AMYLOID DISEASE
AN AUTOPSY REVIEW OF THE DECADES 1937-46
AND 1961-70
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AMYLOID is an amorphous homogenous extracellular material which is laid down in connective tissue. It is of interest and of clinical importance because accumulations of amyloid in various organs results in pressure atrophy of the adjacent "host cells" and thus a disruption of the function of the organ.

Amyloid material can be recognised in tissue sections stained with the usual stains, but when scanty is better demonstrated by methyl violet or Congo red. It also gives an apple green fluorescence with polarised light after staining with Congo red.

Since it was first described by Virchow in 1852 many studies have been made and these are well discussed in recent reviews. Wilks in 1858 recognised the association of amyloid disease with chronic infections, especially chronic tuberculous infections, and with rheumatism. An association with multiple myeloma was noted by Adams and Dowse in 1872. Soyka in 1876 recognised that it could occur with no identifiable cause. Lubarsch in 1929 described such cases and those associated with multiple myeloma as primary amyloid disease. This form most commonly appears in the heart, the blood vessels, and the smooth muscle of the intestinal tract. Senile amyloid found in the heart of patients over 80 years of age is usually included as primary and is so classified in this study. Secondary amyloid is that associated with chronic infections, such as tuberculosis, osteomyelitis, syphilis and bronchiectasis, or with chronic inflammatory diseases such as rheumatoid arthritis and systemic lupus erythematosus. This group also includes amyloid associated with renal cell carcinoma and sarcoid, and the heredofamilial forms. Secondary amyloid most commonly affects the adrenals, kidneys, liver and spleen. Endocrine amyloidosis is that associated with the endocrine tumours such as medullary carcinoma of the thyroid. It is interesting in that it is thought to be related to altered synthesis of the hormone secreted by the tumour.

Differences in the fibril subunit protein may be demonstrated by X-ray diffraction studies and may be related to the primary, secondary, endocrine and senile forms of the clinico-pathological classification, but this has not been possible in this retrospective study.

MATERIAL AND METHODS

All the cases of amyloid disease indexed in the autopsy records of the Pathology Department, Royal Victoria Hospital, during the years 1937-46 and 1961-70 were studied. There were 3,414 autopsies indexed in the first decade and 11,586 in the second decade. The age and sex distribution, organ involvement and associated diseases were noted and the results tabulated.
RESULTS

Of the 3,414 autopsies carried out between 1937 and 1946, 15 were found to have amyloid disease. In the years 1961-70, 11,586 autopsies were carried out and 81 were noted to have amyloid disease. Thus it can be seen that in the earlier decade 0.44 per cent of all autopsies had amyloid disease whereas in the later decade 0.7 per cent of all autopsies were affected.

Age and Sex

There has been little change in the sex distribution of amyloid disease, the ratio of male to female remaining at approximately two to one. (Table I). A marked shift has occurred in the age distribution of the disease (Table I). In the 1937-46 period 60 per cent of cases were less than 50 years of age. In comparison, only 10 per cent of cases between 1961 and 1970 were less than 50 years old.

Organ and Tissue Involvement

Organ involvement has altered (Table II). In the earlier decade the adrenal glands, kidneys, liver and spleen were the organs most commonly affected. In the later decade the heart was added to the above list of organs commonly involved.

Associated Diseases

From Table III, it can be seen that the type of amyloid disease present has altered. There has been an increase in the incidence of primary amyloid from 40 per cent to 53 per cent and a fall in that of secondary amyloid from 60 per cent to 47 per cent. The aetiology of secondary amyloid has changed. In the decade 1937-46, 67 per cent of all cases of secondary amyloidosis were associated with tuberculosis and 22 per cent were associated with bronchiectasis. However, in 1961-70, tuberculosis was associated with only 24 per cent of cases of secondary amyloid and bronchiectasis with 37 per cent. Rheumatoid arthritis, which was not associated with any cases of secondary amyloid disease in the years 1937-46, was the cause of 29 per cent of cases between 1961 and 1970.

Age Distribution of Primary and Secondary Amyloidosis

As can be seen from Table IV the largest single group in the earlier decade is secondary amyloidosis in those aged 50 years and under. In the later decade the largest group is primary amyloidosis in those over 50 years of age.

Discussion

The results of this review show that there has been a clearly detectable increase in the incidence of amyloid disease found at post-mortem examination. With this change there has occurred a dramatic shift in the age groups within which cases occurred. The third important fact which emerged was that secondary amyloidosis has been largely replaced by primary amyloidosis. It is interesting to speculate on the reasons for these changes in the pattern of amyloid disease.

