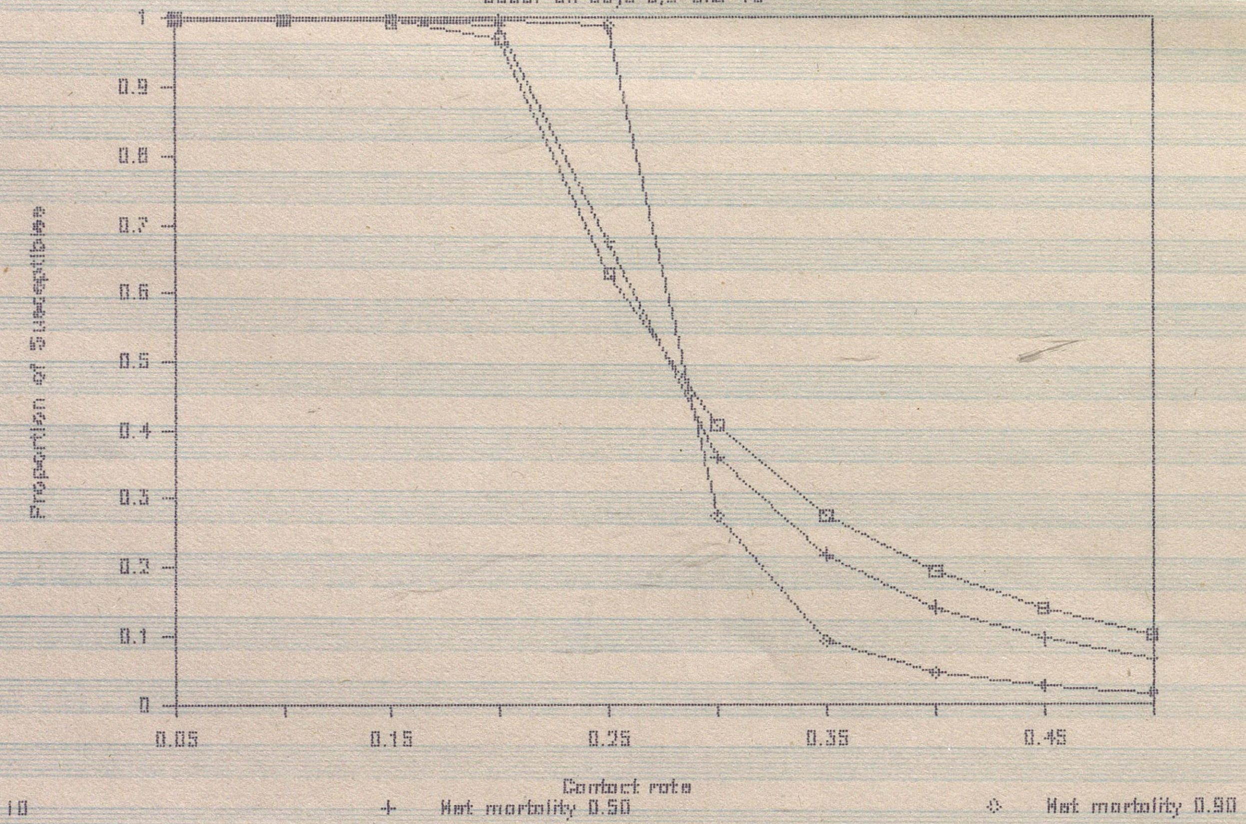
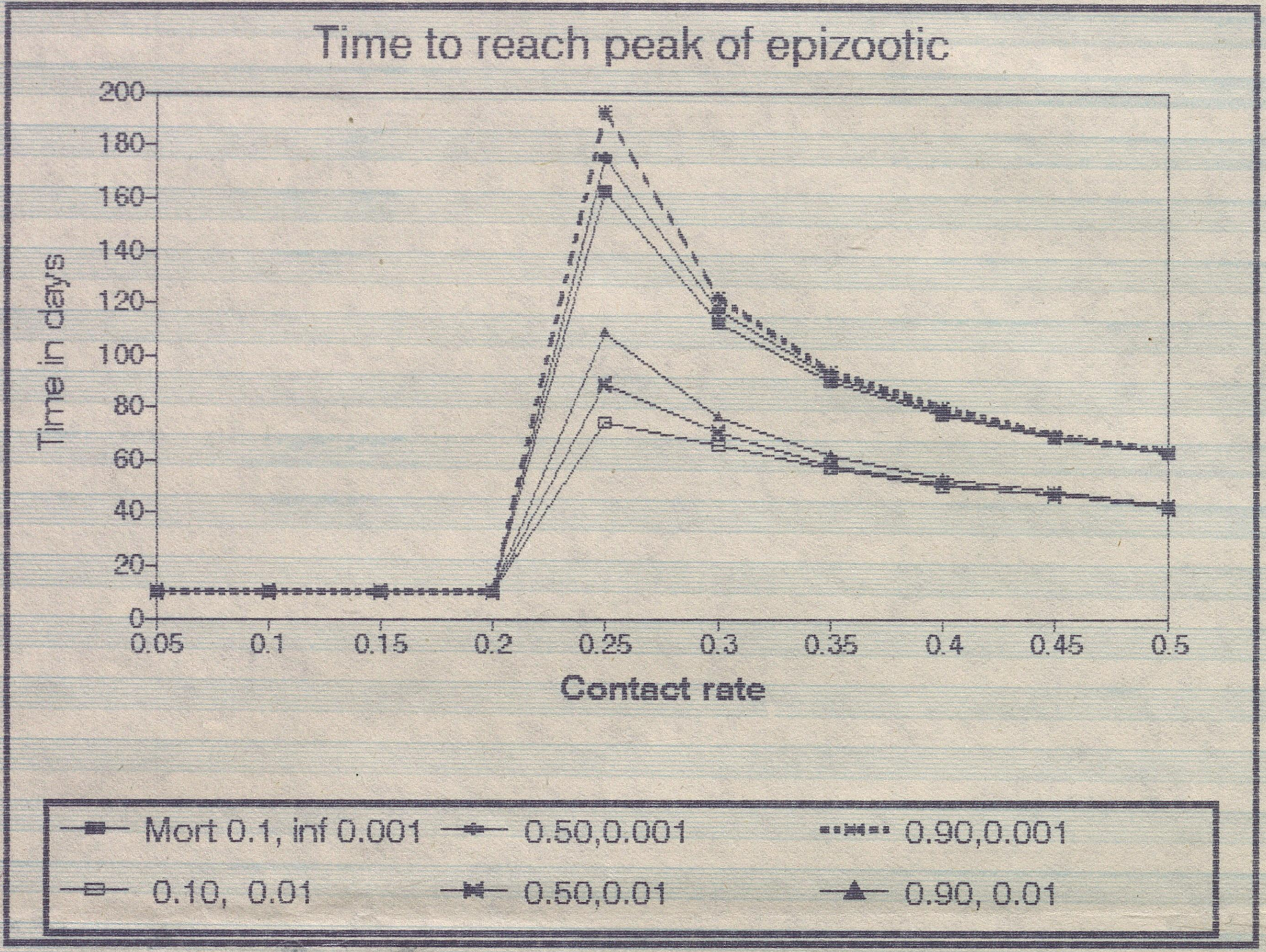


