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Mulder, Jacob

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HAEMOPHILUS INFLUENZAE (PFEIFFER)
AS AN UBQUITOUS CAUSE OF ACUTE AND CHRONICAL PURULENT BRONCHITIS.

SUMMARY.

For about nine years the author has made a systematic study of the incidence and the pathogenicity of the haemoglobinophilic bacteria in acute and chronic diseases of the respiratory tract and of the lungs.

Part of these investigations have been performed in the Natives and Europeans, employed by the Mining-Company „Sinam" (South Sumatra, D. E. I.) and the other part in the Medical Department of the University Hospital at Groningen, Netherlands.

The results of these investigations were as follows:

Bacteriology of the haemoglobinophilic bacteria in general:

It should be realized that the Haemophilus influenzae (PFEIFFER) most probably represents a group of micro-organisms.

The analysis of this group is still at an early stage. A simple routine method is given to determine whether isolated strains require X- and V-factors for their growth. For this purpose agarslants, containing X-factor, which can be easily prepared, are supplied with V-factor by a stab-culture of staphylococci.

The indole test can be easily performed as a ring test on the water of condensation of the Levinthal-agar tubes.

The strains, found in purulent sputa from the bronchi or the bronchioles in cases of acute or chronic supplicative bronchitis (with bronchiectasis) always want X- and V-factors for their growth.

The observations of Miss Pittman in 1932 about the type-specificity of haemoglobinophilic bacteria, cultured from sputum, have been corroborated. The growth of the type-specific strains on Levinthal-agar is different from that of the PFEIFFER bacteria cultured from sputa, namely showing strong iridescence of the colonies in transmitted artificial- or sunlight. Most of the strains from purulent meningitis, cultured in the Netherlands, belong to a definite type (b). They kill rabbits on intravenous inoculation with marked bacteriaemia.

A rapid diagnosis is possible by agglutination with type-specific serum on a slide at a low temperature.

As the bacteria, described with this type b, we propose for the presence as the COHEN-PITTMAN bacterium, as it has nothing to do with the PFEIFFER bacterium. The present occurrence as the strains of type b, once type c, of the PFEIFFER bacterium. The sputa were from cases of pneumonia and postoperative complications observed by ourselves. The prevalence of influenza. With the ability to cause suppuration, was thought to be caused by the COHEN-PITTMAN bacterium. The results of these investigations have been corroborated. The growth of the type-specific bacteria cultured from sputa, namely showing strong iridescence of the colonies in transmitted artificial- or sunlight. Most of the strains from purulent meningitis, cultured in the Netherlands, belong to a definite type (b). They kill rabbits on intravenous inoculation with marked bacteriaemia.

A rapid diagnosis is possible by agglutination with type-specific serum on a slide at a low temperature.

1. H. PFEIFFER as a pathogen of acute and chronic supplicative bronchitis.
2. The cases, in which we isolated the bacteria, were not associated with pneumonia.
3. As subtype b is the most frequent subtype of H. PFEIFFER, it is possible that in a great number of cases of meningitis-strains, subtype b, as judged by the type-specificity of meningitis-strains, that they have unknowingly been exposed to R-strains.

The occurrence of H. PFEIFFER as a pathogen of acute and chronic supplicative bronchitis.

The frequency of the various diseases of the Tropics (1928–1931), was not always high. Suppurative broncho-bronchiectasis, supplicative bronchitis, supplicative tracheitis, and pulmonary tuberculosis were observed. Some cases of broncho-bronchiectasis, as described by Hollows, Eyré and French, ended lethally.
As the bacteria, described by COHEN in 1909, is probably identical with this type b, we propose to designate the whole bacterium group for the presence as the COHEN-PITTMAN type. Miss PITTMAN found already 6 subtypes (a—f) in this group. It is important that this group is also found in purulent sputa. Among about 90 sputum strains we found eight times type-specific strains, among which five times type b, once type c, once type e and once a still undetermined type. The sputa were from cases of chronic bronchitis, pneumococcic-pneumonia and postoperative broncho-pneumonia, all clinically observed by ourselves. The cases were quite independent of the prevalence of influenza. We ascribe to this group of bacteria the ability to cause suppurative bronchitis. The COHEN-PITTMAN type has nothing to do with the aetiology of influenza. R-variants of the COHEN-PITTMAN bacterium, cultured in vitro, have the same appearance as the strains of the PFEIFFER bacterium. We think it utterly improbable, however, that the PFEIFFER bacterium is only to be considered as an R-variant of type-specific strains.

Our opinion is based on the following arguments:

1. H. PFEIFFER as a pathogenic micro-organism, can be isolated from sputum in far more cases than H. COHEN-PITTMAN. Such a high incidence of cases with only R-variants in the foci of infection would stand alone in bacteriology, as far as we know.

2. The cases, in which we isolated H. COHEN-PITTMAN from the sputa, were not associated with unusually severe bronchitis or broncho-pneumonia.

3. As subtype b is the most frequent and probably also the most parasitic subtype of H. COHEN-PITTMAN, it should be expected that in a great number of strains of H. PFEIFFER, the R-variants of subtype b, as judged by agglutination tests, would be of rather frequent occurrence. According to our own experience this is not the case.

