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## ‘GERMANIN’ (‘BAYER 205’) IN THE TREATMENT OF PLAGUE.

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### INTRODUCTION.

EVER since the outbreak of bubonic plague in India, almost every drug which had been favourably reported upon as a possible cure has been tried at the Maratha Plague Hospital, Bombay, but with disappointing results. Choksy (1923) after an experience extending over a period of more than 25 years in the treatment of plague came to the conclusion that ‘all efforts hitherto made to cure the disease by drugs have proved absolutely futile’ and urged the necessity for undertaking further researches into the possibility of preparing a potent anti-plague serum in India, as ‘it is the only remedy that holds out any hope of reducing the excessively high case mortality which has so markedly characterized the epidemics at Bombay.’ Patel, the present Superintendent of the Maratha Plague Hospital, also came to the same conclusion. He (Patel, 1925) observes that chemotherapy of plague with iodine and its preparations, carbolic acid, mercurochrome, salvarsan preparations, etc., has not been found to have any effect either on the mortality or on the course of the disease. Looking to the analogy of other infectious diseases, the only rational treatment, in his opinion, would be with a powerful concentrated antitoxic serum prepared from local strains and given early and in large doses. Until such a potent antitoxic serum becomes available, the medical practitioner called upon to treat cases of plague must necessarily have recourse to one or the other of the drugs which have been commended by his fellow practitioners.

Dr. O. Urchs (1930) of Messrs. Bayer-Meister Lucius, having received a communication from Dr. Vincent of Maymyo of the very good results he had obtained with '*Bayer 205*' in the treatment of some cases of plague, suggested that he would place a sufficient supply of the drug at our disposal should we desire to test its therapeutic value in experimental animals. This paper deals with a brief history of chemotherapy of plague and with our experiments with '*Germanin*,' a preparation of '*Bayer 205*' for human use, in rabbits—animals susceptible to experimental infection with plague.

#### CHEMOTHERAPY OF PLAGUE.

Several drugs have been administered to plague patients either orally, subcutaneously or intravenously, not only to relieve the distressing symptoms which accompany the disease but also with a view to destroying the plague bacilli in the body and effecting a cure. With this latter object, Choksy introduced the method of injecting germicides into buboes during the first epidemic of plague in Bombay.

*Carbolic acid*.—Choksy (1904) injected either pure carbolic acid or equal parts of carbolic acid and liquor iodi in doses of 10 to 20 minims into each bubo. Paton (1908) reported successful results following oral and subcutaneous use of carbolic acid among cases treated at Amoy. Choksy (1918) found that even when pure carbolic acid was administered in doses of 72 to 100 grains per day, it was inert. Patel (1925) also obtained no success with this drug.

*Formalin and its preparations*.—Roehr (1912) suggested the injection of a two per cent solution of formalin into the bubo and Deggeller (1915) treated 5 cases of plague with intravenous injections of formaldehyde sodium bisulphite ('*Fonabisit*') with 3 deaths; but the number of cases treated was too small to allow of any definite conclusion with regard to its therapeutic value.

*Eusol*.—Connor (1916) suggested the subcutaneous injection of eusol in the treatment of plague. Brayne (1917) and Baker (1920) employed eusol but with no benefit.

*Izal*.—Choksy (1904) treated 21 cases of plague with injections of 5 to 10 c.c. of a one per cent solution of izal into buboes; he found that these injections had no influence, either local or general, on the course of the disease or on the mortality. Patel (1926) also employed izal without any benefit.

*Mercury and its preparations*.—Choksy (1918) treated 21 cases of plague by subcutaneous injections of *collosol mercury* with 15 deaths. Andrew Balfour (1924) suggested the use of *mercurochrome-220 soluble* in plague. He (1925) reported later that he had received accounts of a few cases of plague in which the drug had been distinctly beneficial. Patel (1925) treated 6 cases of plague with this drug by the intravenous route and all ended fatally. Still later, he (1929) tried the drug on two more cases but without benefit. We (Naidu and Shamsheer Jung, 1926) found that in

experimentally infected animals, such as rats and rabbits, the injections of *mercurochrome-220* soluble in sublethal doses either single or repeated had no influence on the case mortality. At the Haffkine Institute Caius, Kamath and Naidu (1927) tested the bactericidal action of some organic compounds of mercury on '*B. pestis*' *in vitro* and found that the bactericidal power of these drugs was roughly proportional to the amount of mercury present in each. One of us (B. P. B. N.) tested the therapeutic action of *tetra-acetoxy-mercuri-trypan blue*, a synthetic preparation prepared at this Institute, in experimentally plague infected rabbits as it exhibited very high germicidal property against '*B. pestis*' *in vitro*. But when tested *in vivo* the drug was found to have no influence on the mortality from the disease in these animals.

