MADRAS HEALTH EDUCATION

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SMALLPOX AND ITS PREVENTION

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Smallpox is a highly infectious disease, and causes high mortality particularly among children and is the cause of much disfigurement and even blindness. This is caused by very tiny organism called virus. When a healthy person comes in contact with a smallpox patient he gets the disease through invisible organism floating in the air. These organisms enter his body through the air passages, multiply there and excrete a poison as a result of which the disease is caused. Smallpox affects all people, irrespective of race, occupation, age and sex. No one is naturally immune to the disease.

How it spreads?

The disease is transmitted primarily through the coughs and sneezes of the patient as they contain the smallpox viruses. Transmission may also take place through the bed clothes and other articles that have been soiled by the patient's discharges. It is, therefore, advisable to boil the clothes. If the clothes are dusted dry the particle of smallpox virus settled on them will be scattered. Similarly the scabs and crusts that fall from the body of a patient also contain the virus and when dried get powdered and float in air when blown and thus the air gets contaminated. When the virus enter the body of a person who has not been protected by vaccination, it cause the disease, but fails to produce this disease in people who have been successfully vaccinated few years earlier. A person who is vaccinated during the incubation period (14 days from exposure to infection till the signs and symptoms of Small pox appear) is however likely to get the disease. Similarly, one may get the infection upto eight days after the

vaccination because by that time the immunity does not develop. However in both these cases the attack has been usually found to be milder.

There has been much misconception about the disease, its cause and prevention in the past. . Some lay people have expressed an opinion that defective stomach was the cause of smallpox. If it were so the disease would occur only among people having diseases of the stomach. But smallpox, when it breaks out in a particular area, affects only unvaccinated people. It has been proved beyond doubt that Smallpox is an infectious disease caused by a virus and it has no connection with any bad condition of the stomach whatsoever.

Vaccination—Protects against Smallpox

The only and the sure protection against smallpox is vaccination. There is no consideration for age in connection with vaccination. Infants and persons of all age groups—can get vaccinated and eight days after a successfully primary vaccination and 24 hours after a successful re-vaccination one gets immunity (protection) against smallpox. The vaccination spot swells sufficiently to form pustules. It indicates that vaccination has been successful and the vaccinated persons has become immune to smallpox for many years.

Primary vaccination should be done when infants are three months old, and there should be re-vaccination after every three years. There is no harm, even if a baby is given primary vaccination before it is three months old. Re-vaccination is essential because the immunity once acquired goes down with the passage of time. Whenever there is an epidemic of smallpox in your locality or when one is visiting an area where there have been cases of smallpox, it would be safer to get vaccinated.

Misconceptions about vaccination

There are several misconceptions about vaccination but these should not deter one from getting vaccinated. Vaccination is not harmful on any account but on the other hand it is very beneficial. It does not produce any kind of poison in the human system nor does it cause any disease. It simply gives us immunity (protection) against smallpox. A vaccine is permitted to be used only when it conforms to the standards laid down by the Indian Drugs Act. This vaccine has the quality to protect mankind against the scourge of Smallpox.

In the beginning of the present century, Smallpox was prevalent throughout the world. But it is by systematic vaccination, that many of the countries in the world have successfully eradicated the disease from their midst. Today the whole of Europe, Canada, U.S.A. and some States in South America are completely free from smallpox.

Late Prime Minister's views

Shri Nehru in a message on the occasion of Smallpox Eradication Week in 1963 had expressed his views on smallpox and vaccination as follows :—

"Before discovery of vaccination, smallpox was a major killer of mankind in all parts of the world and it is on record that smallpox killed one out of every five infants before they reached the age of five years.

The countries, that have taken up systematic mass vaccination campaigns, have now completely eradicated smallpox, but in our own country, in spite of vaccination having been in vogue for more than 100 years, smallpox epidemics have been recurring with periodic cyclicity every five to seven years claiming a heavy toll of life. The reason is that there has been no systematic vaccination of all our people so far. It was in view of this that National Smallpox Eradication Programme was launched last year in order to

rid the country of this scourge. This year a concerted drive is being made beginning 25th September to give an increasing tempo to the programme.

No programme in health can, however, succeed without the whole-hearted co-operation of the people. I hope the much needed co-operation will be forthcoming in an abundant measure so that the targets set up by the Ministry of Health are achieved and India becomes free from the stigma of being an endemic home of this perfectly preventible disease."

Most of the advanced countries have eradicated smallpox. Its incidence is quite high in the developing countries and the incidence of disease is very high in Asia and some countries of Africa. In 1961 and 1962 the total number of cases of smallpox throughout the world were 78,430 and 73,778 respectively. Out of this as many as 45,195 cases of smallpox in 1961 and 42,231 in 1963 occurred in India only. This is not all. Most of the patients who recover either lose one or both of their eyes and, are left with ugly pock marks on their faces. Their living thus become a burden to the society. To the extent to which a particular country is developed in the field of preventive health measures can very well be judged from the incidence of smallpox over there. Smallpox is still prevalent with us and it is a stigma to the fair name of the country. It is one of the earliest disease to have been tackled by vaccination. There is no reason why we should not eradicate the disease completely within the shortest possible time.

The Government have launched a national smallpox eradication campaign to rid the country of this scourge. The aim of this campaign is to vaccinate the entire population of the country free of charge. Our people should extend their fullest co-operation in this great and noble task, getting themselves and their families vaccinated against smallpox.

This will help us to get rid of this perfectly preventible disease. Our Government have made arrangements to manufacture freeze dried vaccine and also to procure the same from other countries to meet the urgent requirements of the Nation. This vaccine is of high potency and gives very high success rate and is easy to transport without any less in its efficacy.
efficacy.

Today we are putting all our efforts to strengthen our country's defence. We should not encourage any misconception about vaccination but we should as a rule get ourselves and our families vaccinated periodically and help our Government to rid the country of one of the oldest scourges.

VACCINE PRODUCING INSTITUTES IN INDIA

1. The Institute of Preventive Medicine, Hyderabad (Andhra Pradesh).
2. Government Vaccine Depot, Shillong (Assam).
3. Government Vaccine Institute, Nam Kum (Bihar).
4. Public Health Laboratory, Trivandrum (Kerala).
5. Manpur Lymph Depot, Manpur (Madhya Pradesh).
6. King Institute (Madras State).
7. Vaccine Institute, Nagpur (Maharashtra).
8. Vaccine Institute, Bangalore (Mysore).
9. Vaccine Institute, Belgaum (Mysore).
10. Hygience and Vaccine Institute, Amritsar (Punjab).
11. State Vaccine Institute, Patwadanagar, Nainital (U.P.).
12. Government Vaccine Institute, Calcutta (West Bengal).
13. Calcutta Corporation Vaccine Institute, Calcutta.

Historical Background of the Vaccination

SMALLPOX VACCINATION IN ANCIENT INDIA

DR. (MRS.) H. M. SHARMA,
Director of Public Health, Madras.

Smallpox is one of the oldest diseases in the world. It takes the first place among the epidemic diseases in the tenacity with which it has pursued the human race all over the world, and the tale of the destructive ravages of this pestilence in early times and of the suffering which resulted from it fills the mind with horror.

An extent of the ravage of smallpox during the later part of the 17th and early 18th centuries can be got from the writings of Lord Macaulay, who had stated in his " History of England " of that time, " that disease over which science has since achieved a succession of glorious and beneficient victories, was then the most terrible of all the ministers of death. The havoc of plague had been far more rapid but the plague did visit our shores only once or twice within living memory; but smallpox was always present filling the churchyards with corpses, tormenting with constant fears all whom it had not yet stricken, leaving all those whose lives it spared the hideous traces of its power, turning the babe into a changeling at which lovers shuddered and making the eyes and cheek of the betrothed maiden objects of horror to the lower ". Other writers have stated that at the end of epidemics about 80 per cent of the population represented survivors from attacks of smallpox and many of them suffered from blindness, mutilation and disfigurement. In 1802, Admiral Berkley (in a speech before the House of

Commons) stated " It is proved that in this United Kingdom alone 45,000 persons die annually of smallpox but throughout the world what is it! Not a second is struck by the hand of time but a victim is sacrificed upon the altar of that most horrible of all disorders, that is smallpox ".

In India even as early as 1,500 years ago, history tells us that a wonderful endeavour in preventive medicine, i.e., smallpox inoculation was in vogue in this country.

People felt that instead of getting the loathsome disease in the natural way, it was better and safer to contact t by judicious inoculation so that the resulting attack may be mild and life may not be endangered and immunity against the disease may be acquired.

Tikkadars

We speak of vaccinators today, as though they are something new. But then there existed the Tikkadars or professional inoculators. At least there was one for every eight to ten houses who carried on the practice of inoculation and it was estimated that in the town of Calcutta alone 81 per cent of the population were protected by this indigenous method. The profession of inoculation was followed by Brahmins who had empirically achieved a high degree of knowledge of aseptic methods in inoculation practices and had acquired great proficiency in prescribing a proper regime to be followed before and after inoculation.

