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# Seasonality of thyrotoxicosis

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SUMMARY Study of a large and representative series of thyrotoxic patients showed a higher frequency of diagnosis in the spring and summer. The median interval between onset and diagnosis was 12 weeks, indicating a peak in onset of the disease from January to June. The seasonality of thyrotoxicosis may be related to seasonal variations in iodine intake.

During an investigation of geographical variations in the incidence of thyrotoxicosis in England and Wales an excess of patients presenting in the summer months was noted. As little is known about the aetiology of thyrotoxicosis this observation stimulated a detailed investigation into the seasonality of the disease.

## Methods

Throughout 1982 hospital biochemistry laboratories in England and Wales participated in a prospective study of all new cases of thyrotoxicosis occurring in 12 towns. The method has been described in detail elsewhere.[1] The towns were selected to encompass a range of social and economic conditions and geographical spread within the country. They were Barrow-in-Furness, Chester, Derby, Ipswich, Middlesbrough, Newport (Gwent), Plymouth, Preston, Southampton, Stoke-on-Trent, Wakefield, and York. The records (hospital or general practitioner) of all patients with raised thyroid function tests, that is, values above the normal reference range for free thyroxine index (FTI) or free thyroxine (Free T4), were reviewed. The techniques used to measure FTI or Free $T_4$ differed between laboratories. Hence the reference ranges varied. Patients were included in the study if they were newly diagnosed and thereafter treated for thyrotoxicosis and if they were normally resident in the towns—as defined by the pre-1974 county borough boundaries. The date on which the first abnormal blood sample was drawn from the patient was taken to be the date of diagnosis.

Incidence rates were based on 1981 population data. The statistical significance of seasonality was assessed using the likelihood ratio test described by St Leger.[2] This tests whether the number of cases per month follows a simple harmonic trend.

Climatic data for England and Wales during 1982 were obtained from the Meteorological Office, Bracknell. Mean monthly temperatures were calculated as the average of the mean 24 hour temperatures recorded in 68 locations throughout the country.

## Results

Three hundred and seventy two newly diagnosed and treated cases of thyrotoxicosis (74 men and 298 women) were recorded in the 12 towns during 1982. The overall annual incidence in the combined population of the towns (1 641 949 people) was 22·7 per 100 000. Figure 1 shows the numbers of patients diagnosed monthly. Numbers were above average during each month of the second and third quarters, April to September, giving a six monthly incidence of 13·8 per 100 000, compared with 8·9 during the winter months October to March. This seasonal trend is statistically significant ($\chi^2 = 16{\cdot}7$, $p<0{\cdot}01$, 2 df). Figure 1 also shows the mean monthly temperatures in England and Wales during 1982. They rose progressively from January to a peak in July, after which they progressively declined, in contrast to the numbers of patients, which were almost constant from April to August.

The cases in each town were divided into three equal groups, 'severe', 'moderate' and 'mild', according to the value of the thyroid function tests. (Since the methods of FTI and Free $T_4$ estimation differed between the towns no useful indication of town-to-town variability in tertiles can be derived.) Figure 2 shows the monthly distribution by severity, using the combined results for all towns. Severe cases showed a peak in the second quarter; moderate cases showed an April to September plateau; and among mild cases there was a peak in August. A test for differences between the three groups in the phase or position of the seasonal peak did not reach statistical significance ($\chi^2 = 5{\cdot}5$, $p = 0{\cdot}06$, 2 df).

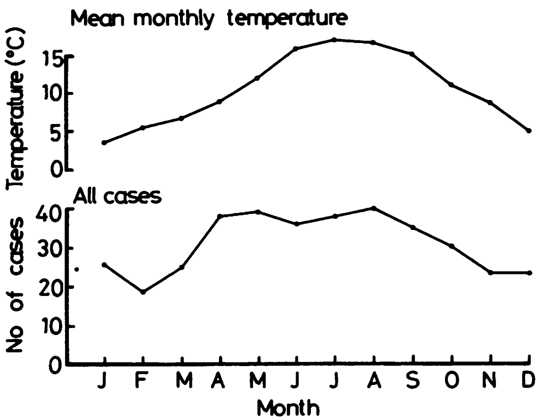


Fig 1 *Upper graph: mean monthly temperature in England and Wales (see text).*
*Lower graph: monthly variation in numbers of cases of thyrotoxicosis in the 12 towns.*