*Silver and its preparations.*—Elliot (1907) reported successful cures in bubonic plague following the intravenous injections of a one per cent solution of collargol. Choksy (1918) employed *colloidal silver* in 93 cases of plague with 60 deaths (64·5 per cent). Denman (1914) found that early cases of plague were benefited by intravenous injections of *electrargol*. In his series the mortality among the treated cases was 60·4 per cent as compared to the mortality of 83·4 per cent among controls. Ilvento and Mazitelli (1914) and Choksy (1918) also employed *electrargol* in the treatment of plague but found the drug to be of little value.

*Salvarsan and allied arsenical preparations.*—Lancelin (1912) and Aumann (1912) employed intravenous injections of salvarsan without benefit in plague. Schut (1921) treated 5 cases of plague by intravenous injections of *neosalvarsan* all of which ended fatally. Ram Mansoor (1922) treated one case of plague with the same drug and it recovered. Marshall and Achhru Ram (1922) reported successful cures in 6 out of 7 cases treated with *neokharsivan*. Patel (1925) found that salvarsan preparations had no effect on the case mortality of plague.

*Iodine and its preparations.*—Choksy was apparently the first to use iodine in the treatment of plague. He (Choksy, 1901) treated 104 cases by the oral administration of *iodine terchloride* with a mortality of 66·3 per cent. Patel (1925) also treated 32 cases with the same drug administered orally and had a mortality of 87·5 per cent. Commissioner Booth Tucker of the Salvation Army (1913) reported successful cures following oral administration of *tincture of iodine*. Connor (1912-13) advocated the use of this drug intravenously in plague and reported that all the three cases he had treated recovered. Liston (1913) conducted an experiment with tincture of iodine among cases admitted to the Maratha Plague Hospital. He classified the cases into four groups according to bacteriological findings: (1) no plague bacilli in 0·25 c.c. of blood, (2) some but less than 10 plague bacilli in 0·25 c.c. of blood, (3) more than 10 but less than 100 bacilli in 0·25 c.c. of blood, and (4) more than 100 bacilli in 0·25 c.c. of blood. He considered such a classification necessary as he had previously observed that all patients who showed more than 10 plague bacilli in 0·25 c.c. of blood invariably died, while a proportion of cases with no plague

bacilli or less than 10 bacilli in 0·25 c.c. of blood recovered. In his series of 60 cases, 20 received the routine treatment adopted by Choksy in his hospital cases, 20 were treated with tincture of iodine by the mouth while 20 were given the drug intravenously. In the first group of 20 cases there was a mortality of 16, in the second 12 and in the last group 17. Among the cases in which recovery was considered possible from bacteriological findings as explained above, in the first group there were 9 cases with 55·5 per cent mortality; in the second there were 12 cases with 33·3 per cent mortality and in the last there were 10 cases with 70 per cent mortality. As the number of cases treated in each group was not sufficiently large, he could not come to any definite conclusion as to the value of this treatment. Choksy (1914) in view of the lesser mortality that followed oral administration of tincture of iodine among the cases treated by Liston, treated 27 cases by the same method and had a mortality of 81·5 per cent. He (Choksy, 1915) made a further trial with tincture of iodine in 88 cases and had a mortality of 72·7 per cent. From these results he concluded that 'plague as observed in Bombay is unaffected and not amenable to treatment by iodine.' Rama Iyer (1916) treated 6 cases of plague with intravenous injections of tincture of iodine and of these 5 recovered. He also reported that Mg. Tha Din treated a few cases in Mandalay by the same method with satisfactory results. Vassallo (1921) treated 20 cases by intravenous injections of tincture of iodine with 4 deaths and attributed his good results to very early treatment. Jeudwine (1923) found that early cases were benefited by intravenous injections of tincture of iodine and stated that Hari Ram had reported 26 cures out of 28 cases treated with intravenous injections and that Gian Chand also reported in the same manner. Pal (1924) treated 2 cases with intravenous injections of iodine; of these one died. He noticed that the injections of iodine resulted in the reduction of the temperature of plague patients even in septicæmic cases, but 'as regards cures the results are as disappointing as with any other form of drug treatment of this dreaded disease.' Naquvie (1924) reported that he had treated about 100 cases of plague by intravenous injections of iodine and that most of his cases recovered and estimated the cures at 75 per cent. Patel (1922) employed 0·6 per cent solution of iodine subcutaneously and also intravenously in 153 cases with a mortality of 73·2 per cent, while the mortality among the 48 control cases was 72·7 per cent. He (Patel, 1924) further reported that he had treated in all 380 cases with tincture of iodine by oral, subcutaneous and intravenous routes with a mortality of 75·7 per cent. Marshall and Ram (1924) reported that the latter had treated 103 cases of plague in Uganda by intravenous injections of iodine and only 16 of these recovered, and that Baker had treated 50 cases by the same method and of these 19 recovered. Bharadwaj (1926) reported that he had treated about 100 cases by the same method and claimed 80 per cent cures. Mallanah (1920) advocated the injection of a solution of *iodine*, *camphor* and *thymol* into the plague bubo and reported that out of 34 cases treated by this method in the Hyderabad Isolation Hospital there were 15 deaths whereas