Previous to the operation the operator takes a piece of cloth in his hand and with it gives dry cleaning upon the part intended for inoculation, then with a small instrument he makes many slight touches about the size of a silver groat just making the smallest appearance of blood. Then opening a lined double rag he takes a small pledget of cotton charged with the various matter (taken from the one-year old pustules) which he moistens with two or three drops of Ganges water,

and applies it to the wound fixing it on with a slight bandage and ordering it to remain on for six hours without being moved. Then the bandages are to be taken off and the pledget to remain until it falls off by itself. Before the inoculations were carried out in any village they directed that the village had to be placed under quarantine restrictions for a period of one month; all inhabitants, except the very old had to have themselves inoculated and after inoculation the village had again to remain under quarantine restrictions for one month.

In the hands of the Brahmin inoculators, results were very gratifying. But, as time went on, individuals from the lower strata of society, whose knowledge of technique and asepsis was poor adopted the profession with disastrous results.

Disadvantages

Inoculation, though a great advance in principle in preventive medicine, was not without its detractors. The spectre of smallpox, despite inoculation, continued haunting the country. The disease unceasingly exacted a heavy toll of life and disfigured for life the survivals some of whom became blind before the boon of vaccination came to offer hope to the people. Sir John Simon has said, about vaccination that, it is a greatest physical good ever given by science to the world.

Milk-maid

The manner in which vaccination came to be introduced in India is of interest and worth recounting. Towards the close of 1799, a British doctor by name Jenner accidentally found from a milk-maid that cow-pox affected persons did not get smallpox which made him conduct his crucial experiments which resulted in the discovery of vaccination as a prophylactic against smallpox. Several efforts were made by Dr. Jenner to send dried lymph to India, but it was soon discovered that the lymph did not retain its potency long enough to permit its despatch in an active state to distant countries

by sea. Finally Jenner succeeded in securing the services of a number of volunteers, who undertook to have themselves vaccinated one after another to keep the lymph passage during the voyage from England to Ceylon thus helping in the transport of lymph over long distances in potent conditions. It was by this method that cow-pox lymph reached India. Another version of the story is, that in 1799 Jenner is said to have sent Dr. De Carro in Vienna a supply of threads soaked in vaccine and from this stock De Carro got good results. He then took two pieces of glass, one with a depression on its surface, placed in that depression, a piece of lint saturated with lymph, applied a drop of oil on the internal surface of the two pieces of glass, tied them together, sealed the edges of glass pieces, and finally dipped them in melted wax so that air was efficiently excluded. This packet was safely conveyed across European and Asiatic countries and over the whole line of deserts to Baghdad. On arrival there, the lymph was found to be still liquid and the veryfirst vaccination carried out with it was successful. This vaccinated child was then sent to Bazra where arm to arm vaccination was carried out and sufficient stocks of vaccine lymph were maintained and by the end of May 1802 some of it was sent to Bombay by the ship " Recovery ". With the lymph thus received, 20 to 30 persons were vaccinated but only in one it was successful. The successful vaccination was carried out by Dr. Scott on the 14th of June 1802, on an arm of Anna Dusthall, a healthy child of three years of age.

By vaccinations carried out with this lymph vaccine was soon produced in sufficient quantities to enable supplies to be sent to Poona, Surat, Hyderabad, Madras, Ceylon, etc.

Tissues

Up to 1870, all vaccinations were done with humanised lymps either from arm to arm or with lymps carried on point glasses or tissues, or secured from vaccine crusts.

Animal vaccination was established in Bombay in 1870 and from this virus some successful experiments were made by Dr. Charales in Calcutta in 1883. In Madras, vaccination with animal lymph was successfully established in 1880–81. Other parts of India then came to adopt animal lymph for vaccination purposes.

For want of correct medical statistics, exact information regarding the occurrence of smallpox till the middle of last century is not available; but we do know that for many centuries before the statistical era, smallpox raged in India with a terrible severity. In support of this statement, the existence all over the country of ancient temples dedicated to the Goddess of Smallpox may be mentioned which indicates that hardly any part of the country escaped it.

With the introduction of vaccination, smallpox has begun to receive, its extent and severity have both abated. The fall in mortality rate has been noticeable in spite of the fact that no systematic countrywide vaccination drive has been attempted. With improved techniques, potent lymph, better trained vaccinators, and better supervision of their work and, above all, with better organization, eradication of smallpox in India is intended to be attempted now. Many a country in the West has eradicated smallpox and so can India.

SMALLPOX ERADICATION PROGRAMME

Smallpox, a quick spreading disease, which disfigures, blinds or kills its victims has been known to man since civilisation began. During the last 100 years, however. spectacular progress has been made towards defeating this scourge. The world figure for smallpox incidence has come down from 4.8 million in 1951 to 2.4 million in 1958 and to 74 thousands in 1959.

The weapon against the disease is preventive repeated vaccination of at least 80 per cent of the population with smallpox vaccine. The success of the method has been proved and has enabled many countries to eradicate the disease from their territory.

The important foci of the disease are now in parts of Asia, especially, India and Pakistan. These and other countries in South East Asia have launched pilot projects which have developed into national campaigns to eradicate the disease.

Smallpox is thought to have originated in Asia and it still persists there as well as in Africa and South America. But since history began, it has recognised no limits of geography or climate, impartially attacking rich and poor, young and old, men and women. In the days of the slave trade, smallpox was considered such an inevitable afflction that a pock-marked individual fetched a much higher price than one with an unblemished skin, for it was recognised even then that a person rarely contracts it twice. This favourable circumstances and the fact that there is no intermediate host-insect, animal or other have made it easy to control the disease. The virus gradually disappears from an area is no susceptible

persons remain or if the infection is not introduced from outside. The means of inducing sound immunity by vaccination have been known since the 18th century.

Dr. Jenner first introduced vaccination. It was not realised at first that vaccination does not necessarily give life long immunity, but gradually wanes, leaving the subject once again susceptible so that re-vaccination is necessary. Many people still, erroneously, believe that one vaccination is good for a life time.

It is now considered that everyone should be vaccinated, first in infancy and subsequently at the beginning and end of school life. People in endemic areas should get themselves vaccinated at intervals no longer than 3 years apart.

According to the WHO administered International Sanitary Regulations, " A Health administration may require any person on an international voyage who does not show sufficient evidence of protection by a previous attack of smallpox, to possess, on arrival a valid certificate of vaccination against smallpox. Any such person who cannot produce such a certificate may be vaccinated or he may be placed under surveillance for not more than 14 days reckoned from the date of his departure from the last territory visited, before arrival ".

Vaccination has been so successfully applied in some countries that smallpox has disappeared. The disease can easily be re-introduced by travellers from endemic areas, however and unless the immunity of the population is good.

Many countries are smallpox-free

The whole of Europe, Canada and the United States were free from indigenous smallpox in the first half of this century. Cases became very rare in many other countries like Hong-Kong, Isreal, Madagascar, Mauritius, Turkey

and Zanzibar. The disease has regressed in Argentine, Ceylon, Chile, Japan, Mexico, the Philippines and even in areas where it is still a serious problem such as in parts of Asia—smallpox has shown a tendency to decline.

Estimated number of cases in the whole world in the last 10 years demonstrates this downward trend. In 1951, the figure was 489,000. In 1958, it was 247,000 of which 88 per cent were in India and Pakistan; in 1959, the total fell to about 74.000 in 1960: the total was only about 60,000 In South East Asia, the disease continues to take a heavy toll. In India, for instance, 44,537 people suffered from smallpox in 1961, of whom 12,312 died.

Menace of fast communications

In the past, people were cut off from contagion because communication between countries was slow and infrequent. Speed of airtravel now makes it possible for a passenger on a plane, who has been infected several days before departure, to reach his destination in apparent good health since the incubation period is from 10 to 14 days. By the time the illness has been diagnosed, the patient may have infected a number of other people. Then the chase is one, searching for contacts and vaccinating them to prevent the infection from going further.

People whose immunity from vaccination is vaning off can develop a modified form without the typical symptoms but still be infectious.

International action

It has always been a matter of concern for the WHO. that smallpox has not yet been completely wiped out. In 1958, the World Health Assembly adopted a policy of eradication which has been actively pursued ever since.

Over 50 countries throughout the world either are engaged in, or are planning eradication programmes, or are stepping up control measures. In two of the most important foci of the disease, India and Pakistan, Pilot Projects are in operation which are the precursors of eradication campaigns. Today, in all the countries of South East Asia, campaigns against smallpox are being carried out in varying degrees of progress.

India is now engaged in a mass programme which aims at the mass vaccination of the entire population in three years. The need for the vaccine is proposed to be met from the output of glycerinated vaccine lymph from India's vaccine laboratories and a gift of 250 million doses of freeze dried vaccine from the USSR. Government.

Eradication seems to present no insurmountable difficulties. When smallpox persists in a locality, it is because vaccination, of the population is neither systematic nor widespread, enough to reach the 80 per cent coverage, which considered necessary to eliminate the endemic foci.

Analysis of the reports of smallpox eradication Pilot Projects has revealed the following beliefs and superstitions and lack of understanding of smallpox :—

(1) Smallpox is caused by Goddess.

