

Résumé

L'auteur présente une étude faite sur 55.000 préparations examinées pendant ces vingt dernières années au laboratoire d'anatomie pathologique de la Faculté de Médecine de Téhéran.

Sur ce nombre, 4718 affections ganglionnaires ont été observés (8,5% du total), parmi lesquelles la tuberculose montre une plus haute fréquence avec 1891 cas, dont 1034 cas chez la femme. Puis par ordre d'importance se présentent les affections sarcomateuses, les adénites banales, lymphogranulomatose, les ganglions irrités, le Brill Symmer's, la Leucémie et la Métastase, montrant d'une manière générale, une plus haute fréquence chez l'homme.

Summary

The author presents a study of 4718 histological examination of lymphatic glands carried out in the Department of Pathology of Tehran Faculty of Medicine in the last 20 years.

Tuberculosis shows a high frequency with 1891 cases of which, 1034 cases were female. Other affections listed below were much more common amongst the male.

After tuberculosis the following conditions were seen in the order of their frequency: sarcoma, simple adenitis, lymphogranulomatosis, Brill Symmer's disease, leukemia and metastasis.

PREVALENCE OF DRUG-RESISTANT STAPHYLOCOCCI IN TEHERAN UNIVERSITY HOSPITAL WARDS

F. Shafa, M.D., Ph. D.

Department of Microbiology, Faculty of Medicine, Teheran university, Iran.

Introduction

When Penicillin was first used in human therapy, about 12% of coagulase-positive stains of Staphylococcus were found to be relatively resistant to it. (25,14,9). Nevertheless most of the clinicians believed that this problem would not constitute a major cause of therapeutic failure with penicillin (7,23). In practice however the wide-spread use of penicillin especially in hospital wards has been accompanied by the appearance of an increasing number of highly resistant stains of Staphylococcus (21,2,5,3,4,6,20,7,12).

The most extensive studies in this field have been carried out in London by Barber and his associates (2,3,5,4). In one of these studies Barber and Rozwadowska Dowzenko (5) have found that the number of resistant stains of Staphylococcus which was 14% in 1946, increased to 38% in 1947, and 59% in 1948. In places where penicillin is used intensively this number has now risen to 65-90%.

It has been stated in literature that penicillin resistant stains of Staphylococcus are most frequently encountered in hospital population where penicillin is used extensively (3,13,25,23), but it should be pointed out, firstly that penicillin is now being administered frequently outside hospitals, and secondly that penicillin resistant strains are spreading diffusely through the population by carriers who are found everywhere.

One of the most significant studies emphasizing the widespread distribution of these penicillin-resistant strains among healthy individuals is that of Martyn (19), in the obstetrical Department of St. Mary's Hospital, in Manchester, England. The nasopharynx and faeces of 130 healthy newborn infants were cultured for Staphylococci. None of the

babies or their mother had received penicillin. Staphylococci were obtained from the nasopharynx of 62% of infants, and from the faeces of 50%. Of the those strains isolated from the nasopharynx, 55.5% were penicillin-resistant, and 58.5% were resistant when cultured from the faeces.

Staphylococci have not only become resistant to penicillin, but also to the most current antibiotics.

At the section for sensitivity tests in the Department of Microbiology, Medical Faculty, Teheran University, it has been noticed that a great majority of Staphylococci were resistant to penicillin and a number of other antibiotics. It was decided therefore to ascertain the incidence of the drug-resistant strains of coagulase positive Staphylococcus by carrying out in vitro tests.

Materials and Methods

- 1) The strains of coagulase-positive Staphylococcus studied were isolated from the nose and wrist of nurses in Teheran University Hospital wards.
- 2) Coagulase test was performed in tubes with citrated rabbit plasma and 24 hours culture of staphylococcus. The mixtures were incubated at 37°C for 3 hours before reading the results.
- 3) Sensitivity tests were performed with high concentration of B.B.L.* Sensi-Discs.

Results

Table (1) shows the sensitivity of 50 coagulase-positive strains of Staphylococcus to penicillin, ten other antibiotics and the triple sulfa.

From this table the following results can be concluded:

- 1) At the present time only 18% of coagulase positive strains of Staphylococcus isolated from hospital nurses in Teheran University wards are susceptible to penicillin, the remainder are fully resistant (54%), moderately resistant (16%) or slightly resistant (12%).
- 2) With penicillin, aureomycin, tetracyclin, terramycin, chloramphenicol, Bacitracin and polymyxin-B, different ranges of susceptibility are observed, confirming the fact that in these antibiotics resistance develops slowly in a stepwise fashion.
- 3) In the case of streptomycin nearly one half of the strains (52%) are fully susceptible and the other half (48%) completely resistant

* Baltimore Biological Laboratory.