when tincture of iodine was injected into the bubo and also orally, all the twenty cases thus treated died. Subbiah Pillai (1921) treated 3 cases by Mallanah's method with 2 deaths. Carman (1927) reported that he had treated 27 cases by the same method with 9 deaths (33·3 per cent). Patel (1929) treated 16 cases by intravenous injections of this mixture with 14 deaths (87·5 per cent). Choksy (1920) reported that he obtained good results following the use of colloidal preparations of iodine. Out of 260 patients treated with these preparations there were 160 deaths (61·5 per cent). Grimes (1926) treated seven cases of plague with *colloidal iodine* and of these only one died. Choksy (1918) treated 63 cases with *iodol* and had 41 deaths (65·1 per cent).

From this review, it is apparent that a very large number of cases of plague have been treated especially with iodine in one form or another but with very divergent results: some claiming cures with this drug to the extent of 80 to 100 per cent while in the hands of others the results have been very disappointing. In spite of these apparently conflicting results iodine continues to be a favourite remedy with many. This is partly due to the fact that its use is unattended with any constitutional disturbance and that a temporary fall in the temperature of the patient very often follows its injection. The divergent results obtained by these several observers may be reconciled when one remembers that in the course of an epidemic several cases of fever resembling plague but in reality not due to infection by *B. pestis* are treated as such. In a series of 276 cases that were sent to the hospital by medical practitioners in which we carried out bacteriological examination both by bubo puncture and by blood culture there were no less than 40 cases in which the diagnosis of plague could not be confirmed. It is obvious that inclusion of such cases among those treated as plague with any special line of treatment will naturally raise the percentage of recoveries depending upon the proportion of such cases treated. Further, even among cases that have been definitely diagnosed as plague and classified according to the severity of blood infection, our observations have shown that in purely bubonic cases in which no plague bacilli were detected in 0·25 c.c. of blood the mortality under ordinary hospital treatment varied only from 25 to 33 per cent, while in septicæmic cases in which less than ten plague bacilli were present in 0·25 c.c. of blood the mortality rose to about 75 per cent and in septicæmic cases in which more than ten bacilli were detected in the same amount of blood the mortality was 100 per cent. From these results it would be evident that for correctly estimating the value of any form of treatment it is necessary not only to confirm the diagnosis of plague by bacteriological examination but also to estimate the severity of infection in each case.

‘GERMANIN’ (‘BAYER 205’).

‘Germanin’ is a loose white powder which dissolves readily in physiological solution of sodium chloride and also in cold distilled water. According to the

manufacturers it is a complex organic combination containing neither arsenic, antimony, mercury nor any other inorganic substance. It is regarded as the best trypanosomicidal drug at present available for the treatment of human trypanosomiasis. The manufacturers emphasize that this drug has produced no satisfactory results in other diseases not caused by trypanosomes. It has been ascertained that in encephalitis lethargica, it has proved to be quite useless, while in other bacterial diseases and in infections caused by spirochaetes it has not been a success. They warn that the drug is not entirely harmless. They, therefore, recommend not to employ it at random, as it would not only do harm but also discredit the drug.