(2) Some consider one vaccination is enough for life long protection. Vaccination is sometimes considered, as a preventive and curative measure for diseases other than smallpox as well.

(3) It is thought to be meant for children only.

(4) For pregnant women it is thought to be undesirable.

(5) Smallpox is confused with chickenpox and if people get chickenpox after vaccination, the faith in vaccination goes down.

Freeze dried vaccine

Studies by WHO to find a potent vaccine that would remain stable under a variety of conditions, particularly very hot weather when no refrigeration was available led to the discovery that freeze dried vaccines developed by laboratories in several countries, were the most satisfactory.

Smallpox must be eliminated. The relative cost of it, is low, not to mention the lives that will be saved and the human suffering avoided.

PRODUCTION OF FREEZE DRIED VACCINE

For production of freeze dried vaccine, four institutes, viz., State Vaccine Institute, Patwadanagar, King Institute, Madras, Institute of Preventive Medicine, Hyderabad and Vaccine Institute, Belgaum, are being equipped with the help of international agencies (WHO/UNICEF). Both State Vaccine Institute Patwadanagar and King Institute, Madras, have produced trial batches of freeze dried vaccine conforming to WHO standards and will soon go into production. With the improved type of shelf dying equipment which is going to be supplied to all the four Institutes by UNICEF, it is expected that by the middle or end of 1965, we should be in a position to manufacture nearly 125 million doses to meet all our needs for the maintenance phase of the Smallpox Eradication Programme.

FIGHT AGAINST SMALLPOX !

An Appeal to the Public

To-day smallpox is a problem of only the undeveloped countries. The maximum number of countries of smallpox are reported from this sub-continent. India and Pakistan alone have 80 per cent smallpox cases occurring in the world. It is well known that smallpox was prevalent throughout the world till some decades back and it is equally well known that it is completely absent in most of the advanced countries of the world. This complete eradication of this dreaded scourge has been possible because of the stringent measures adopted both by the Governments, towards the control of the disease and the wholehearted co-operation of the public towards the satisfactory discharge of the Governments' measures.

Though there is no known cure for smallpox, we have a very potent weapon to prevent smallpox. A successful vaccination almost always prevents smallpox. In the rare instances where smallpox occurs in vaccinated individuals it is mild and uncomplicated. A definity immunity is built up in the body after vaccination to resist injection of smallpox, so that the battle of infection versus resistance may result in success on the side of resistance. It is only by systematic vaccination of all new born children, and repeated periodical vaccinations of all citizens of the country, this disease has been wiped out of the advanced nations of the world.

Some people are still resorting to Pujas, Mantras. magic and to pleace the Goddess Mariamman to cure those attacked with the disease. Many people do not know its cause or its prevention. In spite of vaccination of infants and adults having been compulsory in our State for over fifty

years, because of lack of public participation, appreciable progress has not been achieved in the contact of this disease and it is very much with us, though perhaps not to such an extent as before.

In Madras State, the complications of smallpox are numerous that many who recover from the infection are crippled or blinded. Smallpox is one of the major causes of blindness in our country. Such maimed and crippled people are not only a burden to themselves and their families but also to the State and the country. The valuable manpower lost because of these and the valuable manhours lost because of the prolonged illness due to this disease should be taken as severe losses to the development efforts of the country. The money and the effort expended towards the hospitalisation and cure of this completely preventable disease is something that could easily be spent for some other much more useful purpose.

With a view to avoid these losses, the Government of India have launched the Smallpox Eradication Programme throughout the country. And in line with this programme, the present Statewide Smallpox Eradication Programme has been under way in this State from 1st March 1963. During 1960-61, the eradication programme was carried out in the district of Chingleput on a pilot scale. During 1961-62 it was carried out in North Arcot district.

What has been achieved in other countries is certainly possible of achievement in our country and much more so in our enlightened State. What we need is wholehearted public co-operation and understanding rather joint working by staff and public. Assured of that, we are sure we could make this Scheme a success and keep the State free from smallpox.

RABIES
PREVENTION AND TREATMENT

Dr. VEERARAGHAVAN.
Dr. A. K. THOMAS.

An extract from the Agenda and Notes of the Committee on Rabies.

Ways and means of overcoming the difficulties of control of Rabies.

The Committee was of unanimous opinion that if rabies is to be controlled in the country, the following steps will have to be taken :—

I. Legislation should be enacted and enforced for the destruction of stray and ownerless dogs.

II. Registration and licensing of dogs must be enforced by all local authorities, at all levels.

III. Anti-rabic vaccination should be made compulsory before registration.

IV. *A widespread health education programme should be undertaken all over the country to bring home to the public the need to control the stray dogs population in order to protect the lives of human beings and livestock against rabies.*

V. To be effective, it is imperative that the control programme is carried out all over the country simultaneously.

VI. A small Central Committee be formed to work out the details of a co-ordinated programme.

Destruction of Dogs

Humane methods should be employed for the destruction of dogs. It is desirable that lethal chambers be established wherever possible. Those already existing should be maintained properly throughout the year.

Immunization of pet Dogs

It is preferable to use a chick-embryo adapted live virus vaccine which confers immunity for at least three years. If this is not possible, the single dose phenolised 20 per cent vaccine can be used. It is desirable to repeat the vaccination every six months or at least every year.

The problems relating to the Production of A. R. Vaccine, classification of patients and dosage schedules.

I. Preparation of vaccine :

(*a*) Seed-virus : It is considered essential that seed fixed virus strain used for the manufacture of anti-rabic vaccine should be checked periodically for its properties.

(*b*) Manufacturing institutions, which do not have these facilities should get their strain checked by an established institution or obtain fresh seed virus periodically.

(*c*) Preparation of vaccine : (i) Brains of infected animals showing typical and progressive signs of rabies only should be used.

(ii) The brain emulsion is to be prepared either in buffered saline or saline and incubated for the minimum period of time sufficient to ensure the inactivation of the virus. This time may vary depending on the strain of virus and each laboratory should work out its own data.

(iii) To ensure uniformally potent vaccine, it is considered essential to pool vaccine produced from at least 10 brains. This can be conveniently done either immediately after incubation, in a sterile drum and the requisite quantity of saline added to make a 15 per cent brain emulsion or in the final stage. Extreme care has to be taken to prevent contamination.

(iv) Inactivation test on each batch by the intra-vertebral route in at least six mice using 1 : 10 dilution of the vaccine should be carried out to ensure that no vaccine containing live virus is released for use. Apart from this, tests for sterility and the presence of carbolic should be carried out.

(v) It is essential to have the potency test of random samples carried out by either Habel or antigen extinction method throughout the year.

(vi) The proposal to issue anti-rabic vaccine from treatment centres to practitioners of Western system of medicine, who are fully conversant with anti-rabic therapy, is accepted. They should be held responsible for the return of case-cards to the manufacturing institution.

Decision regarding the use of anti-rabic serum.

Decision regarding the exact dose of serum to be employed has been deferred till the results of the field trials now being carried out, are available. The use of serum in case of severe exposure is recommended.

Problem of paralytic accident and formulation of methods by which their incifence may be rnduced.

1. Reduction of the incidence of paralytic accident can be achieved if a close watch is kept cn the patients during anti-rabic therapy for prodromal signs of the condition. Prompt withdrawal of vaccine therapy in these patients and prompt treatment with corticosteroids may avert or cut-short the illness. This can be ensured only if the Medical Officers examine the patients every day.

2. Since paralytic accident is considered to be an allergic manifestation in those patients where treatment with brain vaccine has been withdrawn and corticosteroids given, it is dangerous to give further injections of vaccine containing brain materials. Such patients, however, should be given inactivated avaianised anti-rabic treatment.

3. A certain number of paralytic accidents are likely to occur inspite of all precautions and the only way to avoid its occurrence is by ensuring that anti-rabic treatment is unnecessary in the community.

Methods for diagnosis of Rabies :

1. It is desirable that pathology departments of all medical colleges undertake the microscopic and biological methods of diagnosis of rabies.

2. The abovementioned methods are not really of help to the clinicians in deciding whether to start anti-rabic treatment or not observation of the biting animal wherever practicable, to rule out rabies, is strongly emphasised.

3. Fluorescent microscopy may prove to be of help in rapid diagnosis of rabies. Intensive study of this method should be undertaken by more laboratories in this field. The necessary equipment for the purpose should be made available to laboratories undertaking the diagonsis of rabies.

Methods for better collection of data in treated patients.

All State Governments should be requested to instruct Medical Officers under their control to fill up the case cards properly and return them promptly. They should also instruct their local authorities to co-operate in ascertaining the health of patients, six months after treatment.

It is also desirable that the main institutions write to the individual patients, to find out about their health.

(Recommendations of the Ad hoc Committee on prevention and treatment of Rabies.)

HEALTH EDUCATION IN SMALLPOX ERADICATION

1. In the whole world, India, though an old and civilised country with good old culture, is in bad position in Smallpox. Eighty-five per cent of World's Smallpox cases are in India and Pakistan.