Table (1)

Antibiotics	Concentration	Fully sensitive		Slightly resistant		Moderately resistant		Fully resistant	
		No.	%	No.	%	No.	%	No.	%
Penicillin	10 units	9	18	6	12	8	16	27	54
Aureomycin	5 mcg	8	16	21	42	10	20	11	22
Tetracyclin	30 mcg	8	16	21	42	10	20	11	22
Terramycin	30 mcg	8	16	21	42	10	20	11	22
Chloramphenicol	30 mcg	34	68	11	22	5	10	0	0
Dihydro-streptomycin	50 mcg	26	52	0	0	0	0	24	48
Kanamycin	30 mcg	39	78	11	22	0	0	0	0
Neomycin	30 mcg	39	78	11	22	0	0	0	0
Erythromycin	15 mcg	50	100	0	0	0	0	0	0
Bacitracin	10 mcg	16	32	25	50	6	12	3	6
Polymyxin-B	30 gr	1	2	1	2	39	78	9	18
Triple-sulfa	1 mgr	0	0	0	0	0	0	50	100

showing that in this antibiotic, resistance develops suddenly.

- 4) Nearly all the strains under examination are still sensitive to newly discovered antibiotics such as erythromycin, neomycin, and Kanamycin.
- 5) Strains which have become resistant to one member of tetracyclines are resistant to other member (complete cross-resistance).
- 6) Strains which have become resistant to streptomycin are slightly resistant to neomycin and Kanamycin (partial cross-resistance).

Discussion

1 - The origin and mechanism of drug-resistance:

a) All the available evidence indicates that the development of drug-resistance both in vitro and in vivo is due to mutation. (22, 16, 1, 11, 2, 5, 15, 20).

These mutations occur spontaneously and independently of the presence of drug. Their rate of occurrence is very low, being of the order of 10^{-10} to 10^{-11} . If the drug is present, the parent sensitive is inhibited and the drug-resistant mutants can grow out. The action of the drug is therefore not to stimulate the development of drug-resistant forms but to select them.

b) Since nearly all penicillin-resistant strains of Staphylococcus isolated from the body produce penicillinase, whereas resistant mutants selected in the laboratory are not penicillinase producers, it can be concluded that the production of penicillinase is not the only cause of resistance, and other mechanisms such as alternation of bacterial metabolism or permeability are also involved.

2 - Cross-resistance:

When microbial variants are resistant to a certain drug and are selected out from the population by that drug, they may also be resistant to another drug to which they have not been exposed. Such relationships exist principally between agents that are closely related chemically, and may be the first clue to the identity of drugs whose chemical structure has not been decided. Here is a list of some antibiotics giving complete or partial cross-resistance.

a) Complete cross-resistance: Tetracyclin (Achromycin), chlortetracyclin (Aureomycin), and oxytetracyclin (terramycin). Streptomycin and dihydrostreptomycin. Kanamycin and Neomycin.

b) Partial cross-resistance: Streptomycin, neomycin, kanamycin and oleandomycin. Erythromycin and carbomycin.

3 - Hospital epidemiology:

Because of the increased prevalence of resistant strains of Staphylococcus in hospitals, the danger of cross-infection and fatal complications in hospitalized patients has become a serious problem. For this reason most of physicians and epidemiologists are trying to find practical solutions for prevention and control of staphylococcal infections in hospitals. (10)

4 - Clinical implications:

From what has been said, it follows that in antibiotic therapy of Staphylococcal infections the following point should be taken into consideration:

a) Before starting antibiotic therapy a sensitivity test should be performed, and among effective drugs the most current one should be used.

b) The newly discovered antibiotics such as vancomycin and Novobiocin should be used as little as possible, since with increase in their use, an increase in the proportion of strains resistant to these drugs must inevitably occur.

c) If the strain of staphylococcus is resistant to one antibiotic the use of chemically related ones which give complete or partial cross-resistance must be avoided.

d) The chemotherapeutic agents should not be casually administered as prophylactics or given for trivial infections from which the patient would certainly recover.

Summary

1) Fifty coagulase positive strains of Staphylococcus isolated from the nose and wrist of Hospital nurses have been examined for sensitivity to penicillin, tetracyclines, chloramphenicol, dihydrostreptomycin, erythromycin, neomycin, kanamycin, bacitracin, polymyxin-B and the triple sulfa. The percentages of fully sensitive strains at the present are as follows:

Erythromycin	100%
Neomycin	78%
Kanamycin	78%
Chloramphenicol	68%
Dihydrostreptomycin	52%
Penicillin	18%

Tetracyclines	16%
Polymyxin-B	1%
Triple sulfa	0%

2) The following topics have been discussed:

- The origin and mechanism of drug resistance
- Cross-resistance
- The hospital epidemiology of Staphylococcus
- The clinical implications of Staphylococcus drug-resistance.