Nevertheless, this drug has been used by some observers for the treatment of plague. Dyce Sharp (1926) reported 8 recoveries out of the 12 cases of plague he had treated with 'Bayer 205,' while Carman (1927) found that this drug had no definite specific action on plague. Very recently, Vincent (1931) published successful results he obtained in four cases of plague with 'Bayer 205.' In view of these apparently good results which are reported to have attended the use of 'Bayer 205' in the treatment of plague we undertook to test this drug in experimental animals.

#### OUR EXPERIMENTS WITH 'GERMANIN.'

##### (1) Germicidal action of 'Germanin' on *B. pestis*.

In the first instance, we attempted to ascertain the germicidal property of this drug on the plague bacillus. A broth culture of *B. pestis* of 48 hours' growth was employed. Equal volumes of this culture and of different dilutions of 'Germanin' were mixed together and allowed to stand at room temperature. At the end of 15 minutes and 24 hours respectively, cultures were made from these mixtures on blood-agar slopes. These subcultures were examined for growth from day to day for a period of seven days. The results showed that the drug has no germicidal action on *B. pestis* even in a dilution of 1 in 20 and after a contact of as long as 24 hours.

##### (2) Toxicity of 'Germanin' for rabbits.

We then proceeded to test the toxicity of the drug. For this purpose rabbits weighing from 1,690 to 1,980 grammes were inoculated intravenously with a single dose varying from 0.01 to 2 grammes of the drug. In another series, rabbits weighing from 1,690 to 2,790 grammes received intravenous injections of the drug in doses varying from 0.1 to 0.5 gramme repeated at intervals of 24 hours for 2 to 7 days, the total amount of the drug injected being 0.7 to 1.25 grammes. The results showed that the drug was not toxic to rabbits up to 0.6 gramme, given either as a single dose or in fractional doses; but was fatal when the dose reached 0.7 gramme and over with a mortality of 100 per cent, death ensuing within about 20 minutes to seven days according to the size and fractioning of the dose employed. These results are summarized in Tables I and II.

From Tables I and II it would also appear that either a single dose of 0.5 gramme or repeated doses of 0.1 gramme on five successive days at intervals of 24 hours were well borne by rabbits.

Following the injection of a rapidly fatal dose rabbits scream, have convulsions, their respirations become hurried and death ensues in a short time. Should the animal survive for a period of 24 hours or longer, as it happened when the doses were given in fractions, the post-mortem appearances in these animals were: (a) hæmorrhages in the walls of the intestines, more particularly in the large intestine, (b) liver presenting appearances of simple congestion to fatty degeneration, (c) spleen congested, (d) lungs presenting appearances of congestion or sometimes of broncho-pneumonia, and (e) pleural, pericardial and in one instance peritoneal effusion.

TABLE I.

| Weight of rabbits in grammes. | Daily mortality following intravenous injections of ' Germanin ' in single dose. |                                      |    |     |    |            |    |     |    |     |    |    |    | Survivors at the end of 30 days after treatment. |
|-------------------------------|----------------------------------------------------------------------------------|--------------------------------------|----|-----|----|------------|----|-----|----|-----|----|----|----|--------------------------------------------------|
|                               | 0                                                                                | 1                                    | 2  | 3   | 4  | 5          | 6  | 7   | 8  | 9   | 10 | 11 | 12 |                                                  |
| 1,730                         | gm. 0.01                                                                         | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,750                         | 0.0125                                                                           | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,690                         | 0.025                                                                            | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,750                         | 0.05                                                                             | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,800                         | 0.05                                                                             | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,820                         | 0.1                                                                              | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,820                         | 0.125                                                                            | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,830                         | 0.25                                                                             | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,900                         | 0.5                                                                              | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,800                         | 0.5                                                                              | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,900                         | 0.6                                                                              | ..                                   | .. | ..  | .. | ..         | .. | ..  | .. | ..  | .. | .. | .. | 1                                                |
| 1,910                         | 0.7                                                                              | Died within one hour after injection |    |     |    |            |    |     |    |     |    |    |    | D                                                |
| 1,900                         | 0.8                                                                              | do.                                  |    | do. |    | 20 minutes |    | do. |    | do. |    |    |    | D                                                |
| 1,940                         | 1.0                                                                              | do.                                  |    | do. |    | do.        |    | do. |    | do. |    |    |    | D                                                |
| 1,980                         | 2.0                                                                              | do.                                  |    | do. |    | do.        |    | do. |    | do. |    |    |    | D                                                |
| TOTAL 15                      |                                                                                  |                                      |    |     |    |            |    |     |    |     |    |    |    | 11                                               |