2. Our Pilot Projects experience, in Madras City, North Arcot and Chingleput districts show that, it is not easy to get 85 per cent expected target, unless this programme is dealt as a national movement, and many workers, other than health workers help to educate people.

Particularly women can help a great deal in educating our village families.

3. (*a*) Smallpox is a disease carried by a living organism.

(*b*) It spreads from one person to another by (1) breath, (2) contagion-from Smallpox Pustules, scabs.

(*c*) Vaccination is the best method to prevent and eradicate Smallpox.

Eighty-five per cent of people and 100 per cent of children should be vaccinated within one year of Smallpox Eradication Programme period. (This really means one week in each village under question.)

(*d*) All those who have not had vaccination within the previous three years, must have revaccination to protect themselves and their village against Smallpox.

(*e*) The age group 15—50 (wage earners). It is seen in the past, have been missing the benefit of vaccination, when vaccination team visits the village. So women and men

workers—both Professional and Voluntary, should concentrate their attention and see that this age group stay in the village on the vaccination days, during vaccination time and get themselves vaccinated.

Vaccination teams work both in the mornings and in the evenings and nights to help wage earning groups.

It is as much the duty of wage earners, like others to see that the whole village (men, women and children) gets vaccinated within the one week programmed for vaccination for each village.

(*f*) Doubts of villagers should be answered by women workers after they themselves get the answers for such doubts.

(i) Some believe that the reaction is so much as to affect some people going to work. It is not so. Only those who had not revaccination for a long time, get a " typical primary reaction " which is described as severe reaction. The reaction is not severe as to stop a person from working. Some difficulty has to be faced by us if we want to overcome the greater calamity of Smallpox coming to our village every now and then and in epidemic form once in 5 or 6 years. All other countries in the world have eradicated them, because of all the people—men and women co-operated and took to vaccination in a large scale at the same time, as is now organised in Smallpox Eradication Programme.

(ii) This does not cause problem in pregnant women. On the other hand, unprotected pregnant women, when they get Smallpox, it is said by experts, that have a tendency to get the most dangerous form of Smallpox—Haemorrhagic Smallpox.

—*Health Education Bureau.*

PREGNANCY AND SMALLPOX

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Since Gregg's (1941) incrimination of rubella, as a factor in the aetiology of congenital malformations, a lot of interest has been evinced to find out the effects of other virus infections in general, on the termination of pregnancy, the life of the foetus and the life of the mother, besides congenital malformations when a pregnant woman contracts such diseases. But, there is another aspect of this most interesting problem, which has not been studied to a great extent and that is the effect of "pregnancy status" of the individual on the nature of the attack and the course of the disease when she contracts it. This is a very important question which is of great interest to both the clinician as well as public health administrator.

According to Bavinbridge (1918) pregnancy stimulates most of the tumours except the epitheliomata. Williams (1926) held that with the exception of scarlet fever, pregnancy does not seem to increase the resistance of the body to any other infections. Working on animals, Sprunt *et al.* (1932) found that pregnancy in rabbits altered the reactivity of the

tissues to the virus of infectious myxomatosis. Roshan *et al.* (1936) showed that in a large number of rabbits, pregnant animals were more resistant to vaccinia infection than non-pregnant ones and the females were more refractory than males. Manwaring *et al.* (1928) stated that pregnancy and parturition make it more difficult to sensitise the guinea-pig. MacGoogan (1932), Aycock (1946) and several others reported increased severity of poliomyelitis in pregnant women. Thus we have many interesting but somewhat conflicting reports regarding pregnancy and infection.

As regards smallpox in particular, several authors reported that pregnant women fare badly with this disease. By (1923) observed that the prognosis of smallpox is more serious in the pregnant women owing to their liability to abortion. Marsden (1951) held that the association of pregnancy with smallpox is bad both for the mother and the child. Downie (1959) stated that a pregnant woman seemed to fare particularly badly when she contracts smallpox.

The authors have confirmed the above statements in this paper by comparing the attacks in pregnant women with those in non-pregnant ones and meals of the same age-group. There is a great need for further study as to why the pregnant woman fares so badly with smallpox. Certain aspects of this question are also discussed in this paper.

Materials and methods

Smallpox cases were admitted to the Infectious Diseases Hospital, Tondiarpet, Madras. during the period of 38 months between May 1st 1959 and June 30th, 1962, were studied. 8,133 cases of smallpox were admitted during this period and of these, 255 were pregnant women who contracted the disease at various periods of gestation and a few in the post-partum period. In this paper, these 255 cases are presented of whom 244 were pregnant when they developed the disease and 11 developed the disease within 20 days afte

confinement; excepting 2, the remaining cases were infected while still pregnant and confined only during the incubation period.

Two aspects of the question were studied :—

1. The effect of smallpox on the termination of pregnancy, the life of the foetus and the life of the mother :

For this purpose, all the 255 cases were studied and the effect was noted till the patient was discharged cured or was dead. This paer does not deal with what happened to the child after birth, nor does it deal with the pregnancy if it did not terminate during the course of the disease. These aspects form the subject for a separate study.

2. The effect of the 'Pregnancy Status' of the host on the nature of the attack and the course of the disease :

For this purpose, admissions of one year from July 1st, 1961 to 30th June 1962 were taken up. In all, 1,910 cases of smallpox were admitted during this period, of whom 94 were pregnant. Since none of the pregnant females were below the age of 15 or above the age of 45 years, the authors have taken the age-group 15 to 45 years as the susceptible age-group for pregnancy, and compared the nature of the attack and the course of the disease in these 94 pregnant women with those of non-pregnant females and males of the same age group. The results of the comparison and the possible causes as to why the pregnant subjects fare badly with smallpox are discussed.

Before the results are presented it is necessary that the method of classifying the types of smallpox cases in this hospital should be explained. After treating nearly fifteen to twenty thousand cases of smallpox during the last 20 years, the senior author feels that the classification of smallpox cases into the usual discrete, semi confluent, confluent and modified types with only the number of lessions and their density as

the sole criterion is not an effective way of assessing the severity and prognosis of a case. The following classification is followed in this hospital.

Classification

The smallpox cases are broadly divided into four types :

Type 1 (*Haemorrhagic*).—All cases that have haemorrhages through the mucous membranes and into the skin at one stage or the other of the disease are grouped in this type, which has two sub-types.

Type 1 (*a*) (*haemorrhagic early*) : These are cases where the prodromal stage is very severe and toxic, and haemorrhages into the skin and through the mucous membrane occur even before the focal lesions are seen or well developed. This corresponds to the type described as variola purpurica or primary haemorrhagic smallpox.

Type 1 (*b*) (*haemorrhagic late*) : These are cases where haemorrhage occur through the mucous membranes and into the skin and lesions apear late in the course of the disease after appearance of focal lesions. This corresponds to the type described as variola pustulosa haemorrhagica. This term does not seem to be happy because it appears to mean that haemorrhages occur only during the pustular stage whereas actually in this type, haemorrhages may occur at any stage of the disease after appearance of lesions.

Type 2 (*Flat*).—These are cases where the focal lesions are exceedingly slow to nature and the vesicales at the usual time of maturity seem to be hurried in this skin. They contain very little fluid, do not project on the skin and do not present umbilication. These cases usually have severe prodromal stage and the constitutional symptoms do not abate even after the onset of the focal lesions, but containue during the disease. Majority of the lesions shows haemorrhages into their bases but not into the skin or through te mucous membranes. This type is far more common in the unvaccinated

children. Depending upon the number of lesions and their density this type has three sub-types : (*a*) Flat—Confluent, (*b*) Flat—Semi-confluent, (*c*) Flat—Discrete.

Type 3 (*Ordinary*).—These are cases where usually there is abatement of constitutional symptoms of the prodromal stage with the onset of rash and the focal lesions develop normally and go through all the classical stages, present almost all the characteristic features, round in their pattern, project nicely over the skin, present umbilication, etc. In this type again, depending upon the number of lesions and their density, we have 3 sub-types : (a) Ordinary—Confluent, (b) Ordinary—Semi-confluent, (c) Ordinary—Discrete.

Type 4 (*Modified*).—The modification of the disease may be (i) in the severity of the prodromata, (ii) in the characteristics of the lesions and (iii) in the course and evolution of lesions. So, even a confluent smallpox may still be modified if the course of the disease is accelerated and scabbing occurs right after the vesicular stage. Any case of smallpox which presents any type of modifications as described above comes under this category, and again depending upon the number of lesions and their density this type is further subdivided into : (*a*) Modified—Conuuent, (*b*) Modified—Semi-confluent, (*c*) Modified—Discrete, (*d*) Variola *sine* eruptionae.

Thus, we have four main types of case with 2 sub-type in Type 1, three sub-types in each of Types 2 and 3, four sub-types in Type 4 and all these types are arranged in the order of their severity. In this classification, greater importance has been given to the nature of the lesions, rather than to the number, since the prognosis depends more upon the nature and not upon the density of rash. A 'modified confluent' is never fatal, and 'ordinary confluent' is less fatal than even the 'flat discrete'. In this paper the description of cases is given according to the above classification.

