

## GONORRHOEA-TREATED WITH INTRAVENOUS PENICILLIN

by

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*“Mary had a Gonococcus  
with bean shaped twins  
It followed Mary every where;  
And Mary was no bore”  
( With apologies to Butter-Field )*

*Historical*:— Gonorrhoea appears to be as old as humanity, existing from the earliest times. Many believe that the words “an issue of seed” in the old Testament refers to this disease.

Though gonorrhoea was known from time immemorial doctors in the Renaissance period believed that gonorrhoea was only an initial stage of syphilis and not an independent disease.

John Hunter ( 1767 ), unfortunately by a self inoculated experiment, which ultimately cost him his life, mistakenly concluded that both gonorrhoea and syphilis were caused by the same organism. His reputation was so great that no contemporary physician could dare contradict his statement which resulted in confusion worse confounded in the proper understanding of gonorrhoea.

Jean Francois Hernandez ( 1812 ) experimentally produced gonorrhoea in a human guineapig. a male prisoner without showing any signs or symptoms of syphilis. Still there were some sceptics who considered such experiments as inconclusive. Record ( 1830 ) properly delineated the two diseases, syphilis and gonorrhoea as two different disease entities. Albert Neisser ( 1897 ) ultimately settled all controversy by demonstrating the organism responsible for gonorrhoea and named it as gonococcus.

*Nomenclature*:— Galen ( 130 A. D. ) is given the credit as the first to employ the term gonorrhoea.

Gonorrhoea means “ a berry like organism that causes a flow of semen”. Etymologically this nomenclature is a misnomer as neither the gonococcus resembles a berry nor the resulting discharge is seminal in nature.

Gonorrhoea produces blindness in new born innocent children, great morbidity in women, sterility in both sexes, besides local and metastatic complications, some-times resulting in death.

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**Diagnosis:**— The diagnosis of gonorrhoea is much more difficult in women than men because of the anatomical structure and of the normal flora of the vagina. Often non-gonococcal gram negative diplococci are present in the genitalia of female children and women. Though the ideal method is to culture the suspected material and perform the fermentation tests for confirming the diagnosis, it is time consuming and not always successful. Routine smear examinations with Gram's stain is often sufficient under the guidance of an experienced venereologist.

**Incidence:**— It is very difficult to assess the true incidence of gonorrhoea in a community because of the short incubation period, rapid course, reinfections, superinfections and the frequent early asymptomatic state in women. Though the disease is more common in the poorer sections of the population, no strata of society is exempt from the disease.

Married men seldom bring their wives for examination and treatment. A frequent excuse is that either the wife is permanently separated, or that she is in a state of advanced pregnancy. The single women, women separated from their husbands, deserted wives and widows who attend the V. D. Clinic are either habitually promiscuous or often members of the oldest profession. Contact tracing becomes practically impossible as in most of the cases sexual intercourse takes place clandestinely in obscure places, sometimes with casual acquaintances so that it is not possible to elicit correct identity of the individuals. Even when a definite address is provided by the patient, it often turns out to be a false one to mislead the social worker. Many women who are carriers of the disease are often blissfully ignorant of their infection and transmit the disease to their sexual partners without fear or favour.

Gonorrhoea is prevalent throughout the world affecting homosapiens of all colours, creeds, castes and countries without distinction. The incidence of gonorrhoea reached the peak along with the other Venereal Diseases during the world war-II. From 1945 to 1956 there was a steady decline of venereal diseases. since then the trend has been reversed and there has been yearly increase. This has been reported from almost every country in the world, even from some of the iron curtain countries.

***Incidence of gonorrhoea in the V. D. Clinic, Government General Hospital, Guntur***

Year	Males	Females	Children below 15 Years	Total
1965	1107	235	5	1347
1966	969	235	1	1199
1967	1087	347	7	1441
1969	1179	387	12	1579

From the statistical study of the cases of gonorrhoea treated in the V. D. Clinic, Government General Hospital, Guntur for a 5 year period from 1965

to 1969 shows that there is a slight fluctuation in the annual incidence of gonorrhoea in the males but there is a definite increase in the females and in the children below 15 years. There is also an increase in the total incidence of gonorrhoea in 1969 when compared to the previous years. Since only a fraction of the cases of gonorrhoea attend the V. D. clinic for treatment, this does not reflect the true incidence in the community. However these figures indicate a disturbing trend that gonorrhoea perhaps with other venereal diseases is increasing in incidence.

*Treatment of Gonorrhoea:* The treatment of gonorrhoea has become so simplified that 90% of the cases are being treated by persons both qualified and quacks who have either grossly inadequate knowledge or no knowledge about the disease.