D = Died.

TABLE II.

| Weight of rabbits in grammes. | Daily mortality following intravenous injections of 'Germanin' in repeated doses. |      |      |      |      |     |     |    |    |    | Survivors at the end of 30 days after treatment. |    |
|-------------------------------|-----------------------------------------------------------------------------------|------|------|------|------|-----|-----|----|----|----|--------------------------------------------------|----|
|                               | 0                                                                                 | 1    | 2    | 3    | 4    | 5   | 6   | 7  | 8  | 9  |                                                  | 10 |
|                               | gm.                                                                               | gm.  | gm.  | gm.  | gm.  | gm. | gm. |    |    |    |                                                  |    |
| 1,820                         | 0.5                                                                               | 0.5  | D    | ..   | ..   | ..  | ..  | .. | .. | .. | ..                                               |    |
| 1,800                         | 0.5                                                                               | 0.5  | D    | ..   | ..   | ..  | ..  | .. | .. | .. | ..                                               |    |
| 1,750                         | 0.5                                                                               | 0.5  | D    | ..   | ..   | ..  | ..  | .. | .. | .. | ..                                               |    |
| 1,690                         | 0.5                                                                               | 0.5  | D    | ..   | ..   | ..  | ..  | .. | .. | .. | ..                                               |    |
| 1,870                         | 0.25                                                                              | 0.25 | 0.25 | 0.25 | D    | ..  | ..  | .. | .. | .. | ..                                               |    |
| 1,990                         | 0.25                                                                              | 0.25 | 0.25 | 0.25 | 0.25 | ..  | D   | .. | .. | .. | ..                                               |    |
| 2,020                         | 0.25                                                                              | 0.25 | 0.25 | 0.25 | 0.25 | D   | ..  | .. | .. | .. | ..                                               |    |
| 2,070                         | 0.25                                                                              | 0.25 | 0.25 | 0.25 | 0.25 | ..  | D   | .. | .. | .. | ..                                               | .. |
| 2,010                         | 0.1                                                                               | 0.1  | 0.1  | 0.1  | 0.1  | ..  | ..  | .. | .. | .. | ..                                               | 1  |
| 2,220                         | 0.1                                                                               | 0.1  | 0.1  | 0.1  | 0.1  | ..  | ..  | .. | .. | .. | ..                                               | 1  |
| 2,220                         | 0.1                                                                               | 0.1  | 0.1  | 0.1  | 0.1  | ..  | ..  | .. | .. | .. | ..                                               | 1  |
| 2,230                         | 0.1                                                                               | 0.1  | 0.1  | 0.1  | 0.1  | 0.1 | ..  | .. | .. | .. | ..                                               | 1  |
| 2,790*                        | 0.1                                                                               | 0.1  | 0.1  | 0.1  | 0.1  | 0.1 | 0.1 | .. | .. | .. | ..                                               | D  |
| TOTAL<br>13                   |                                                                                   |      |      |      |      |     |     |    |    |    |                                                  | 4  |

\* Died seven days after the last injection. D = Died.