Two more terms that are used in this paper require clarification. 'Unvaccinated' are those persons who were never vaccinated in their life so far those who say that they were vaccinated in infancy, but show no visible marks, and those who were vaccinated for the first time during the incubation period of the present attack. 'Vaccinated' are those who present successful marks of having been vaccinated at least once in their life time. In our experience we have not had any case of smallpox excepting one or two isolated instances amongst persons in whom marks of primary vaccination as well as of successful revaccination with two years before the attack were present.

Results - Effects of smallpox

Out of 8,133 cases of smallpox that were admitted during the period of 38 months ending with June 30th, 1962, 244 were pregnant women in various periods of gestation and 11 post partum at varying time intervals within a maximum period of 20 days after confinement. For the purpose of this paper, all the 255 patients were taken as one group. Specific incidence of smallpox amongst the pregnant could not be stated, and compared with that in the non-pregnant since no data were available regarding the number of pregnant women in the City during this period.

Table 1 shows the total number of admissions of smallpox cases month by month, the number of pregnant women amongst them and the proportion of pregnant women to the total admissions in each month. The incidence of smallpox was high, as usual in the months of February to April with the peak in March. 38 per cent of the total annual admissions occurred in these 3 months and similarly 43 per cent of the total pregnant women with smallpox took admission during this period. But, when we compare the proportionate incidence of the pregnant to the total number of cases in each month, it is found to vary from month to month, and it is maximum with 5.1 per cent in the month of June and

TABLE 1.—*Total number of cases of smallpox and number of pregnant women with smallpox (in italics) admitted monthwise.*

	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sep.	Oct.	Nov	Dec.	Total.
1959	—	—	—	—	113	77	114	277	284	201	115	135	1,316
					2	*2*	*4*	*4*	*4*	*4*	*4*	*1*	*25*
1960	164	247	227	208	116	147	246	154	188	171	99	21	2,177
	4	*4*	*5*	*8*	*6*	*5*	*6*	*1*	*2*	*2*	*3*	*2*	*48*
1961	301	423	655	621	391	336	314	190	139	93	51	152	3,666
	11	*21*	*18*	*10*	*7*	*21*	*14*	*6*	*8*	*6*	*2*	*5*	*129*
1962	216	277	160	153	106	62	—	—	—	—	—	—	974
	10	*14*	*10*	*4*	*11*	*4*							
Total	681	947	1042	982	726	622	674	621	611	465	265	497	8,133
	25	*39*	*33*	*22*	*26*	*32*	*24*	*11*	*14*	*12*	*9*	*8*	*255*
Mean per month..	227·0	315·6	347·3	327·3	181·5	155.5	224·6	207·0	203·6	155·0	88·3	165·6	—
	8·3	*13·0*	*11.0*	*7·3*	*6·6*	*8·0*	*8·0*	*3·6*	*4·6*	*4·0*	*3.0*	*2·6*	
Proportion of pregnancy to total in per cent ..	*3·6*	*4·1*	*3.1*	*2·2*	*3·5*	*5·1*	*3·5*	*1·7*	*2·1*	*2·6*	*3·4*	*1·6*	—

TABLE 2.—*The number of cases of smallpox with pregnancy admitted, with reference to the stage of pregnancy, the case fatality, the nature of termination of pregnancy, and the state of foetus at birth.*

Stage of pregnancy (months).	No. of cases.	Deaths.	C.F.R.	Cases died before termination.	No. who survived the termination.	No. actually terminated during the course of the disease.	Termination rate (percentage).	Nature of termination and state of foetus at birth									
								Abortions and miscarriages.	Abortion rate.	Premature				Full term			
										L.B.	S.B.	Term rate.	S.B. rate.	L.B.	S.B.	S.B. rate.	No. of haemorrhagic cases.	Incidence of haemorrhagic cases.
1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
2	4	2	50	1	3	3	100	3	..	..	..	..	..	..	..	..	..	..
3	17	5	29	2	15	7	46·6	7	..	..	..	..	..	..	..	..	1	6·0
4	21	4	19	3	18	4	22·2	4	..	..	..	..	..	..	..	..	3	13·3
5	20	6	30	1	20	9	45·0	9	..	..	..	..	..	..	..	..	4	20·0
6	24	6	25	3	20	8	15·0	3	..	..	..	..	..	..	..	..	7	25·0
7	43	12	28	4	39	16	41.0	..	..	8	8	..	50	..	..	..	7	16·3
8	27	12	44	4	23	13	56·5	..	..	6	7	..	54	..	..	..	4	14·3
9	24	10	42	3	21	12	57·1	..	..	9	3	..	25	..	..	..	5	20·8
FT	75	24	32	2	73	65	89·0	..	..	..	..	..	..	58	7	10·7	16	21·3
Total	255	81	32	23	232	132	56·9	26	34·2	23	18	49·4	43·9	58	7	10·7	47	18·4

L.B.=Live births S.B.=Still births C.F.R.=Case fatality rate.

minimum with 1.6 per cent in the month of December. These facts do not seem to have any bearing with the incidence of smallpox in those months. This may be explained by the fact that there are perhaps more susceptible pregnant women in the population in the month of June and the least in the month of December. It is a fact that births also do not occur uniformly in the City every month. They are more in the last quarter of the year than other quarters.

Table 2 and Fig. 1 show the number of pregnant cases admitted with reference to their periods of gestation at the time of admission, the nature of the termination of pregnancy the state of the foetus at birth and the case fatality.

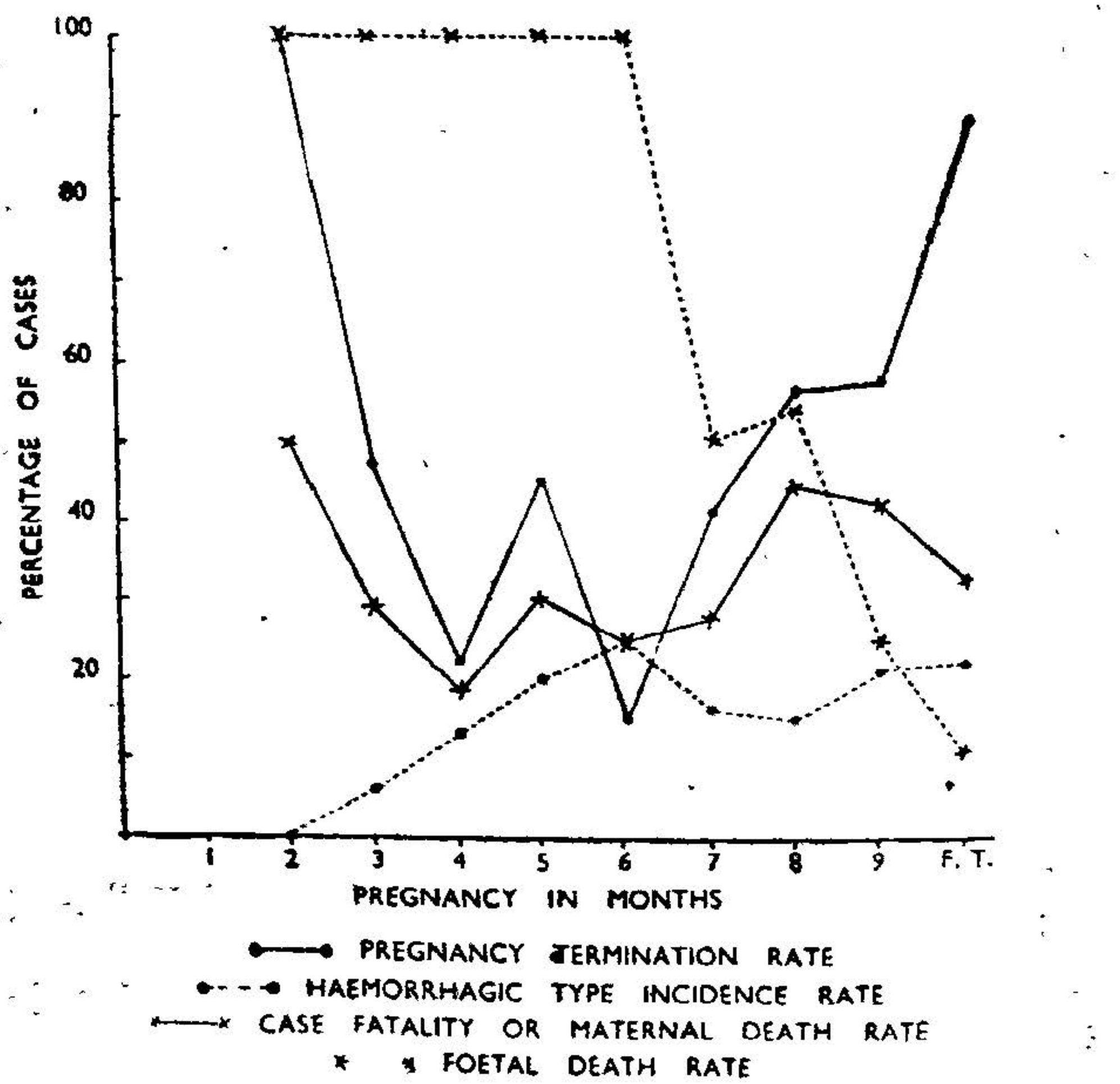

FIG : THE PREGNANCY TERMINATION RATE, MATERNAL AND FOETAL DEATH RATES AND INCIDENCE OF HAEMORRHAGIC SMALLPOX IN THE PREGNANT SERIES WITH REFERRENCE TO THH STAGE OF PREGNANCY.

