A PHANTASY

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'Wot ye not that such a man as I can certainly divine?' (Gen. 44 : 15).

ADVANCES IN TREATMENT, 1966 : RESPIRATORY INFECTIONS

As early as 10 years ago practitioners were well aware that respiratory infections accounted for well over 90% of all infectious disease seen in practice. Today this vast unclassified group accounts for almost 100% of the minute amount of infectious disease still seen in the western world. With the recent introduction of multi-superimmunization techniques, virostatics, bactericidals and parasiticides, there are virtually no other infections that have not been conquered. Respiratory infection itself has now dropped to negligible proportions in the western world, and medical schools are having difficulty in finding cases for demonstration to students, most early infections having already been 'nipped in the bud' by the use of BGX.

Mucoviscidosis

The brilliant work at Los Angeles culminated in the epoch-making paper of Bloch[1] on β globulin X (BGX). In truth it may be said that the road to his discovery was paved through the way of paediatrics—in the paper by Anderson[2] on the subject of what used to be called fibrocystic disease of the pancreas. The emphasis in this disease later shifted to the lungs: mucoviscidosis was the magic term that wrought a revolution in thought on respiratory infection. It was then realized that emphasis should be shifted away from the infecting agent, and that the 'soil' should be studied instead. What was it, in the nasal, the pharyngeal, the bronchial mucosa, that permitted micro-organisms to enter and thrive? It was soon found that the respiratory secretion was abnormal, and that perhaps all types of respiratory infection was based on this chemico-pathological anomaly. In 1954 Geddes[3] hazarded the view that bronchiectasis was a congenital disorder due to a localized nidus or a generalized area of lack of normal bronchial secretion. Six years later the daring experiments in Peiping[4] demonstrated the truth of this hypothesis both in bron-

chiectasis and also in tuberculosis. However, of the numerous studies on bronchial pathology and chemistry, that of Thomas[5] in Boston is pre-eminent. Since his qualitative analysis of bronchial mucosal biopsies and secretions on 489 individuals with various respiratory diseases and 162 controls, the way was open for Southam[6] in Alabama to demonstrate that the lack of β globulin X (BGX) in epithelial secretions was the factor responsible for the occurrence of respiratory infections.

BETA-GLOBULIN X (BGX)

Purified the same year and synthesized by Ethichem laboratories in 1961, it became available for large-scale trials in America and in England. The results were dramatic. It has been hailed as the greatest advance in replacement therapy since insulin. Using it as a 1% aerosol inhalant Crackers[7] reported on 81 patients with serious respiratory infections—all cured in a matter of hours. He also used bactericidins and virostatics, but showed clearly that the results were better than could be obtained by the use of these alone. Engelhoff and Van Goon[8] followed with an account of the value of BGX in coughs, colds and 'flu, and in the same year the Medical Research Council of Great Britain published its controlled studies[9] on 304 patients with respiratory infections treated with BGX plus VSBCC (Virostatic-Bactericidin Compound, Biopharm labs.) and 109 treated with VSBCC alone. The earlier rate of improvement in the former group was stated to be statistically significant—indeed very much so—and it was hailed (albeit cautiously) as a great advance in the therapeutic armamentarium of this modern age.

In Tokio, Kutisaki's work amply confirmed the English results,[10] and dispelled the pessimistic doubts of Shoenholler *et al*.[11] Further, its value as a prophylactic in all forms of undifferentiated respiratory infection has been noted by many workers[12–15] and has been stressed by Cherbakov[16] who showed that the exhibition of BGX does not interfere with the local mucosal production of antibodies in the presence of asymptomatic infection.