## (3) Treatment of plague in experimentally infected rabbits.

Rabbits were infected subcutaneously with our test dose, namely, 0.003 milligram of spleen of a rat dead of acute plague. They were treated with varying amounts of 'Germanin.' In one series, the first dose was injected immediately after infection. Some of the infected animals received a single dose while in others the doses were repeated at intervals of 24 hours. Out of 10 rabbits treated with a single dose varying from 0.1 to 0.5 gramme intravenously, all died by the eighth day after infection. Of the 10 rabbits treated with repeated doses in total amounts varying from 0.3 to 0.5 gramme, 9 died by the twelfth day of infection, while the mortality among the ten control rabbits was 80 per cent during the same period. In another series, treatment was commenced after 24 hours of infection and the

TABLE III.

| Weight of rabbits in grammes. | Treated with ' Germanin ' intravenously. Daily mortality following infection. |     |     |     |     |    |    |    |    |    |    | Percentage of mortality at the end of 30 days after infection. | Weight of rabbits in grammes. | Treated with anti-plague serum intravenously. Daily mortality following infection. |      |      |      |    |    | Percentage of mortality at the end of 30 days after infection. | Weight of rabbits in grammes. | Untreated controls. Daily mortality following infection. |    |    |    |    |    |    |    |    | Percentage of mortality at the end of 30 days after infection. |    |    |    |
|-------------------------------|-------------------------------------------------------------------------------|-----|-----|-----|-----|----|----|----|----|----|----|----------------------------------------------------------------|-------------------------------|------------------------------------------------------------------------------------|------|------|------|----|----|----------------------------------------------------------------|-------------------------------|----------------------------------------------------------|----|----|----|----|----|----|----|----|----------------------------------------------------------------|----|----|----|
|                               | 0                                                                             | 1   | 2   | 3   | 4   | 5  | 6  | 7  | 8  | 9  | 10 |                                                                |                               | 11                                                                                 | 0    | 1    | 2    | 3  | 4  |                                                                |                               | 5                                                        | 6  | 7  | 8  | 9  | 1  | 2  | 3  | 4  |                                                                | 5  | 6  | 7  |
|                               | gm.                                                                           | gm. | gm. | gm. | gm. |    |    |    |    |    |    |                                                                |                               | c.c.                                                                               | c.c. | c.c. | c.c. |    |    |                                                                |                               |                                                          |    |    |    |    |    |    |    |    |                                                                |    |    |    |
| 1,990                         | 0.1                                                                           | ..  | ..  | ..  | ..  | .. | .. | D  | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,780                         | 0.1                                                                           | ..  | ..  | ..  | ..  | D  | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,710                         | 0.1                                                                           | ..  | ..  | ..  | ..  | .. | .. | D  | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,640                         | 0.1                                                                           | ..  | ..  | ..  | ..  | .. | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,560                         | 0.1                                                                           | ..  | ..  | ..  | ..  | .. | .. | D  | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,980                         | 0.5                                                                           | ..  | ..  | ..  | ..  | D  | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,840                         | 0.5                                                                           | ..  | ..  | ..  | ..  | D  | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,710                         | 0.5                                                                           | ..  | ..  | ..  | ..  | D  | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,630                         | 0.5                                                                           | ..  | ..  | ..  | ..  | D  | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,530                         | 0.5                                                                           | ..  | ..  | ..  | D   | .. | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,970                         | 0.1                                                                           | 0.1 | 0.1 | 0.1 | 0.1 | .. | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,660                         | 0.1                                                                           | 0.1 | 0.1 | 0.1 | 0.1 | D  | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,620                         | 0.1                                                                           | 0.1 | 0.1 | 0.1 | 0.1 | D  | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,810                         | 0.1                                                                           | 0.1 | 0.1 | 0.1 | 0.1 | .. | .. | .. | .. | .. | .. | ..                                                             | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,520                         | 0.1                                                                           | 0.1 | 0.1 | 0.1 | 0.1 | .. | .. | .. | .. | .. | .. | D                                                              | ..                            | ..                                                                                 | ..   | ..   | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 2,130                         | 0.1                                                                           | 0.1 | 0.1 | 0.1 | ..  | D  | .. | .. | .. | .. | .. | ..                                                             | 2,190                         | 1                                                                                  | 1    | 1    | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 2,000                         | 0.1                                                                           | 0.1 | 0.1 | 0.1 | ..  | .. | D  | .. | .. | .. | .. | ..                                                             | 2,010                         | 1                                                                                  | 1    | 1    | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,940                         | 0.1                                                                           | 0.1 | 0.1 | 0.1 | ..  | .. | .. | D  | .. | .. | .. | ..                                                             | 1,970                         | 1                                                                                  | 1    | 1    | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,830                         | 0.1                                                                           | 0.1 | 0.1 | 0.1 | ..  | .. | .. | D  | .. | .. | .. | ..                                                             | 1,840                         | 1                                                                                  | 1    | 1    | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,670                         | 0.1                                                                           | 0.1 | 0.1 | 0.1 | ..  | D  | .. | .. | .. | .. | .. | ..                                                             | 1,700                         | 1                                                                                  | 1    | 1    | ..   | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 2,240                         | ..                                                                            | 0.1 | 0.1 | 0.1 | 0.1 | D  | .. | .. | .. | .. | .. | ..                                                             | 2,370                         | ..                                                                                 | 1    | 1    | 1    | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,800                         | ..                                                                            | 0.1 | 0.1 | 0.1 | 0.1 | .. | D  | .. | .. | .. | .. | ..                                                             | 2,050                         | ..                                                                                 | 1    | 1    | 1    | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,670                         | ..                                                                            | 0.1 | 0.1 | 0.1 | 0.1 | .. | .. | D  | .. | .. | .. | ..                                                             | 2,030                         | ..                                                                                 | 1    | 1    | 1    | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 2,000                         | ..                                                                            | 0.1 | 0.1 | D   | ..  | .. | .. | .. | .. | .. | .. | ..                                                             | 1,720                         | ..                                                                                 | 1    | 1    | 1    | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |
| 1,880                         | ..                                                                            | 0.1 | 0.1 | D   | ..  | .. | .. | .. | .. | .. | .. | ..                                                             | 1,680                         | ..                                                                                 | 1    | 1    | 1    | .. | .. | ..                                                             | ..                            | ..                                                       | .. | .. | .. | .. | .. | .. | .. | .. | ..                                                             | .. | .. | .. |