Fig. 6

Effect of Contact rate & Mortality

Death on days 8,9 and 10





Obtain figs in QPRO such that 2 fig/page

FIG1PPR.W21

FIG6PPR.W21

DEE-PEE COMPUTER FORMS PVT LTD DEHRADUN

EPIDEMIOLOGICAL MODELLING OF PPRV AND RINDERPEST OUTBREAKS

This project is being carried out in collaboration with Prof. M.S. Shaila of the Department of Microbiology and Cell Biology, Indian Institute of Science, Bangalore.

PART - II

1. Preface

Infection of domestic as well as wild animals by the Rinderpest Virus (RV) has been known in India since the last century. Reports of the outbreaks of Peste des Petits Ruminants Virus (PPRV) are, however, of a recent origin (Shaila et al 1989, Shaila et al 1990). As implied by the name, PPRV affects small ruminants like goats and sheep. Rinderpest virus primarily affects cattle, but has a broader host-range, which includes goats and sheep as well. Nevertheless, PPRV is highly infectious and leads to high levels of morbidity and mortality (Losos, 1981; Scott, 1990). Over the last few years, PPRV seems to be taking an increasingly heavy toll in Karnataka, Tamil Nadu, Andhra Pradesh and Maharashtra (Shaila et al, manuscript in preparation; see also Ramachandran and Nayak, 1992).