*Penicillin:* Penicillin the wonder drug, the first of the antibiotics, though discovered in 1929 by Fleming was therapeutically made useful only in 1943 by Mahoney and his colleagues.

Gonococcus was one of the earliest victims and one of the most susceptible organisms to penicillin therapy. Soon after the introduction of penicillin attempts were made to show that penicillin when combined with sulphonamides gave better results (Hargraves 1947). Later it was demonstrated that penicillin alone was sufficient and sulphonamides only caused avoidable complications.

In spite of many broadspectrum antibiotics that were subsequently introduced, penicillin is still the drug of choice in the treatment of gonorrhoea, unless the patient is sensitive or the organism is resistant to penicillin. The penicillin of choice is P A M (Procaine Penicillin in arachis oil and 2% aluminium monostereate). The optimum concentration necessary to cure acute gonorrhoea is about 1 unit of penicillin per c.c. of blood for a minimum of 24 hours.

#### GONORRHOEA RESISTANT TO PENICILLIN THERAPY

Any antibiotic when in use sufficiently long is likely to induce partial or complete resistance in the organisms once susceptible. Their usefulness gradually decreases and for the same infection higher doses for longer periods may be necessary. This metamorphosis has also taken place even in the case of penicillin therapy for gonorrhoea. In 1954, 100% of cases of gonorrhoea were cured with penicillin. By 1966 about 13% of cases of gonorrhoea have become resistant to penicillin therapy. In 1948, a single injection of PAM 150,000 to 300,000 Units was more than sufficient to cure acute gonorrhoea but now a total dosage of 1,200,000 to 2,400,000 units are recommended. This indirectly indicates that to cure gonorrhoea higher concentration for longer period are necessary. This is also confirmed in some of our cases which were resistant to conventional therapy with PAM by the intramuscular route but were positive for sensitivity tests for penicillin. This indicates that the organisms were only partially resistant to penicillin. These factors prompted us to try a method of penicillin therapy where higher concentrations were achieved by directly injecting penicillin into the blood. This has the added advantage that it eliminates the possibility of defective absorption when penicillin was given by the intramuscular route. Since penicillin is injected directly into the blood, the individual idiosyncrasy of penicillin metabolism can be eliminated for assessment of the therapy. Moreover the chances of developing further resistance of the gonococcus to penicillin are remote as very high concentration of penicillin is maintained in the blood. Unless the organism is already absolutely resistant to penicillin, cure is a certainty by the intravenous method.

### TREATMENT OF GONORRHEA BY INTRAVENOUS PENICILLIN IN RESISTANT CASES

This paper relates to cases of acute gonorrhoea apparently resistant to penicillin therapy treated with intravenous penicillin. Care was taken to exclude reinfections and superinfections. In conjugal cases of gonorrhoea both partners were treated simultaneously.

The following routine treatment was given in cases of acute gonorrhoea after confirming the diagnosis.

*Males* :— 6 Lakhs P. A. M., I. M. on two consecutive days total 1.2 M. U.

*Females* :— 6 Lakhs P. A. M., I. M. on three consecutive days total : 1.8 M U. ,

Whenever there was a suspicion or where-ever there was even a remote possibility of reinfection, a second course of P. A. M. was given. Culture and sensitivity tests were done in most of the cases. All the cases clinically resistant to P. A. M. therapy were confirmed by bacteriological examination and admitted in the V. D. wards of hospital. These cases were unselected consecutive patients willing for admission in the hospital' After testing for penicillin sensitivity of the patients, intravenous penicillin therapy was administered.

*Dose and Duration* : 10 Lakhs of crystalline penicillin G. was given intravenously, daily, single dose for 5 consecutive days.

TABLE I.  
*Cases treated with Intravenous Penicillin for 5 days*

S. No.	Code number.	Age	Sex.	Marital status.	V- D. R. L.	Results of Treatment.
1.	M. V. 2303/61	18	M	Single.	4 Dils.	Cured.
2.	F. V. 197/69	25	F	Married.	Neg.	Cured.
3.	M. V. 397/69	28	M		Neg.	Cured.
4.	F. V. 217/69	25	F	Married.	Neg.	Cured.
5.	M. V. 990/69	30	M		Neg.	Cured.
6.	F. V. 589/69	25	F	Married.	8 Dils.	Cured.
7.	M. V. 2496/69	30	M		Neg.	Cured.
8.	F. V. 1305/69	22	F	Married.	Neg.	Cured.
9.	M. V. 4585/69	30	M		Neg.	Cured.
10.	F. V. 1318/69	22	F	Married.	Neg.	Failure.
11.	M. V. 5592/69	27	M		Neg.	Failure.
12.	F. V. 1434/69	21	F	Married.	Neg.	Cured.
13.	M. V. 6106/69	28	M		Neg.	Cured.
14.	M. V. 5940/69	24	M	Single.	Neg.	Failure.
15.	M. V. 3906/69	22	M	Single.	Neg.	Cured.
16.	M. V. 70/70	21	M	Single.	Neg.	Cured.
17.	M. V. 179/70	22	M.	Single.	Neg.	Cured.
18.	M. V. 484/70	24	M	Single.	Neg.	Cured.
19.	M. V. 424/70	24	M.	Single.	Neg.	Cured.
20.	M. V. 494/70	21	M.	Single.	Neg.	Cured.