The failures of previous investigators to demonstrate the pathogenicity of meningitis-strains for rabbits, are probably due to the fact that they have unknowingly carried out their experiments with R-strains.

The occurrence of H. Pfeiffer in common catarrhs of the respiratory tract.

The frequency of the various catarrhal affections, observed in the Tropics (1928—1931), was as follows:

<table>
<thead>
<tr>
<th>Affection</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suppurative broncho-bronchitis</td>
<td>20</td>
</tr>
<tr>
<td>Suppurative bronchitis, respectively tracheo-bronchitis</td>
<td>110</td>
</tr>
<tr>
<td>Suppurative tracheitis</td>
<td>75</td>
</tr>
</tbody>
</table>

Some cases of broncho-bronchitis showed the same clinical pictures as described by HAMMOND, ROLLAND, SHORE, ABRAHAMS, HOLLOWES, EYRE and FRENCH at the English front in 1917. None of these cases ended lethally, however.
Up till now this question cannot be answered with certainty. The
COHOF!-P[TDA :-' bacterium represents the only clearly differentiated

H. Pfeiffer as a ubiquitous

Previous investigations

3. Can H. Pfeiffer play a primary pathogenic rôle or does it only cause
   secondary infections in association with preceding or simultaneous
   invasion of a filtrable virus or other micro-organisms?

   In common colds, measles and whooping-cough, H. Pfeiffer certainly
   plays a secondary part. The discovery of the influenza virus (SMITH,
   LADLOW, and ANDREWES) made the secondary part of H. Pfeiffer in
   influenza nearly a certainty. Further H. Pfeiffer plays a primary
   infectious part in conditions of decreased resistance after operations
   (anaesthesia) or in exhausting infective diseases.

   At the present time we do not yet know for certain whether H.
   Pfeiffer may be the primary aetiologic agent in epidemics of acute
   supplicative catarrhal inflammation of the mucous membranes of the
   respiratory tract.

   It is possible that such epidemics are due to primary infections
   with filtrable viruses; at any case their occurrence is secondary
to certain meteorological circumstances, both in the Tropics and in
the frigid zone. The nature of these circumstances is not known.

   In the Tropics refrigeration certainly does not play a predominant
   part; in Europe it may be a factor.

4. Where does H. Pfeiffer produce its primary lesion?

   H. Pfeiffer is a surface parasite. Some cases of pneumonia are said
to be caused by H. Pfeiffer. This expression causes confusion. The
majority of infections with H. Pfeiffer do not produce larger pulmonary
lesions. At most miliary lobular pneumonias (and atelectasis) develop.

   Only in epidemics of influenza exceptions have been observed
(MAC CALLUM), probably because immunity markedly decreases in
cases of influenza.

   Thus it is a rarity that H. Pfeiffer acts as an invader of pulmonary
tissue, which differentiates it markedly from pneumococci, strepto-
cocci and staphylococci in a biological sense.

5. What clinical pictures are produced by H. Pfeiffer?

   The acute catarrhal suppurations of the mucous membranes of
the respiratory tract are admitted by many authors to be caused in
some cases by H. Pfeiffer. In chronic supplicative bronchitis H.
Pfeiffer is generally considered as a saprophyte. We are of the opinion
that this view is untenable and consider H. Pfeiffer as the aetiological
agent in both acute and chronic suppurations of the bronchial
mucous membrane.

   Primarily acute suppurative parasitic subtypes of H. Pfeiffer
which is generally caused however, that infections with
H. Pfeiffer as a ubiquitous commensal parasite of the respiratory tract.

Previous investigations give the impression that H. Pfeiffer is sometimes found in cases of acute and chronic bronchi(ol)itis. Some investigators still consider the bacterium to be the aetiologic agent in influenza, may it be then as an obligatory "microbe de sortie" (NICOLLE) of the influenza virus.

On the ground of our investigations we have come to the conclusion, however, that the bronchial mucous membrane can be infected by but few groups of micro-organisms and that among these the group of Haemophilus is the principal and most parasitic. Besides this group the micrococcus catarrhalis plays a less important rôle in the causation of bronchitis, but the latter rarely penetrates far into the bronchial tree.

Whether the pneumococcus alone is able to produce acute suppurative bronchitis is still uncertain and in our opinion improbable. The streptococcal group plays, except during an epidemic prevalence of influenza or measles, a subordinate part in the causation of bronchitis.

The chief result of our investigations is that H. Pfeiffer is rarely missed in purulent sputum from cases of acute or chronic bronchitis.

Did we come to the conclusion that, among the few invaders of the mucous membrane of the respiratory tract, the Haemophilus group is chiefly found as a parasite, then it is conceivable, why among diseases which are the cause of an increased susceptibility to infections of the respiratory tract and the lungs in general, H. Pfeiffer is found in the majority of those cases which are associated with a suppurative bronchi(ol)itis, together with broncho-pneumonia or not. As many bacteriologists did not sufficiently take account of this fact and did not search for influenza bacteria until a new pandemis broke out, a great many cases again presented the (deceptive) picture of influenza, obligatory associated with infection with Haemophilus of the respiratory tract.