There have been several attempts to model the epidemiology of RV (James and Rossiter 1989, Tille et al 1991). However, there has been little or no work to model the outbreaks of PPRV, especially in India, where both the viruses cause separate cycles of infection in small ruminants. The regular migration of nomadic communities, which in turn leads to the movement of sheep and goats over large distances, makes the problem of modelling PPRV more challenging. The structure of the metapopulation of small ruminants

- population of a say district being subdivided into demes at the village level, with some amount of mixing brought about by the weekly markets where livestock of many adjoining villages are bought and sold; or the metapopulation of a village divided into demes corresponding to individual households, where mixing takes place at the common grazing grounds - is likely to lead to complex patterns of the spread of PPRV epidemics.

It is known that animals immunized against RV are able to resist challenge by PPRV and vice versa (Losos, 1981; Scott, 1990). Against this backdrop, it would be interesting to investigate the competition between RV and PPRV in the arena of a rural livestock ecosystem - cattle, sheep, goats etc. - both from an epidemiological as well as an evolutionary point of view. It may be possible to extend these studies to include the interaction between domestic and wild animals (e.g. gaur) which occurs at the periphery of wildlife sanctuaries.

The mathematical models developed to describe PPRV epidemics may also be generalized to include the effects of vaccination. These would be helpful in devising optimal vaccination strategies so as to minimize the risks of the outbreaks of RV or PPRV epidemics in a cost-effective manner.

2. Abstract of the project

A deterministic mathematical model has been developed to investigate the propagation of a PPRV epizootic in an isolated, non-reproducing herd of arbitrary size. The parameters corresponding to incubation period and virus excretion period were obtained from published literature. Since different strains of PPRV, different geographical areas and different breeds of hosts show considerable variations in the proportion of animals succumbing to the disease, the model was run for three different levels (high, medium and low, i.e., 0.9, 0.5 and 0.1) of

mortality rates. Since little or no information is available for the contact rate/transmission efficiency, this parameter was also varied over a wide range of values. For every combination of parameter values and for varying levels of the initial infection rate, the model simulated daily changes in the proportion of susceptible, infected, infectious, recovered/immune and dead animals, till they reached nearly constant values.

It is seen that more or less independently of the initial infection level, but with a sensitive dependence on the contact rate, the infection either peters off, or builds up into an epizootic with a large proportion of animals contacting the disease. A set of simulations was carried out to determine the dependence of onset, magnitude and duration of the epizootic on the virulence level and the contact rate/transmission efficiency of the PPR Virus.

3. Highlights of the findings achieved in the project

(i) A modified approach was developed for evaluating the probability of disease transmission, based on statistically more appropriate Poisson distribution, in contrast to the binomial distribution based investigations of the dynamics of rinderpest epizootics reported in veterinary literature.

(ii) In conformity with other epidemiological models, a threshold effect is observed for the contact rate / transmission efficiency such that for values even slightly lower than the threshold, the initial infection dwindles away, and for even slightly higher values, an epizootic sweeps through the herd. This emphasizes the need for developing more detailed, explicit and reliable theoretical as well as experimental techniques for determining the values of this crucial parameter for real-life situations.

(iii) Interestingly, the magnitude of the epizootic is higher for more virulent strains (higher mortality rates).

4. Detailed report of the work done on the project

a) Summary of the objectives

(i) To set up detailed deterministic models for the spread of PPRV in an isolated herd, and explore the range of parameters (permitted by the available data) such as duration of infection, contact rate, extent of production of infective particles, mortality rates etc. which would lead to outbreaks.

(ii) Modify the models to include stochastic variations, to obtain estimates of the reliability of the predictions made from the deterministic models.

(iii)Generalize the models to include spatial movements (and mixing) of the herds.

(iv) Investigate the effects of subjecting the populations to various degrees of vaccination.

(v) Explore the competition between PPRV and RV from epidemiological as well as evolutionary perspectives.

b) Methodology

An isolated, nonreproducing herd of arbitrary size is assumed to contain freely and randomly mixing individual animals. Four main categories into which the animals can be divided are :

* Susceptible, who have not yet contacted the disease,

* Infected animals, who have not yet become infective,

* Diseased animals, who excrete virus and are thus infective

* Recovered animals, who are immune against further infection, and

* Animals which have died due to the disease.