Effect on the termination of pregnancy.—Out of 255 cases, 23 died before termination, and of the remaining 232, only 132 terminated during the course of the disease with a termination rate of 56·9 per cent. Of the 180 cases, who were admitted before term, 21 died before termination of pregnancy and of the remaining 159, 67 had the termination of pregnancy prematurely, with a premature termination rate of 42·1 per cent. In general, the termination rate is greater in persons who contracted the disease after the foetus had become viable than in those who contracted the disease within six months of pregnancy, the rates being 49·4 per cent and 34.2 per cent respectively. When we compare different periods of gestation there is a greater tendency to termination in the very early weeks of pregnancy and again in the fifth month and in the very late months of pregnancy.

Effect on the life of the foetus.—Of the 232 cases who survived till the termination of pregnancy, only 132 terminated during the course of the disease in the hospital. The present study does not include the results of the termination that occurred after the patients had been discharged cured. Of these 132 terminations that occurred during the course of the disease, in 51 cases the foetus was dead *in utero*, with a foetal death rate of 38·6 per cent. The stillbirth rate was far less in the full term cases, being only 10·7 per cent as against 44 per cent in the 41 premature terminations we had during this study.

Effect on the life of the mother.—Of the 255 pregnant patients admitted, 81 died, with case fatality rate of 31·7 per cent. In general, there were more deaths in those cases who contracted the disease after six months of pregnancy than in those who got the disease in the earlier months, the rates being 34·3 and 26.7 per cent respectively. But with reference to different periods of gestation, it is found more in the early weeks of pregnancy, before two months and then it declined

till the fourth month with a sudden rise in the fifth month. Thereafter, it declines in the sixth month, to rise again till the eighth month with tendency to fall later.

The effect of pregnancy status on the nature of attack and the course of the disease

For this aspect of study, smallpox cases admitted during the period of 12 months from July 1st, 1961 to June 30th, 1962 were taken. During this period, 1,910 cases were admitted and of these, 94 were pregnant women. These pregnant cases were compared with the non-pregnant females and also male belonging to the same age-group (15 to 45 years), and admitted during the same period of study. Table 3 shows the distribution of cases in these three groups. Hence, in this study a comparison has been made between 502 males, 348 non-pregnant females and 94 pregnant females, all belonging to the same age-group. Table 4 shows the details of the admissions, the deaths and the type of the attack with reference to the vaccinal status.

TABLE 3—*The distribution of cases among the three groups under study.*

Groups.	No. of cases in 15–45 yrs age-group.	No. of cases not in this age-group.	Total No. of cases.
Males	502	452	954
Non-pregnant females ..	348+3*	511	862
Pregnant females ..	94	..	94
Total	944+3*	963	1,910

* Records of these three cases were not available and hence omitted from this study.

Table 4.—*The types of attacks, number of cases and deaths with reference to vaccinal status in the three groups under study.*

Typing code	Sub types		Unvaccinated				Vaccinated				Total			
			Males	Non-pregnant females	Pregnant females	Total	Males	Non-pregnant females	Pregnant females	Total	Males	Non-pregnant females	Pregnant females	Total
							Haemorrhagic type							
T_1	a Early	C	2	1	2	5	2	2	10	14	4	3	12	19
		D	2	1	2	5	2	2	10	14	4	3	12	19
	b Late	C	3	2	1	6	3	8	1	12	6	10	2	18
		D	3	2	1	6	3	8	1	12	6	10	2	18
							Flat type							
T_2	a Conf.	C	5	4	2	11	5	5	4	14	10	8	6	25
		D	4	4	2	10	5	..	4	9	9	4	6	19
	b S. Conf.	C	1	2	1	4	..	..	1	1	1	2	2	5
		D	..	1	1	2	..	..	..	..	..	1	1	2
	c Disc.	C	..	..	..	..	..	1	..	1	..	1	..	1

TABLE 4.—*The types of attacks, number of cases and deaths with reference to vaccinal status in the three groups under study*—cont.

Typing code	Sub-types		Unvaccinated. Males	Unvaccinated. Non-pregnant females	Unvaccinated. Pregnant females	Unvaccinated. Total	Vaccinated. Males	Vaccinated. Non-pregnant females	Vaccinated. Pregnant females	Vaccinated. Total	Total. Males	Total. Non-pregnant females	Total. Pregnant females	Total. Total
							Ordinary type							
T_3	a Conf.	C	30	26	4	60	34	32	8	74	64	58	12	134
		D	8	8	3	19	3	2	2	7	11	10	5	26
	b S. Conf.	C	20	13	2	35	33	26	10	69	53	39	12	104
		D	1	1	..	2	..	..	..	..	1	1	..	2
	c Disc.	C	11	15	..	26	217	145	27	389	228	160	27	415
							Modified type							
T_4	a Conf.	C	..	..	..	..	..	1	..	1	..	1	..	1
	b S. Conf.	C	..	..	..	..	..	..	..	..	..	..	..	..
	c Disc.	C	3	3	..	6	133	60	21	214	136	63	21	220
	d V.S.E.	C	..	..	..	..	..	2	..	2	..	2	..	2
Total number of cases.		..	75	66	12	153	427	282	82	791	502	348	94	944
Total deaths		..	18	17	9	44	13	12	17	42	31	29	26	86
Case fatality rates.		..	24	25·7	75	28·7	3·0	4·2	20·7	5·3	6·1	8·3	27·6	91

Effect on the case fatality rate.—Irrespective of the vaccinal status, the case fatality rates were 6.1, 8.3 and 27.6 per cent in the males, the non-pregnant females and the pregnant females respectively.

If a comparison is made with reference to the vaccinal status, the case fatality rates are found to be—in the unvaccinated 24, 25.7 and 75.0 per cent and in the vaccinated 3.0, 4.2 and 20.7 per cent in males, the non-pregnant females and the pregnant females respectively.

Effect on severity of the attack.—As per the clinical classification of smallpox cases followed here, Type 1 (*a*) and (*b*), viz., the haemorrhagic cases are most fatal, with the case fatality rates of 100 per cent in Type 1 (*a*) and 95 to 100 per cent in Type 1 (*b*). Next in severity comes the Type 2—the flat type, which has a case fatality rate of 80.0 to 90.0 per cent and then follows Type 3 (*a*)—ordinary confluent, which has a case fatality rate of about 40 per cent for all age-groups irrespective of the vaccinal status, with about 10.0 per cent in the vaccinated and 50.0 per cent in the unvaccinated. Hence, Type 1 (*a*) and (*b*), Type 2 (*a*), (*b*) and (*c*) and Type 3 (*a*) are considered to be severe and the incidence of these types has been compared in these three groups of cases. Table 5 shows the proportionate incidence of the severe varieties of smallpox, the case fatality rate amongst them with reference to the vaccinal status in all the three groups under study. The proportionate incidence of these severe types is 54.6, 53.0 and 83.3 per cent in the unvaccinated, 10.3, 17.0 and 29.2 per cent respectively in the three groups. Comparing the deaths due to these severe varieties, the case fatality rates are 41.5, 45.6 and 90.0 per cent in the unvaccinated and 29.9, 25.0 and 70.8 per cent in the vaccinated males, in the non-pregnant females in the pregnant females respectively.

The proportionate incidence of the invariably fatal variety, namely, the haemorrhagic, was 6.6, 4.5 and 25.0 per cent in the unvaccinated and 1.1, 3.5 and 13.4 per cent in the vaccinated in the three groups respectively. All the cases were fatal (Table 6).

TABLE 5.—*Incidence of severe types in the three groups and their case fatality rate (C.F.R.).*

Groups.	Unvaccinated.				Vaccinated.				Total.			
	Incidence.	Incidence percentage.	Deaths.	Case fatality rate.	Incidence.	Incidence percentage.	Deaths.	Case fatality rate.	Incidence	Incidence percentage.	Deaths.	Case fatality rate.
Males	41/75	54·6	17/41	41·5	44/427	10·3	13/44	29·5	85/502	16·9	30/85	35·3
Non-pregnant females.	35/66	53·0	16/35	45·6	48/282	17·0	12/48	25·0	83/348	23·8	28/83	33·7
Pregnant females ..	10/12	83·3	9/10	90·0	24/82	29·2	17/24	70·8	34/94	36·1	26/34	76·5
Total	86/153	56·2	42/86	43·8	116/791	14·5	42/116	36·2	202/944	21·4	84/202	41·5

Denominators indicate total number of cases.