D=death from plague.

infected animals received three doses of 0.1 gramme of the drug at intervals of 24 hours. All the five rabbits so treated died by the eighth day after infection.

For purposes of comparison, ten other infected rabbits were treated at the same time with our local anti-plague serum. All these serum-treated animals survived, while four out of the five control rabbits died within 9 days after infection. These results are summarized in Table III.

#### CONCLUSIONS.

1. 'Germanin' ('Bayer 205') when tested *in vitro* was found to possess no germicidal action upon *B. pestis* even in a dilution of 1 in 20.
2. The minimum lethal dose for rabbits was found to be 0.7 gramme whether given as a single dose or in fractional doses administered in the course of 2 to 7 days.
3. When tested in experimentally infected rabbits in tolerant doses it was found to possess no curative property against plague.

#### REFERENCES.

- AUMANN (1912) .. .. *Deut. Med. Woch.*, **38**, 46, pp. 2166-2168. Abst. in *Trop. Dis. Bull.*, **1**, 6, p. 316.
- BAKER, C. J. (1920) .. *Uganda Protectorate Annual Med. San. Report*, pp. 64-66. Abst. in *Trop. Dis. Bull.*, **19**, 5, p. 369.
- BALFOUR, ANDREW (1924) .. *Brit. Med. Jour.*, Dec. 6, p. 1081.
- Idem.* (1925) .. *Ibid.*, July 11, p. 86.
- BHARADWAJ, A. C. (1926) .. *Ind. Med. Gaz.*, **61**, 2, pp. 63-64.
- BRAYNE, W. F. (1917) .. *Ibid.*, **52**, 9, pp. 322-323.
- CAIUS, J. F., KAMAT, S. A., and NAIDU, B. P. B. (1927) .. *Ind. Jour. Med. Res.*, **15**, 2, pp. 327-333.
- CARMAN, J. A. (1927) .. *Kenya and East African Med. Jour.*, **4**, 7, pp. 196-200. Abst. in *Trop. Dis. Bull.*, **25**, 4, p. 318.
- CHOKSY, N. H. (1901) .. Report to the Municipal Commissioner, Bombay, on cases treated with Prof. Lustig's serum, etc.
- Idem.* (1904) .. *Annual Report of the Executive Health Officer, Bombay Municipality*, p. 44.
- Idem.* (1914) .. *Ibid.*, pp. 81-82.
- Idem.* (1915) .. *Ibid.*, p. 66.
- Idem.* (1918) .. *Ibid.*, p. 90.
- Idem.* (1920) .. *Ibid.*, pp. 54-55.
- Idem.* (1923) .. *Times of India*, May-June.
- CONNOR, F. P. (1912-13) .. *Jour. Lond. Trop. Med.*, **2**, pp. 148-149.
- Idem.* (1916) .. *Ind. Med. Gaz.*, **51**, 2, p. 73.
- DEGGELLER, O. (1915) .. *Geneesk. Tijdschr. v. Nederl. Indie*, **55**, 1, pp. 23-34. Abst. in *Trop. Dis. Bull.*, **5**, 7, p. 396.
- DENMAN, R. (1914) .. *Brit. Med. Jour.*, June 6, p. 1236.
- DYCE SHARP, N. A. (1926) .. *Trans. Roy. Soc. Trop. Med. Hyg.*, **19**, 8, pp. 482-484.
- ELLIOT, A. M. (1907) .. *Lancet*, Aug. 17, p. 477.
- GRIMES, C. (1926) .. *Bull. Soc. Path. Exot.*, **19**, 6, pp. 407-409.
- ILVENTO, A. and MAZITELLI, M. (1914) .. *Malaria e Malat Paesi Caldi*, **5**, 4, pp. 277-296. Abst. in *Trop. Dis. Bull.*, **5**, 7, p. 396.