Initially (time T=0), the herd is assumed to contain only susceptible animals, except for a small proportion of introduced infected animals. The PPRV infection follows an approximately five day incubation period where the animals are not infective. In the next three to five days, the animals excrete virus (Losos, 1981; Taylor, 1984) and are therefore able to produce infections in other animals which come in contact with them. At the end of this period, a proportion 'd' of these infected animals die, and the remaining proportion '(1-d)'recover into an immune state. A single contact with an infected animal is assumed to be adequate for contacting the disease. Each infected animal is assumed to make an average of 'c' contacts with other animals (a value of c less than 1.0 can thus model a low transmission efficiency). If Ps, Pinf, Ptr and Pim denote the proportions of susceptible, infected (but not infective), infective (transmitting) and immune animals respectively at time 'T', the average number of contacts, 'Cav', received by an animal is given by

$$Cav = Ptr / (Ps + Pinf + Ptr + Pim)$$

The number of contacts received by the animals is assumed to follow a Poisson distribution. Hence, the probability of an animals receiving ZERO contacts is Exp (- Cav). The probability of contacting the disease, 'inf', is therefore the probability of receiving AT LEAST one contact, which is given by

$$inf = 1.0 - Exp (- Cav)$$

A proportion (Ps X inf) of the susceptible animals is thus seen to enter the infected state at time 'T+1'.

A FORTRAN program was developed to simulate the above situation for a given set of parameter values. The run was continued till the day to day changes in the proportion of animals in each of the above state were smaller than a prespecified value. In situations when an epizootic developed in the population, the program also recorded the magnitude (highest proportion of infected+infective animals reached) of the epizootic and the day on which the peak was attained.

In a modified version of the model, infective animals were assumed to have a constant daily mortality rate over the period 3-5 days from their becoming infective (8-10 days from the infection date). For a comparison of the results of the two models, the parameters were so chosen that the net mortality rate was identical in both the cases.

c) <u>Results</u>

The overall behaviour of the dynamics of the spread of PPR epizootic in a herd is similar to standard epidemiological models (Bailey, 1975; Anderson and May, 1982). The quantity which decides whether an epizootic will take off or not is the net 'reproductive rate' of the virus, which is equal to the average number of new infections produced by a single infected individual. This, in turn, is a function of the contact/transmission rate, and in many instances, of the mortality rate as well. When the net 'reproductive rate' is smaller than 1.0, a small initial infection gradually dwindles away (as seen in Fig.1, for contact rate of 0.10). On the other hand, for values of the reproductive rate greater than 1.0, an epizootic builds up (Fig.2 for contact rate 0.40). The proportion of infected individuals increases to a peak value, and then decreases since the infected individuals either recover into an immune state or die, and the number of susceptibles keeps on decreasing, so there are fewer individuals who can be infected.

One of the ways in which the epizootic can be quantified is the proportion of susceptible individuals remaining in the population after the epizootic has run its course. This value is depicted as a function of contact rate in Fig.3 for two different values of initial infection. The threshold-like property of the contact rate is clearly seen, with a sharper transition when the initial infection is low. Since in the first version of the model death can take place only on the 10th day, the proportion of susceptibles is independent of the mortality rate.

Three other descriptors of an epizootic are (a) magnitude of the peak , i.e., the maximum proportion of infected individuals reached during the course of the epizootic, (b) the time to reach the peak and (c) the duration of the epizootic i.e., the time at which there is little or no net change in proportions of the different categories of animals. The peak magnitude increases with increasing contact rate, once the threshold value is crossed (Fig.4). The initial level of infection seems to have little or no effect; the pairs of curves in Fig.4 are close together. The figure also shows that increasing rates of mortality lead to higher peak values. On the other hand, as seen from Fig. 5, a smaller initial infection implies longer time to attain the peak, as expected (top three curves vs bottom three curves). The mortality rate has an opposite effect, such that higher the mortality, slower is the peak reached (Fig.5). The variation in the duration of the epizootic with contact rate, with initial infection levels and with different mortality rates is given in Table I. For super-threshold contact rate, the duration increases with increasing contact rates, with increasing level of initial infection and decreases with increasing mortality rates.