TABLE 6.—*Incidence of haemorrhagic types in the three groups and their case fatality rate (C.F.R.)*

Groups.	Unvaccinated.				Vaccinated.				Total.			
	Incidence.	Incidence percentage.	Deaths.	Case fatality rate.	Incidence.	Incidence percentage.	Deaths.	Case fatality rate.	Incidence.	Incidence percentage.	Deaths.	Case fatality rate.
Males	5/75	6·6	5/5	100	5/427	1·1	5/5	100	50/502	2·0	10/10	100
Non-pregnant females.	3/66	4·5	3/3	100	10/282	3·5	10/10	100	13/348	3·7	13/13	100
Pregnant females ..	8/12	25·0	3/3	100	11/82	13·4	11/11	100	14/94	14·9	14/14	100
Total	11/153	7·1	11/11	100	26/791	3·3	26/26	100	37/944	3·9	37/37	100

Denominators indicate total number of cases.

Effect of the stage of pregnancy on the incidence of haemorrhagic smallpox.—The relationship between the incidence of haemorrhagic type of smallpox and the stage of pregnancy is shown in Table 2. The least incidence is in the 1st trimester. The incidence rises as pregnancy advances, to a peak in the sixth month. Thereafter it falls in the seventh and the eighth month to rise again till term.

We thus find that the disease has a definite deleterious effect on the termination of pregnancy, the life of the foetus and the mother, and further the pregnant females are far more susceptible to severe types of smallpox, especially in the haemorrhagic type, and the case fatality rates are very high in the pregnant females compared with those in the other two groups.

Discussion—

This study has confirmed more or less the results reported by various authors, especially Schamberg (1923), Bull (1945), and Dixon (1962). It was found that there is a greater risk of premature termination of pregnancy if the woman contracts the disease either in the very early months or very late months of pregnancy. The stillbirth rate is far less in full-term termination than in premature terminations. As regards the mother, though much depends upon the severity of attacks, yet irrespective of the severity and the vaccinal status, the case fatality rate is more in the first trimester and again in the last months of pregnancy. In the fifth month of pregnancy, there is a sudden rise both in the termination rate as well as in maternal fatality rate, which appears very interesting. Thus, we find that smallpox infection has an evil effect on the termination of pregnancy, the life of the foetus as well as that of the mother. Considering the other aspect of the question, how the pregnancy status of the host alters the nature of the attack and course of the disease, this study shows that pregnant women fare very badly with smallpox. On comparison with males and non-pregnant females of the same age-group.

admitted during the same period of study, it was found that the pregnant woman faces three times greater risk of dying if she was unvaccinated and five to seven times greater risk if she was vaccinated only in infancy. The severe varieties of smallpox seem to occur more frequently in the pregnant, and the case fatality rate from these varieties is about three times greater in the vaccinated and twice as great in the unvaccinated, when compared to the other patients of the same age-group.

Of greater interest is the incidence of haemorrhagic varieties. The pregnant female seems to be far more vulnerable to this type. Amongst the unvaccinated, the incidence of this type in the pregnant is 4 to 5 times higher than that in the males and the non-pregnant females. It is still worse in the vaccinated and is twelve times more than males and four times more than the non-pregnant females.

Thus, considered from all aspects, there is no doubt that the pregnancy status on the whole makes the disease more severe. But the question is, why? In what way does the pregnancy status in the woman enhance her susceptibility to infection or reduce her resistance to the infective process? There may be several factors playing a role in this matter.

1. *Lack of immunity*.—Can this severity of the disease in the pregnant female be due to simple lack of immunity ? In general, among the admissions of smallpox cases in this Hospital about 70 per cent of the total unvaccinated cases occur in the age-group 0 to 10, and nearly 70 per cent of the vaccinated cases occur in the age-groups beyond 30 years. So the severe varieties of smallpox usually occur in unvaccinated children under the age of 10, and in the adults once vaccinated in infancy, in the age-groups beyond 30, because of the waning immunity in them due to the age. This is true with all the severe varieties of smallpox except the haemorrhagic types. This particular type is found very rarely in children under 15 years though a majority of them are unvaccinated.

The most vulnerable age-group for this type is 21 to 45. and it is equally prevalent in the unvaccinated as well as in the vaccinated. These indicate that there must be something very peculiar to this age-group which is responsible for the occurrence of this variety and lack of immunity may not have much to do with the incidence of this type.

Taking the haemorrhagic types, it is seen, that in spite of the vaccinal status, the pregnant woman faces for greater risk of contracting this type of attack than others. Thus the pattern of the incidence of these varieties is quite different in the pregnant than in others, and the vaccination does not seem to have any bearing on this, as otherwise, if the lack of immunity is the criterion, the incidence of these varieties should have the same pattern in all patients belonging to the same age-group.

2. *Hypermetabolic state in pregnancy*.—It may be true that several things hapen in the pregnant, and the pregnancy state itself is a great stress on the host and she will be in a hypermetabolic state. But if this has some role to play, why is it that all the pregnant women do not fare badly to the disease, and further why they do not behave in the same way with all other virus infections? We had occasions to see hundreds of cases of chickenpox with pregnancy, a few cases of measles and mumps also in the pregnant, but none of them had any unusual course. These, therefore, suggest that this particular factor may not be playing any important role.

3. *Inability to form antibodies*.—Smallpox is generally fatal and perhaps it is possible that the course of the disease is influenced by the ability of the host to prepare antibodies to infection, quite early in the disease, so that further damage by the virus could be arrested. In other virus infections this apparent inability of the pregnant to prepare the antibodies may not be appreciably noted since even otherwise those diseases are not so fatal as smallpox and poliomyelitis. So this may be a reason for the pregnant faring badly with

these diseases. But one may question whether these antibodies are really essential for recovery from the viral infections. It is said that in the agammaglobulinaemic children, no antibodies are detectable though they get virus infections and recover from them, and it is also said that they are immune to further infections from the same virus though they have no antibodies in their circulation. So it is reasonable to question whether these are necessary for the recovery of the case. If that is so, the question of this factor playing a role in the aggravation of the disease does not arise at all, but it is generally assumed that the immunity to infection, and the recovery from an infection are related to the antibody levels, and perhaps the agammaglobulinaemic children are exceptions. And hence it may be possible that the pregnant has some factor that may be inhibiting early formation of the antibodies.

4. *Hormonal factors.*—Gamzell (1953) measured blood levels of 17-hydroxycorticosteroids in pregnant women and concluded that these were elevated during the pregnancy and that the levels dropped to normal within 6 days of the delivery. Working on a greater number of cases Robinson *et al.* (1955) estimated the 17, 21 dihydroxy 20 ketosteroids in plasma during and after pregnancy. They examined 104 pregnant women, 71 at different stages of pregnancy and the remaining at various intervals of time post partum. They also compared the levels with 25 normal subjects and 8 non-pregnant females suffering from various pathological disorders. They summarised that the level of these ketosteroids is significantly high during pregnancy and after delivery the level tends to fall, although in many patients they were somewhat elevated up to 6 to 9 weeks post partum.

Similarly, to assess the adrenocortical function, the 17, 21 dihydroxy 20 ketosteroidh response to intravenous administration of ACTH has been employed by several authors. Nicholas *et al.* (1955) found that there is a subnormal rise in plasma

level occurring in patients suffering from hypopituitarism, and congenital adrenal hyperplasia; no rise in cases of Addition's disease; and in excess over normal in the normal pregnant women especially during the third trimester and patients with Cushing's syndrome.

Whatever be the source of the high levels of this hormone in the blood of the pregnant female (which is still a debated question), there is no doubt that the pregnant women has these circulating at high levels. Can this be responsible in making the pregnant woman to take the disease of smallpox seriously?

Schwartzman (1950) working with animals concluded that ACTH or cortisone or their combination produced a marked acceleration of poliomyelitis infection in mice and an extraordinary enhancement of susceptibility to the infection in hamsters giving rise to a violent and uniformly fatal disease. His experiments indicate the existence of a significant relationship between adreno-cortical function and susceptibility of mice and hamsters to experimental poliomyelitis infection.

Several authors have reported the disease-enhancing activity of cortisone in a wide variety of experimental virus infections Rose *et. al.* (1952) investigating the effect of cortisone in experimental vaccinia infection found diminished local inflammatory reaction to the intracutaneous infection of the live virus as well as increased quantity of virus in the blood, brain, liver, spleen, kidneys and adrenals of the cortisone-treated rabbits. Bugbee *et al.* (1960) conducting the experiments on rabbits found that cortisone has a definite enhancing effect on the vaccinia infection in the rabbits. Paul (1955) states that the pregnant women are more vulnerable to poliomyelitis and quotes Aranson and Schwartzman (1953) who confirmed the relationship between the susceptibility to infection and cortisone.

These experiments indicate that cortisone has definitely a disease-enhancing effect and that may be perhaps what we find in the pregnant women. In cases of haemorrhagic smallpox, there is very little local reaction on the skin and the virus could be isolated continuously from the blood of the cases till death whereas in the non-haemorrhagic variety, the virus disappears from the blood stream on the third day (Downie, 1953).