- JEUDWINE, W. W. (1923) .. *Ind. Med. Gaz.*, **58**, 12, p. 561.
- LANCELIN (1912) .. *Arch. de Med. et Pharm.*, **98**, 11, pp. 353-374. Abst. in *Trop. Dis. Bull.*, **1**, 6, p. 310.
- LISTON, W. G. (1913) .. *Annual Report of the Bombay Bacteriological Laboratory*.
- MALLANAH, S. (1920) .. *Ind. Med. Gaz.*, **55**, 7, pp. 255-256.
- MARSHALL, H., and ACHHRU RAM (1922) *Uganda Protectorate Annual Med. San. Report*, pp. 68-69. Abst. in *Trop. Dis. Bull.*, **21**, 1, p. 67.
- Idem.* (1924) .. *Trans. Soc. Trop. Med. Hyg.*, **18**, 4, pp. 207-209.
- NAIDU, B. P. B., and SHAMSHER JUNG (1926) *Ind. Jour. Med. Res.*, **14**, 2, pp. 323-328.
- NAQVIE, S. Z. (1924) .. *Ind. Med. Gaz.*, **59**, 6, p. 319.
- PAL, R. D. (1924) .. *Ibid.*, **59**, 7, p. 348.
- PATEL, P. T. (1922) .. *Annual Report of Executive Health Officer, Bombay Municipality*, p. 54.
- Idem.* (1924) .. *Ibid.*, p. 50.
- Idem.* (1925) .. *Ibid.*, p. 48.
- Idem.* (1926) .. *Proceedings of the 13th Ind. Sc. Congress*, p. 286.
- Idem.* (1929) .. *Annual Report of Executive Health Officer, Bombay Municipality*, p. 48.
- PATON, B. LEWIS (1908) .. *Brit. Med. Jour.*, Aug. 29, p. 599.
- RAM MANSOOR (1922) .. *Ibid.*, July 22, pp. 127-128.
- RAMA IYER, S. (1916) .. *Ind. Med. Gaz.*, **51**, 10, p. 371.
- ROEHR, C. G. (1912) .. *New York Med. Jour.*, **96**, 16, pp. 800-801. Abst. in *Trop. Dis. Bull.*, **1**, 6, p. 316.
- SCHUT, H. (1921) .. *Geneesk. Tijdschr. v. Nederl. Indie*, **61**, 1, pp. 65-70. Abst. in *Trop. Dis. Bull.*, **18**, 5, p. 350.
- SUBBIAH PILLAI, N. (1921) .. *Ind. Med. Gaz.*, **56**, 3, pp. 98-99.
- TUCKER, BOOTH (1913) .. *Pioneer* (Indian daily paper), May 4.
- URCHS, O. (1930) .. Personal communication.
- VASSALLO, S. M. (1921) .. *Jour. Trop. Med. Hyg.*, **24**, 7, pp. 92-93. Abst. in *Trop. Dis. Bull.*, **17**, 5, p. 395.
- VINCENT, G. W. (1931) .. *Ind. Med. Gaz.*, **66**, 3, pp. 126-127.