A second version of the model permits death to take place on day 8, 9 or 10 from infection, while maintaining the net mortality at a prespecified value. As a result of this modification, animals are infective, on an average, for a relatively shorter duration. The net reproductive rate thus becomes a function of the mortality rate as well, and decreases with increasing mortality. This effect is clearly evident from Fig.6, where threshold values of the contact rate have shifted to the right for higher values of mortality rates.

d) <u>Discussion and Analysis</u>

An important detail in which this model differs from the previous models of rinderpest epizootics is the use of Poisson distribution for computing the range of contacts experienced by the animals, in contrast to the binomial distribution used earlier. Especially for large herd sizes, the Poisson model is statistically somewhat more appropriate. It is also more reasonable from a biological point of view, since a range of values of contacts 0,1,.... is permitted in this formulation, in contrast to the fixed number of contacts experienced by each animal in the earlier formulations. However, as far as the present simulation is concerned, the assumption of 'c' contacts from an infected animal is equivalent to the earlier assumption of fixed number of contacts, since in the present deterministic version (corresponding to an infinite population), it is only the **mean** number of contacts that governs the dynamics. The stochastic model, to be explored in future, would be sensitive to the variation in the number of contacts as well, and is therefore likely to differ from the earlier stochastic models in a significant manner. It is also relatively straightforward to extend this formalism to simulate the more realistic clumped distributions, and this would be taken up in the next phase where the spatial dimension may be explicitly introduced.

One of the interesting patterns seen from the present model is the effect of mortality rate on the peak value of the epizootic, and on the time needed to reach it. Higher levels of mortality lead to higher peak values, but at a relatively later time. This may possibly be due to the assumption of a fixed, nonreproducing herd. Higher mortality rates reduce the population faster, and a lower number of immune animals leads to an effectively higher number of contacts per animal and hence a faster transmission. A lower mortality rate on the other hand converts animals from susceptible to immune state with a higher efficiency, and there being no new susceptible animals, a higher proportion of infected animals cannot be obtained. A more realistic model to be developed in the next phase would include reproduction as well as influx of new animals by immigration. It would be desirable to see if the present pattern of mortality dependence is still retained.

If c is the contact rate, then in the first model, since an infected individual is infective for 5 days, it will on an average infect 5c individuals before it dies or recovers. Thus, the threshold will be reached when 5c is greater than 1.0, or when c is greater than 0.2. This is clearly borne out by Fig. 3. On the other hand, in the second model, if m is the mortality rate per day, an individual will be infective for 3 days with probability m, for 4 days with probability m(1-m), and for 5 days with probability (1-2m+m*m). The net reproductive rate will then be given by

$$c\,(\,5 - 3m + m*m\,)$$

This is less than 5c for all the values of m, and in fact monotonically decreases from 5c to 3c as m increases from 0 to 1. The threshold thus increases from 0.2 for m=0 to 0.33 for m=1. This difference in thresholds is clearly seen in Fig.6 especially for the two mortality rates of 0.10 and 0.90.

One of the objectives of this project is to evaluate the effect of different vaccination strategies. Preliminary simulations indicate that vaccinating a certain proportion of individuals brings down the peak infection by a corresponding amount. This in turn implies that vaccination on a large scale may be needed to ward off epizootics, and this does not seem prima facie a very cost-effective approach.

A question of considerable biological as well as practical interest would be to determine the factors/parameters which lead to persistence (enzootic) of PPRV in the population, without either dying out or leading to epizootics. The current 'closed population' model is clearly unsuitable for this purpose. Earlier workers had somewhat arbitrarily equated persistence beyond 12 months as indicative of enzootic state. A geographically structured population with some episodes of mixing, to be investigated in the next phase, may lead to a better criterion for defining the enzootic state.

e) <u>Tables; Charts</u>

Table I. Duration of the epizootic

The table gives the duration (in days) for which the epizootic lasted, having begun on day 0 with a small proportion of infected animals. Two different values of initial infection level, and three different values of mortality rates were used in the simulation. The epizootic was considered to have completed its course by the somewhat arbitrary criterion of the net day-to-day change (added over all the categories) was less than 0.00001.

