Supplementary:  i) Sepsis in Adult

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At Keio University Hospital, septicemia was most frequently encountered in patients with hematological disorders such as leukemia and aplastic anemia, particularly in patients who developed severe granulocytopenia.

In aplastic anemia, there have been little variation in the occurrence of septicemia every year, while the incidence of septicemia has been increasing in acute leukemia since powerful anti-leukemic agents were introduced for treatment of acute leukemia. The majority of these septicemias occurred during induction therapy.

The main causative organisms were gram-negative rods, that is, Pseudomonas aeruginosa, Klebsiella pneumoniae, E. coli and Enterobacter although the incidence of the causative organisms varies every year among gram-negative rods, depending upon the antibiotics available.

No case of septicemia was accompanied by disseminated intravascular coagulation in our series. Septic shock was one of the frequent complications in the past, but less frequently encountered in recent years.

Our regimens for treatment of septicemia were the combination of β-lactam and aminoglycoside anti-microbial agents. CZE and CBPC were the choice of β-lactam antibiotics, while GM or TOB were that of aminoglycoside antibiotics. All drugs were given intravenously and the dosage of CBPC (SBPC), CEZ, GM and TOB were 20–32 g, 8–12 g, 160–240 mg and 240–300 mg per day respectively. All patients were successfully treated with this regimen when the causative organism was susceptible to these antibiotics in vitro.

As far as the side effect of antibiotics was concerned, prolongation of bleeding time associated with inhibition of platelet functions (platelet aggregation and adhesiveness) was recorded in a patient with reticulum cell sarcoma when he was placed on CBPC, CEZ and GM as mentioned above. Discontinuation of the antibiotics resulted in improvement of platelet function. Platelet aggregation was also shown to be inhibited by CBPC in vitro.

Supplementary:  ii) Importance of Hemophilus Influenzae on Chronic Respiratory Infectious Diseases

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We regard the pathogenic organisms detected more than 10⁷/ml by our quantitative culture method of sputum as the causative pathogens of infections. We summed up respiratory infectious diseases at the First Department of Internal Medicine of Tohoku University from 1971 to 1974 and those at the Department of Internal Medicine of the
Institute for Tropical Medicine of Nagasaki University from 1975 to 1976, and found that *Hemophilus influenzae* was the outstanding pathogen: more than 25% were due to this organism. *Streptococcus pneumoniae* came up to 38.9% in 1971, but about 20% annually since 1973. In 1976, 471 strains of pathogens were isolated more than $10^7$/ml from 1046 specimens by our method. Among the isolated strains *Pseudomonas aeruginosa* was found most frequently (40.1%) and *Hemophilus influenzae* was the second (25.7%). The reason of the result appears to be the fact that *Pseudomonas aeruginosa* easily obtains resistance against antibiotics and so it continues to be isolated from the same patients. On the other hand, *Hemophilus influenzae* is rather eradicable by antibiotics, however, it is apt to be isolated repeatedly as recurrent infections after antibiotics being ceased.

We usually use modified Fildes agar for the isolation of *Hemophilus influenzae*.

No ampicillin resistant *Hemophilus influenzae* has been experienced in our laboratory. Serotypes of 104 strains of recently isolated *Hemophilus influenzae* were studied, and 15% of them could be typed and 85% were not typable.

We had a chance to observe 22 cases of chronic broncho-bronchiolitis for a long period. *Hemophilus influenzae* was isolated as a causative agent in 17 cases of them. 11 of 17 cases were repeatedly infected only with *Hemophilus influenzae* for a long term. There were 7 cases in which the causative pathogen altered from *Hemophilus influenzae* to *Pseudomonas aeruginosa*. These two organisms are extremely important in chronic broncho-bronchiolitis.

Serum antibody against *Hemophilus influenzae* increases apparently after acute exacerbation of chronic broncho-bronchiolitis due to this organism. On this occasion, increase of the antibody belongs to IgM was shown to antecede the increase of that belongs to IgG.