The alteration in the age distribution of the disease can to some extent be explained by the change in the age structure of the population. In 1937, 6.8 per cent of the population of Belfast were aged 65 years and over, and by 1961 this figure had risen to 10.1 per cent. By the end of the second survey period 12.8 per cent were over
# Table I

**Distribution of Amyloidosis by Age and Sex**

| Age | 1937-46 | 1961-70 |
|-----|---------|---------|
|     | Male | Female | Total | Male | Female | Total |
| 0—29 | 3    | 2      | 5     | 2    | 1      | 3     |
| 30—49 | 2    | 2      | 4     | 4    | 1      | 5     |
| 50—69 | 4    | 1      | 5     | 22   | 11     | 33    |
| 70—89 | 1    | 0      | 1     | 22   | 14     | 36    |
| 90+   | 0    | 0      | 0     | 3    | 1      | 4     |
| Total | 10   | 5      | 15    | 53   | 28     | 81    |

# Table II

**Organ and Tissue Involvement in Amyloidosis**

|                | 1937-46 | 1961-70 |
|----------------|---------|---------|
| Adrenal        | 10      | 43      |
| Bladder        | 0       | 2       |
| Blood vessels  | 1       | 10      |
| Gastrointestinal tract | 1      | 6       |
| Heart          | 1       | 31      |
| Kidney         | 13      | 50      |
| Liver          | 9       | 27      |
| Lung           | 0       | 4       |
| Pancreas       | 1       | 2       |
| Parathyroid    | 0       | 3       |
| Pituitary      | 0       | 3       |
| Spleen         | 12      | 32      |
| Thyroid        | 0       | 9       |
| Skeletal muscle | 0    | 1       |
| Testis         | 1       | 0       |

# Table III

**Associated Disease**

| Primary                     | 1937-46 | 1961-70 |
|-----------------------------|---------|---------|
| No associated disease       | 5       | 40      |
| Multiple myeloma            | 1       | 3       |
| Secondary                   |         |         |
| Bronchiectasis              | 2       | 14      |
| Osteomyelitis               | 1       | 0       |
| Tuberculosis                | 7       | 9       |
| Sarcoidosis                 | 0       | 1       |
| Syphilis                    | 0       | 1       |
| Rheumatoid arthritis        | 0       | 11      |
| Systemic lupus erythematosus| 0       | 1       |
| Renal cell carcinoma        | 0       | 2       |

Note: One patient had 2 possible causes of secondary amyloidosis and both have been included in the above table.

# Table IV

**Age Distribution of Primary and Secondary Amyloidosis**

| Age | 1937-46 | 1961-70 |
|-----|---------|---------|
|     | Primary | Secondary | Total | Primary | Secondary | Total |
| 0—29 | 1       | 4        | 5     | 0       | 3         | 3     |
| 30—49 | 2       | 2        | 4     | 1       | 4         | 5     |
| 50—69 | 2       | 3        | 5     | 14      | 19        | 33    |
| 70—89 | 1       | 0        | 1     | 24      | 12        | 36    |
| 90+   | 0       | 0        | 0     | 4       | 0         | 4     |
| Total | 6       | 9        | 15    | 43      | 38        | 81    |
65 years of age. Better social conditions and more effective medical treatment of many diseases have been responsible for much of the rise in the numbers of very old people.

The marked fall in the incidence of amyloid disease secondary to tuberculosis is as expected, since the incidence of tuberculosis itself has been reduced by improved social conditions, BCG vaccination and the introduction of anti-tuberculous drugs. This change is most noticeable in the deaths occurring in the younger age groups. One might reasonably have predicted also a fall in the incidence of cases of amyloidosis secondary to bronchiectasis. However, the figures in fact show a significant increase. Could it be that, on account of better therapy, more patients with bronchiectasis survive long enough to develop amyloid disease?

It is interesting to surmise why rheumatoid arthritis, while implicated in 29 per cent of cases of secondary amyloidosis between 1961 and 1970, was not associated with any cases in the earlier decade. Were there less cases of rheumatoid arthritis in the population or did fewer come to autopsy? The patients may have died earlier in the course of their disease before developing secondary amyloid disease.

Perhaps the most significant finding was that in the first decade there were no cases of amyloidosis in those aged 80 years and over, whereas in the second decade 28 per cent of all cases were in those over 80 years of age. The majority (91 per cent) of cases in this latter group were of primary type and were almost entirely due to the appearance of senile cardiac amyloidosis. It could be suggested that the high incidence of this condition is due to the marked rise in the number of elderly people in the population.

SUMMARY

This review has shown that there has been an increase in the incidence of amyloid disease found at autopsy. Secondary amyloidosis associated with tuberculosis in the younger age groups has been largely replaced by senile cardiac amyloidosis.

ACKNOWLEDGEMENTS

I would like to thank Dr. Claire M. Hill and Professor E. F. McKeown for their help and encouragement. I am grateful to Professor J. E. Morison for his most helpful advice in the preparation of this paper.

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