	InitialInfection 0.001			InitialInfection 0.01		
	Mortality			Mortality		
Contact Rate	0.1	0.5	0.9	0.1	0.5	0.9
0.05	30	30	30	43	43	44
0.10	47	47	47	73	73	74
0.15	99	100	100	150	150	161
0.20	862	1114	2452	405	528	1070
0.25	422	432	410	311	330	323
0.30	268	264	238	216	214	192
0.35	205	198	177	169	164	144
0.40	169	162	145	142	135	119
0.45	147	140	126	123	117	103
0.50	131	125	112	110	104	92

f) Figures

The six figures (Fig.1 to Fig.6) referred to in the 'Results' section as well as in the 'Discussion and analysis' section have been appended at the end of the report. Each figure is suitably titled, labeled and provided with legend to make it self-explanatory.

g) **Likely impact of the work on the scientific potential of our country**

The modelling work described above is at a preliminary stage. Moreover, detailed data on the population structure, mortality rates, movement patterns etc. from the locations where PPRV outbreaks have occurred is not yet available. It would therefore be premature to evaluate the impact of the work carried out so far on the scientific potential of our country.

h) **Bibliography**

1. Shaila M.S., Purushothaman V., Bhavsar D., Venugopal K. and Venkatesan R.A. (1989). *Vet. Rec.* 125 : U602.

2. Shaila M.S., Venugopal K., Purushothaman V. and Venkatesan R. A. (1990). *Indian Vet. J.* 67 : 385-386.

3. Losos, G.J. (1981). 'Infectious tropical diseases of domestic animals' (Longmans)

4. Scott, G.R. (1990). in 'Virus infections of Vertebrates vol. 3 : Virus infections of ruminants', eds. Dinter, Z. and Morein, B. (Elsevier)

5. Ramachandran, S. and Nayak, R. (1992). *Curr. Sci.* 63 : 55

6. James A.D. and Rossiter P.B. (1989). *Trop. Anim. Health Prod.* 21 : 59-68.

7. Tille A., Lefevre C.L., Pastoret P.P. and Thiry E. (1991). *Epidemio. Infect.* 107 : 441-452.

8. Taylor, W.P. (1984). *Prev. Vet. Med.* 2 : 157-166

9. Bailey, N.T.J. (1975). 'The mathematical theory of infectious diseases and its applications'

(Charles Griffin)

10. Anderson, R.M. and May, R. M. (1982). 'The population biology of infectious diseases' (Springer Verlag)

11. Anderson, Roy M. (1982). 'Population dynamics of infectious diseases' (Chapman and Hall)

PART - III

1. **Recommendations including remedial measures relevant to the environmental problems studied under the scheme :**

   The investigations envisioned in this project are yet to reach a stage when recommendations can be made.

2. **List of research papers published/accepted in the research work done under the scheme :**

   Nil

3. **Whether any research fellow associated with the scheme has been awarded Ph.D. etc. :**

   Not applicable.