Diagnosis and Selection of Cases

Patterson and his group,[17] in London, counsel caution in BGX therapy. They feel that the irresponsible and frivolous prescription of BGX for minor respiratory infections is unwarrented and that care should be exercised in its use. Findlay[18] has decried the tendency to high concentrations of BGX and has reported toxicity in the form of severe nausea in 4 patients who swallowed large quantities of aerosol. Bergstrom[19] insists that BGX should not be exhibited unless there is a definite indication for its use, a point also made—with rather more vehemance—by Brailsford.[20] They feel that a diagnosis of bronchial mucosal BGX lack should first be established, and that BGX should not be used indiscriminately. They both point out that with modern anaesthesia, bronchoscopy by a competent chest physician is completely safe, and examination of bronchial secretion by chemical means and by Mamanicolaou's technique will either confirm or vitiate a diagnosis of congenital aglobulinic mucosis. While ben Yussef[21] concurrs with Bergstrom, he points out two factors that must be kept in mind:

(*a*) One bronchial aspiration is not sufficient for diagnosis. A lack of BGX at one examination occurs not uncommonly—for reasons yet obscure. Repeated examinations must be performed in order to distinguish permanent from temporary hypo- or aglobulinic mucosis.

(*b*) Aspirations must be performed separately from all accessible bronchi, as the aglobulinic area may be quite small and localized.

There does appear to be some evidence to substantiate Patterson's views on the injudicious use of BGX. Belanger's report[22] appears to demonstrate that the constant use of aerosol can decrease or even completely stop the normal production of BGX in the bronchial mucosa.

Weisberger *et al*[23] are at present engaged on spectrophoretic analyses of plasma BGX levels, which they feel may do away with the need for bronchoscopy, but as Kowalski[24] of the Institute of Chest Physicians points out—the plasma BGX level is not necessarily an index of bronchial mucosal BGX level. Kowalski has in fact stressed that bronchial smear examination is insufficient, and that a diagnosis of aglobulinic mucosis can only be made by bronchial biopsy. While Rogers[25] agrees with this view he feels that the danger of haemorrhage after biopsy is too great to warrant this procedure as a routine. He points out that bronchoscopy with aspiration of secretion is sufficient in the large majority of cases, and Zsst's controlled study[26] on this subject would appear to give a correlation of 91·6% accuracy between bronchial aspiration and biopsy.

Roux[27] has since demonstrated a small number of patients whose infections are not significantly improved by BGX. He theorizes that BGX is not one substance, but a whole conglomeration of protective globulins, and that some patients are lacking a separate factor which he calls BGX_2. Larner's preliminary report[28] lends credence to Roux's theory, and seems to open up a whole new vista—reminiscent of the multitudes of vitamins.

Smadding[29] classifies respiratory infections under 3 headings:

1. Infections in a normal respiratory tract.
2. Infections in a respiratory tract partially lacking mucosal BGX.
3. Infections in a congenitally aglobulinic mucosa.

He suggests that in cases in group 1, therapy should be limited to a VSBC compound. All patients known to be in group 3 should have daily prophylactic aerosol BGX. He regards this as replacement therapy in aglobulinic mucosis—in the same manner that insulin is replacement therapy in diabetes. If a respiratory infection should supervene—and its incidence should be negligible if prophylaxis is regular and adequate—treatment should be as in group 1—with VSBCC. Recovery can be expected in a few hours. In group 2, BGX need not be used as a prophylactic measure, but should any symptoms occur which might conceivably be due to respiratory infection, BGX and VSBCC should be given early and energetically.

Disappearance of Respiratory Infection

Respiratory infection is finally disappearing because of scientific treatment directed toward two goals: (*a*) Destruction or immobilization of the infecting agent, and (*b*) augmentation or replacement of defective 'respiratory mucosal infection-resisting β globulin X'. The problems thus facing medical science have become crystallized. The main unsolved enigmas are still accidents—cancer, cardio-vascular-renal disease, rheumatism, neuroses psychoses and mental deficiency, skin diseases and allergic disorders.

SUMMARY

An account is given of the work leading to the discovery of the protein fraction lacking in the respiratory mucosa of people suffering from respiratory infections.

It is felt that BGX should be used prophylactically as replacement therapy in aglogulinic mucosis.

In hypoglobulinic mucosis BGX should not be used unless an infection is known to have supervened, when it can be given at the same time as VSBCC.

Examination of bronchoscopic washings is almost as useful as biopsy in establishing a diagnosis of aglobulinic mucosis.

REFERENCES

(*Owing to lack of space the reference list will be published in our next issue*, 31 *April* 1967.—*Editor*.)