Résumé

1) Cinquante souches de staphylocoque à Coagulase positive ont été isolées de la cavité nasale et du poignet des infirmières de l'hôpital et leur sensibilité a été examinée à l'égard de Penicilline, de Tétracycline, de chloramphenicol, de Dihydrostreptomycine, d'Erythromycine, de Neomycin, de Kanamycin, de Bacitracin, de Polymyxin-B et de Triple-sulfa. Le pourcentage de souches pleinement sensibles est actuellement comme suit :

Erythromycine	100%
Néomycin	78%
Kanamycin	78%
Chloramphenicol	68%
Dihydrostreptomycine	52%
Penicilline	18%
Tétracyclines	16%
Polymyxin-B	1%
Triple-Sulfa	0%

Les problèmes suivants ont été discutés :

- L'origine et mécanisme de résistance médicamenteuse.
- La résistance croisée.
- L'épidémiologie de staphylocoque de l'hôpital.
- Les implications cliniques des staphylocoques résistants.

References

- Anderson, D.G., Howard, L.G. and Rammelkamp, C.H. (1944): Penicillin in the treatment of chronic osteomyelitis, Arch. Surg. 49,245.
- Barber, M. (1947): Staphylococcal infection due to penicillin resistant strains, Brit. M.J., 2, 865.
- Barber, M. (1947): Coagulase-positive staphylococci Resistant to penicillin, J. Path. and Bact. 59,373.
- Barber, M., Hayhoe, F.G.J. and Whitehead, J.E.M. (1949): Penicillin resistant staphylococcal infection in maternity Hospital; Lancel, 2,1120.
- Barber, M., and Rozwadowska Dowzenko, M. (1948): Infection by penicillin-resistant staphylococci, Lancel 2,641.
- Berger, K. (1949): Veber die Heufigkeitszunahme penicillin resistenter pathogener koken, Wien. med. wchnschr. 99,536.
- Beigelman, P.M., and Rantz, L.A. (1950): The clinical importance of coagulase-positive, penicillin resistant staphylococcus aureus, New England J. Med, 242,353.

- Bloomfield, L., Kirly, W.M.M., and Armstrong, C.D. (1944): A study of "penicillin failures", J.A.M.A., 126 685.
- Bondi, Jr., A., and Dietz, C.C. (1945): Penicillin-resistant staphylococci, Proc. Soc. Exper. Biol. and Med., 60,55.
- Brown, J.W., (1956): Hygiene and Education Within hospitals to prevent staphylococcal infections, J.A.M.A., 166, 1185-1191.
- Buchman, J. and Blair, J.E. (1945): Penicillin in the treatment of chronic osteomyelitis, Arch. Surg., 51,81.
- Finland, M., Frank, P.F. and Wilcox, C. (1950): In vitro susceptibility of pathogenic staphylococci to seven Antibiotics with note on changing resistance staphylococci to penicillin., Am. J. Clin. Path. 20 325.
- Forbes, G. B. (1949): Infection with penicillin-resistant staphylococci in Hospital and general practice, Brit. M.J., 2,569.
- Gallardo, E. (1945): Sensitivity of Bacteria from infected wounds to penicillin. II. Results in one hundred twelve cases War. Med., 7,100
- Hirsh, H.I., Dowling, H.F., and Robinson, J.A., (1948): Organisms resistant to penicillin obtained from patients, Arch. Int. Med., 82,310
- Lyons, C., (1943): Penicillin therapy of surgical infections in U.S. Army, J. A. M. A. 123, 1007.
- Martin, R., Chabbert, Y., Surean, B., and Demoures, C., (1950): Un problème d'actualité en penicillin thérapie: les staphylocoques producteurs de penicillinase, Presse Med. 58, 197.
- Martin, T.D.M., and Witehead, J.E.M., (1949): Carriage of penicillin-resistant staph. pyogenes in Healthy Adults, Brit. M.J., 1,173.
- Martyn, G., (1949): Staphylococci in the Newborn, their coagulase production and Resistance to penicillin and Streptomycin Brit. M.J., 1,170.
- Nichols, D.R. and Needham, G.M. (1949): Aureomycin in the treatment of penicillin-resistant staphylococcal Bacteremia, Proc. Staff. Meet., Mayo Clin., 24,309.
- North, E.A. and Christie, R., (1945): Observation on the sensitivity of Staphylococci to penicillin, M.J. Australia, 2,44.
- Rammelkamp, C.H. and Maxon, T., (1942): Resistance of Staphylococcus aureus to the action of penicillin, Proc. Soc. Exper. Biol. and Med., 51,386.
- Rountree, P.M. and Thomson, E.F., (1952 Lancet II,262.
- Spink, W.W., Hall, W.H., and Ferris, V. (1948): Clinical significance of staphylococci with natural or acquired resistance to the sulfonamides and to penicillin, J.A.M.A. 128,555.
- Spink, W.W., Ferris, V. and Vivion, J.J., (1944): Comparative in vitro Resistance of staphylococci to penicillin and to sodium sulfathiazole, Proc. Soc. Exper. Biol. and Med., 55,207.
- Vourekka, A., and Hughes, W.H., (1949): Frequency of penicillin-resistant staphylococci, Brit. M.J., 1,395.