Fig. 1: Sub-threshold contact rate 0.10

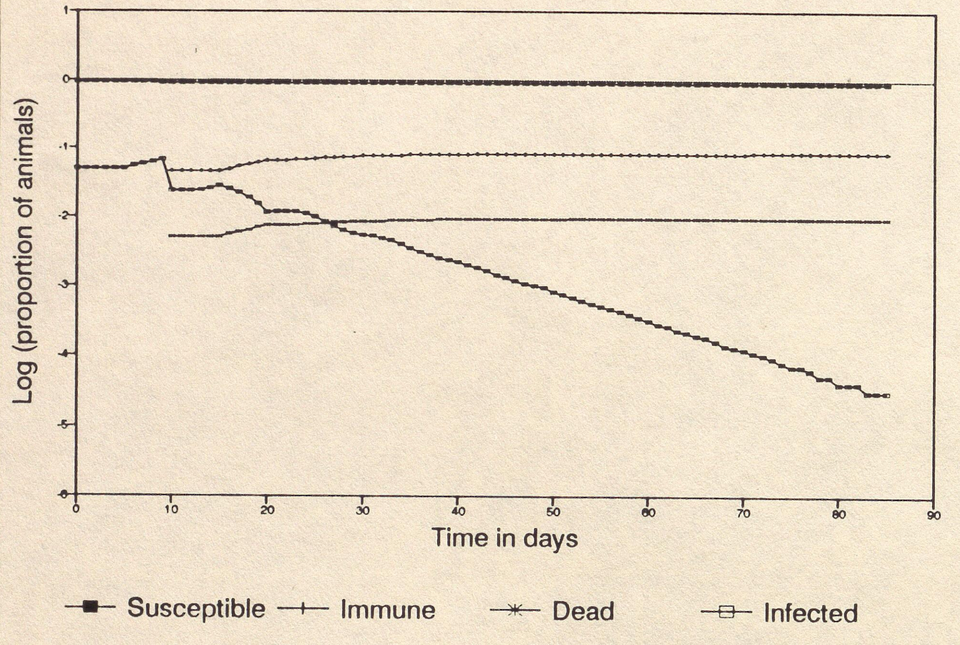


Fig.2: Super-threshold contact rate 0.40

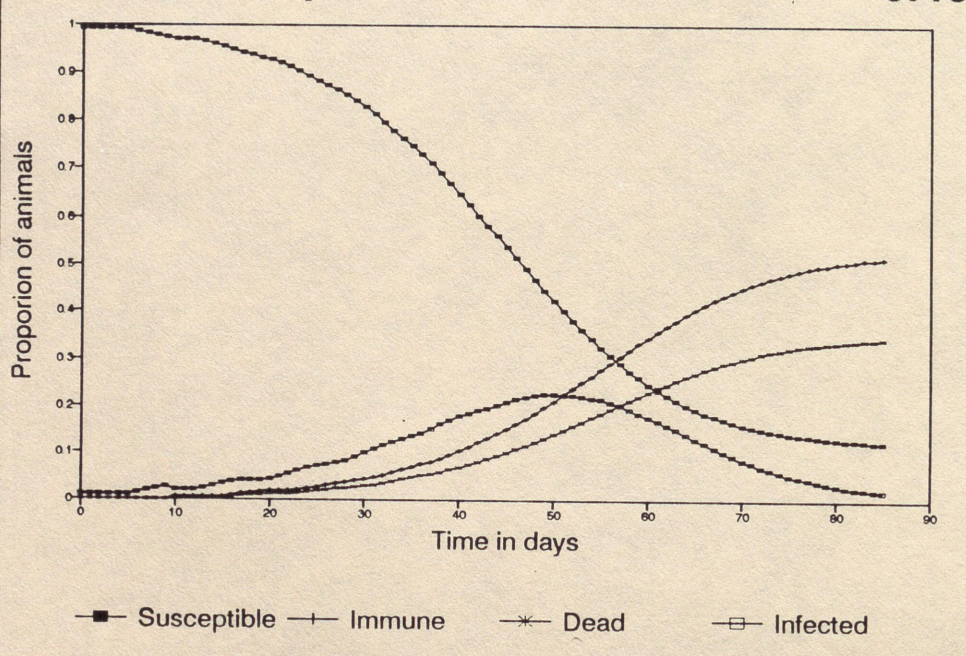


Fig.3: Effect of Contact Rate

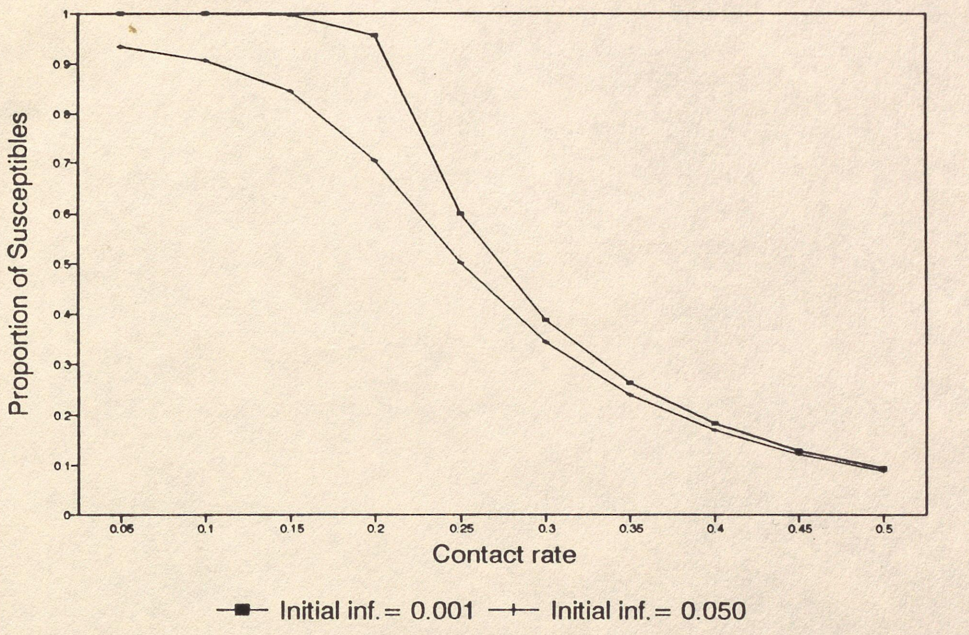