It is quite possible that the high level of steroids in the pregnant woman may be the reason for the increased severity of the disease and greater fatality due to smallpox. Perhaps the same may be the reason why even vaccination does not prevent them from getting severe attacks. Schwartzman (1953) pointed out that cortisone makes a non-susceptible animal susceptible; similarly, this hormone in the pregnant may make even an immune woman less immune to the virus infection. One more interesting feature which requries further study is that in general, women fare a little more badly when compared to men of the same age group. It has been found that the corticosteroid excretion in the urine of non-pregnant females changes from day to day depending upon the stage of the menstrual cycle. It has also been found that 17-hydroxycorticosteroids excretion during the 2nd and 3rd weeks of the menstrual cycle was significantly higher than that during the first and the last weeks. Is it possible, therefore, that if a woman gets infected with smallpox or gets the viraemia during the second and third weeks of the menstrual cycle when the corticosteroid level is high, she will develop a severe viriety ? This requires further study.

If cortisone is responsible for the enhancement of the disease due to virus infection, how does it act? Does it enhance the virulence of the virus or reduce the resistance of the host and make her susceptible to infection or interfere with the formation of the anti body after the development of the disease.

Estimating the various anti body titres from different types of smallpox cases, Herlich, *et al.* (1958) found that in all varieties except the haemorrhagic early, by the tenth day of the disease, 96 to 100 per cent of the cases were positive for HAI antibodies; 65 to 80 per cent of the cases were positive for precipitation antibodies; 52 to 80 per cent were positive for CF antibodies to V antigen, and 24 to 40 per cent were positive for CF antibodies to the S. antigen. Amongst these the HAI antibodies are the first to appear. But the haemorrhagic early cases are reported to show quite a different pattern and it is quite possible therefore that cortisone may be inhibiting the formation of these antibodies and thus giving the virus an upperhand with the result that the blood of these cases is loaded heavily with the virus and they die of intense viraemia and the virus toxaemia with extensive involvement of all the internal and vital organs. This perhaps may happen not only in the pregnant women but even in others where due to some pathological condition the corticosteroid levels may be high and they may develop these fatal types of smallpox. But since the levels of the corticosteroids are invariably high in the pregnant subjects this is more commonly found in them. Now the question is why then all the pregnant cases do not develop these fatal varieties? Perhaps it may be due to the fact that each one varies from the other in their levels of this hormone as could be seen from the figures of Robinson *et al.* (*loc. cit.*). It also depends upon the stage of pregnancy when these women get infected. The hormone level is found to rise markedly only after six months. The incidence of haemorrhagic smallpox in the pregnant seems also to rise only after 6 months of pregnancy. Up to 5 months this incidence is only 13 per cent, whereas it is 23·9 per cent in those who got infected after the fifth month of pregnancy. Therefore, there seems to be some correlation between the level of the hormones and the incidence of haemorrhagic smallpox. The maximum incidence is in the 6th month and again in the last 4 to 6 weeks of pregnancy.

If this hormone is responsible for the enhancement of the disease, does it make the host susceptible to infection or does it interfere with the recovery or both? In the case of pregnant women, since the infection is occurring in persons who are already having high level of this hormone, it looks as though it makes them more susceptible to infection. But the continuance of high level of the hormone in the circulation, after the infection has occurred and the disease has set in, perhaps still aggravates the condition by interfering with the mechanism of the antibody or interferon formation. If all this is true, what happens if a person with normal level of this hormone gets infected and develops the disease and then he is administered high doses of cortisone ? Does it enhance the disease process by interfering with the early formation of the antibodies against the infection? These are problems that will crop up if we say that cortisone has some role to play in this disease-enhancing phenomenon that we find in the pregnant woman. Unfortunately, the authors had no facilities to estimate in any of the cases of smallpox the levels of this hormone, which if done might have thrown some light on this problem.

It will be very interesting to make a thorough study of the corticosteroid levels of different types of cases of smallpox and at different stages of the disease and see how far this hormone is responsible for the enhancement of the disease, and whether it has any relationship with either the formation of the antibodies or the interferon in the viral infections.

Summary

A study of 255 cases of pregnant women with smallpox admited to the Infectious Diseases Hospital, Tondiarpet, Madras, during the period of 38 months ending with June 30th, 1962, has been presented.

The effect of smallpox on the termination of pregnancy, the life of the foetus and the life of the mother during the course of the disease was studied.

The termination rate was 56.9 per cent during the course of the disease. The premature termination rate was 42.1 per cent with 50 per cent in the later months of pregnancy after the foetus has become viable and 34 per cent in the earlier months of pregnancy before the foetus became viable.

38.6 per cent was the overall foetal death rate with stillbirth rate of 44.0 per cent in premature termination and only 10.7 per cent in full term termination.

The maternal fatality rate was 31.7 per cent with 34.3 per cent in the later months of pregnancy and 26.7 per cent in the earlier months. Both the maternal fatality as well as pregnancy termination rates are higher in the first few weeks of pregnancy, they decline with the increase in the stage of pregnancy up to the 5th month and thereafter decline in the 6th month and go up again.

The effect of the pregnancy status of the host on the nature of the attack and course of the disease was studied by comparing 94 pregnant women admitted with smallpox during a period of 12 months ending with June 30th 1962 with 348 smallpox cases of non-pregnant females and 502 smallpox cases of males belonging to the same age-group (15 to 45 years) admitted to this hospital during the same period of study.

The case fatality rate in the pregnant women was 27.6 per cent as against 6.1 and 8·3 per cent in the males and non-pregnant females respectively of the same age-group.

With reference to vaccinial status, the case fatality rate in the pregnant in the vaccinated was 20.7 per cent as against 3 and 4.2 per cent in the males and non-pregnant females respectively and in the unvaccinated, it was 75.0 per cent in the pregnant as against 24.0 and 25·7 per cent respectively in the males and non-pregnant females.

The effect of pregnancy status on the nature and course of the disease was then compared with males and non-pregnant females.

The proportionate incidence of severe varieties of smallpox, viz., the haemorrhagic, the flat and the ordinary confluent types, when compared, the percentage incidence of the varieties to the total cases in each of the groups was, in the unvaccinated 54.6, 53.0 and 83.5 per cent and in the vaccinated 10.3, 17.0 and 29.2 per cent respectively in the males, non-pregnant females and pregnant females. Similarly, the case fatality rates amongst the same varieties were 41.5, 45.6 and 90.0 per cent in the unvaccinated, 29.5, 25.0 and 70.8 per cent in the vaccinated in the males, non-pregnant females and pregnant females respectively.

If the incidence of the fatal haemorrhagic types only are compared, the proportionate incidence was 6.6, 4.5 and 25.0 per cent in the unvaccinated and 1.1, 3.5 and 13.4 per cent in the vaccinated respectively in the males, non-pregnant females and pregnant females.

Thus it has been shown that smallpox takes a more serious and fatal form in the pregnant. The various possibilities for this unusual enhancement of the disease in the pregnant are discussed.

Work done by several authors regarding the blood corticosteroid level in the pregnant has been referred to and also the experiments done on the animals regarding the disease-enhancing property of cortisone discussed. It has been suggested that the high level of this hormone in the blood of the pregnant may be one of the factors responsible for the high susceptibility of pregnant women to the severe varieties of smallpox.

It has been further suggested that cortisone may increase the susceptibility to infections as well as the disease-enhancing property due to inhibitory effect on the production of antibodies or interferon during the course of the disease. All aspects of the question need further and elaborate study.

Conclusion

This study confirm the published reports of the various authors in that the disease, smallpox, tends to cause a high premature termination of pregnancy, high foetal and maternal death rates when pregnant women contract smallpox.

Further, the "pregnancy status" has a disease-enhancing property with the result that the pregnant woman faces far greater risk of developing severe varieties of smallpox, especially the haemorrhagic variety and dying, when compared to the males and non-pregnant females of the same age-group. It is suggested that this disease-enhancing property of the pregnancy status may be due to the high level of circulating corticosteroid in the blood of the pregnant woman. It is likely that in these cases corticosone may be inhibiting the formation of antibodies during the course of the disease with the result that the virus multiplies unhampered and the patient dies of viraemia and virus toxaemia and intensive viral involvement of the internal and vital organs.

However, it has been pointed out that a detailed study of the levels of this hormone in the various types of smallpox cases at various stages along with estimation of titre of different antibodies may throw more light on this question.

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RESEARCH ON MASS IMMUNISATION.

Dr. Gardner Middlebrook, Director of Research at National Jewish Hospital in Denver, sand in a Press Conference, that the whole populations can be immunised against disease with out the use of needles or pills, but human fears prevent use of the new technique. He further adds that mass immunisation, through airborne vaccines, is possible as a means of preventing Tuberculosis, Polio and Measles.

Dr. Middlebrook, a pionees in the research on immunising by inhalng vaccines, developed an airborne infection apparatus several years ago. The device is being used to test this technique on animals at several research centres.

Since 1951, U.S. Scientists have made great strides in developing the technique which they call aerogenic immunisation.

Dr. Middlebrook said that mass immunisation by the airtious technic could be used theoritically to fight any infectious disease. A big problem now is, development of the hghly infective but non-disease producing vaccines. He predicts that a major result of research into mass airborne immuunisation could be the world's first, real defence against germ warfare.