All the cases were examined and investigated every day during the course of treatment and once a week after treatment for three consecutive weeks and considered cured only when gonococci could not be demonstrated at the end of three weeks after treatment.

Table I shows that a total of 20 cases were treated with intravenous penicillin therapy for 5 days. There were 14 males and 6 females. Among them were 6 married couples and 8 single men. Out of the 20 cases in this series there were three treatment failures. Two were in husband and wife (M. V. 5592/69 and F. V. 1318/69) and the third in a single male (M. V. 5940/69). In all the three cases culture and sensitivity tests revealed that the organisms were resistant to penicillin. The organism in the husband and wife (M. V. 5592/69 and F. V. 1318/69) was found to be sensitive to terramycin and in the single male (M. V. 5940/69) was sensitive to synermycin. They were given the appropriate drug and were subsequently cured. Further in the case of the single male (M. V. 5940/69) the organism was reported as gram negative diplococci but not gonococci. The possibility of the organism belonging to the mimeae group has to be considered in this case.

The results of the 5 day treatment was so encouraging and the gonococci disappeared from the urethral discharge in 24 hours to 48 hours after treatment that we reduced the duration of treatment from 5 days to 3 days in the following series of cases.

TABLE II.  
*Cases treated with I. V. Penicillin for 3 days*

Sl. No.	Code number.	Age	Sex.	Marital status.	V. D. R. L.	Results of Treatment
1.	M. V. 5244/69	26	Male	Married.	Negative.	Cured.
2.	F. V. 1461/69	25	Female	Married.	Negative	Cured.
3.	M. V. 947/70	24	Male.	Single.	8 Dils.	Failure.
4.	M. V. 1960/70	23	Male.	Single.	Negative.	Cured.
5.	M. V. 3054/70	35	Male.	Married.	Negative.	Cured
6.	M. V. 3394/70	18	Male.	Single.	16 Dils.	Cured.
7.	M. V. 3705/70	45	Male.	Married.	Negative.	Cured.

Table II shows that a total of 7 cases were treated by intravenous penicillin therapy for 3 days. There were 6 males and 1 female. Among them were one married couple and 5 single men. Among the cases in this series there was one treatment failure and the sensitivity tests revealed that the organism was resistant to penicillin.

This study reveals that the majority of the so called penicillin resistant cases of gonorrhoea are only partially resistant which required higher concentration of penicillin in the blood for a longer period.

The dose and the duration of treatment were purely empirical. From the observation and follow up of cases, we feel that the optimum dose is 10 lakhs crystalline penicillin for a minimum of 3 days. However the estimation of penicillin concentration in the blood would yield greater information regarding the determination of optimum dose and duration of treatment. Unfortunately we could not undertake such a study for want of facilities for estimation of penicillin in the blood.

There were no reactions or constitutional disturbances in any of the cases treated.

### SUMMARY

The historical aspect, the nomenclature and the incidence of gonorrhoea are briefly discussed.

In the first series of 20 consecutive cases of acute gonorrhoea which were resistant to PAM therapy; were treated by I. V. penicillin, 10 lakhs daily for 5 days. They comprised of 14 males and 6 females and among them were 6 married couples and 8 single men. There were 3 treatment failures in this series. One of the three cases which failed to respond to the therapy was probably caused by mimeae organism.

In the second series of 7 consecutive cases of acute gonorrhoea which were resistant to PAM therapy were treated by I. V. penicillin, 10 lakhs daily for 3 days. They comprised of 6 males and one female and among them was one married couple and 5 single men. There was one treatment failure.

Culture and sensitivity tests were done as a routine in most of the cases.

There were no reactions or constitutional disturbances in any of the cases treated by intravenous penicillin therapy.

We are of the opinion that the optimum dose 10 lakhs of penicillin for a minimum period of 3 days is necessary for acute gonorrhoea.

### CONCLUSIONS

Majority of the so called penicillin resistant cases of acute gonorrhoea are really, only partially resistant requiring higher concentration of penicillin for longer period

Intravenous penicillin is a simple, safe and sure therapy in such cases unless the organisms are absolutely resistant to penicillin or the patient is sensitive to penicillin. ✓

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