Fig.4: Peak proportion of infection

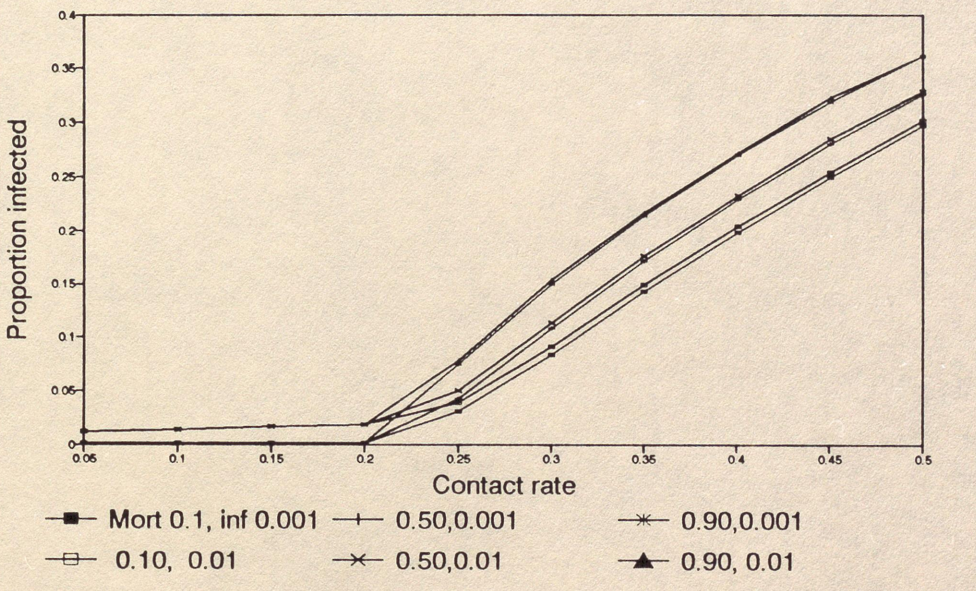


Fig. 5: Time to reach peak of epizootic

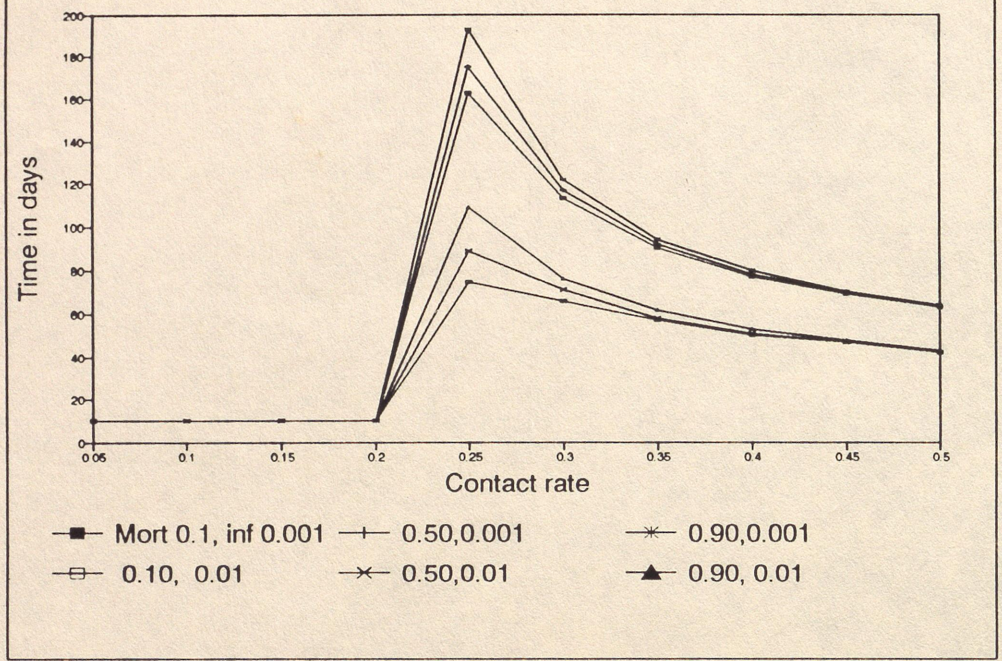


Fig.6: Effect of Contact rate & Mortality Death on days 8,9 and 10