From the present investigation it follows that H. Pfeiffer is a commensal parasite (VAN LOGHEM). The susceptibility of healthy men is very low, which follows from the poor results obtained in experimental infections and from the fact that acute and chronic suppurative cases of bronchitis are not infectious.

Increased susceptibility for the infection with H. Pfeiffer may be constitutional (exudative diathesis); there is also increased susceptibility in the debile infant, in old age, after operation, in exhausting infective diseases, diabetes, nephritis and congestion of the lungs.

Such diseases as measles, influenza, whooping-cough also debilitate otherwise healthy children and adults for H. Pfeiffer, but also for pneumococci and streptococci.

Primary acute suppurative bronchitis may be caused by more parasitic subtypes of H. Pfeiffer, comparable with lobar pneumonia, which is generally caused by type I (in Holland). It is conceivable, however, that infections with filtrable viruses also play a rôle here.
but minding the clinical symptoms of these affections we do not think it probable.

Clinical application of the examination for haemophilic bacteria to diagnosis and therapy of acute and chronic bronchitis.

The practical significance of the occurrence of H. Pfeiffer is the fact that its presence indicates an acute or chronic suppuration of the bronchial mucous membrane in the case in question. Davis (1906) and Lüetscher (1911) already availed themselves of this fact, which enabled them to consider tuberculosis improbable, at an early stage. We, too, experienced that in many cases of „common“ acute or chronic bronchitis, respectively broncho-bronchitis with broncho-pneumonia one thought much too long of tuberculosis. The sputa were ad nauseam examined for tubercle bacilli, while the flora of the haemophilic bacteria was overlooked or considered to be of no importance.

It is, indeed, known to every specialist-internist, how often chronic supplicative bronchitis is mistaken for tuberculosis for years.

It should always be borne in mind, however, that the acute or chronic supplicative bronchitis, due to H. Pfeiffer, may be associated with a tuberculous process. The same can be said of all sorts of other processes.

Thus a supplicative bronchitis, due to haemophilic bacteria, may develop e.g. under an obstructive bronchial tumour or foreign body.

The importance of the occurrence of H. Pfeiffer with exception of the occurrence in sputa from tuberculous cavities and from nasopharynx and sinus of the nose, is, however, that the diagnosis of bronchitis can be made with certainty.

Cases in which supplicative chronic or acute bronchitis is found together with old tuberculous lesions, become susceptible to ready diagnosis; thus avoiding that the whole process is mistaken for tuberculosis.

The occurrence of the bacteria in cases of acute pneumococcal infection of the lungs, indicates the presence of an acute or chronic supplicative bronchi(in)sitis, together with pulmonary lesion. Chronic processes are generally accompanied by bronchiectasis. The unusual clinical course of some pneumonias may be caused by simultaneous infection with H. Pfeiffer in the bronchioles.

For an exact analysis of the clinical pictures denoted as broncho-pneumonia, the examination for H. Pfeiffer are indispensable.

Primarily there is the clinical picture of the acute and subacute broncho-bronchiolitis (capillary bronchitis) together with miliary (microscopical) lobular pneumonias and atelectases, which are caused by this bacterium and secondarily, pneumococcal broncho-pneumonia is, according to our experience very often accompanied by a supplicative broncho-bronchiolitis, due to Haemophilus of the respiratory tract. This combined infection of pneumococci (generally types II and I) the common picture of „broncho-suppurative bronchitis with older patients.

Further detailed investigations in pneumonias is desirable.

Therapy:

It stands to reason that, in such cases, vaccine therapy should be given of autogenous vaccines was of this method. At Groningen with chronic supplicative and chiefly prepared form H. Pfeiffer.

It is difficult to draw conclusions.

In a number of these cases we do not themselves to some degree.

In many of the cases we do not of the vaccine therapy.

The number of cases of acute and sufficient to attempt an eval.
tract. This combined infection of the lungs and bronchi with pneumo-
cocci (generally types II and III and X-types) and H. Pfeiffer produces
the common picture of "broncho" pneumonia in cases of chronic suppurative bronchitis with bronchiectasis or in weakened and (or) older patients.

Further detailed investigation on the pathogenesis of such broncho-
 pneumnias is desirable.

Therapy:

It stands to reason that, in cases of subacute or chronic suppurative bronchitis, besides the ordinary methods of treatment vaccine therapy should be given a trial. In the Tropics the preparation of autogenous vaccines was too laborious for systematic application of this method. At Groningen we have treated a number of cases with chronic suppurative bronchitis with an autogenous vaccine, chiefly prepared form H. Pfeiffer.

It is difficult to draw conclusions as to the effect of this treatment.

In a number of these cases the acute exacerbations will subside of themselves to some degree.

In many of the cases we did not see, however, the slightest success of the vaccine therapy.

The number of cases of acute bronchitis we have observed, is not sufficient to attempt an evaluation of vaccine treatment in such cases.