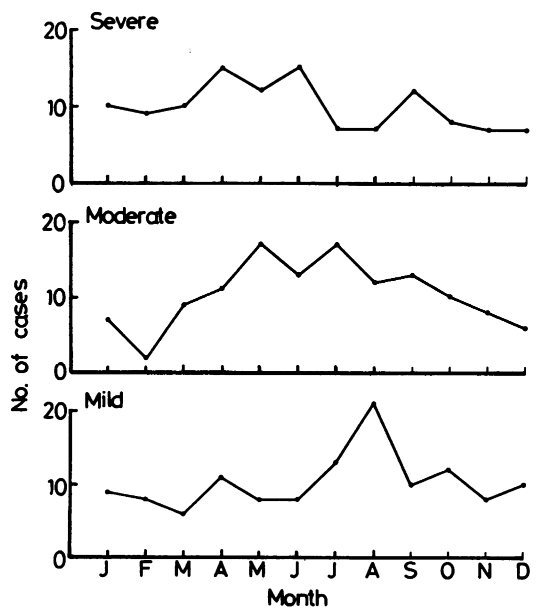


Fig 2 *Monthly variation in thyrotoxicosis according to severity of the disease (see text).*

The age specific incidences of thyrotoxicosis calculated from these data are bimodally distributed, one peak occurring in the middle aged (55–64), the other in the elderly (75–84). It is likely that these correspond with the peaks in the incidence of the two major causes of hyperthyroidism, Graves' disease in the younger age group and toxic nodular goitre in the elderly. The patients were divided into two groups, above and below 67·5 years, 65–69 years being the lowest point of the trough between the two peaks. While both groups show seasonality (fig 3), this is more marked in the younger age group than in the older.

Data on the month of onset of symptoms were obtained from the records (hospital and general practice) of patients in two of the towns, Stoke and Plymouth. In the 51 cases for whom adequate information about onset was recorded the median interval between onset and diagnosis was 12 weeks (range 2 weeks to 18 months). Among cases diagnosed in the summer months, April to September, the median was 12 weeks compared with a median of 15 weeks in the winter months, October to March.

## Discussion

This study in 12 towns in England and Wales has shown a marked seasonality in the presentation of patients with thyrotoxicosis, highest rates being in the second and third quarters of the year (fig 1). This seasonal pattern in diagnosis could have arisen because symptoms of the disease are less tolerable in warmer weather. However, it is difficult to use this explanation to relate the sustained April to September plateau in numbers of patients to the progressive rise and fall in mean monthly temperature (fig 1). Furthermore, data on the median interval from onset of symptoms to diagnosis

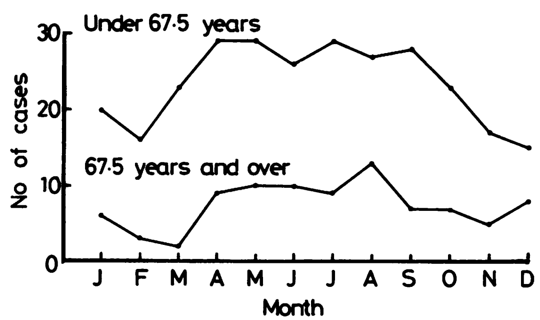


Fig 3 *Monthly variation in thyrotoxicosis in two age groups, above and below 67·5* years.

showed only a three week difference between patients diagnosed in April to September and those diagnosed during October to March. It is therefore concluded that the monthly variation in frequency of diagnosis of thyrotoxicosis, which occurs at all levels of severity of the disease (fig 2), reflects a monthly variation in onset such that the peak period of onset is from January to June.

Iversen described a summer excess in thyrotoxic patients presenting to hospitals in Copenhagen during 1938–45.[3] Three earlier reports from Germany had indicated, respectively, a spring excess in representation, a summer excess in presentation, and a February to May peak in onset.[4-6] All these studies were, however, on hospitalised patients in whom the diagnosis was based only on clinical assessment or measurement of the basal metabolic rate. In the present study, ascertainment of cases was based on laboratories accessible to both hospital staff and general practitioners. The recent advent of reliable and inexpensive measurements of thyroid function makes it unlikely that thyrotoxicosis will now be diagnosed without laboratory confirmation. The 372 cases in the study are therefore a more representative series than those studied previously.

Experimental and clinical studies have suggested that excessive iodine intake is an aetiological factor in thyrotoxicosis.[7,8] Seasonality in the onset of thyrotoxicosis may therefore result from seasonal changes in iodine intake. In Britain, milk, the major source of dietary iodine, has a higher iodine content in winter and early spring because artificial feed for cattle is supplemented with iodine. Analysis of milk samples during 1959–63 showed at least fivefold variation in mean monthly iodine content, from a trough in August to a peak in February to April.[9] More recent investigations have likewise shown a fivefold difference between winter and summer milk.[10] Since the seasonality in thyrotoxicosis is seen at all ages it is suggested that seasonal changes in iodine intake influence the occurrence of both Graves' disease and toxic nodular goitre.

Dr D I W Phillips is a Wellcome Research Fellow.

## References


1. Barker DJP, Phillips DIW. Current incidence of thyrotoxicosis and past prevalence of goitre in twelve British towns. *Lancet* 1984 (in press).
2. St Leger AS. Comparison of two tests for seasonality in epidemiological data. *Appl Statist* 1976; **25:** 280–6.
3. Iversen K. *Temporary rise in the frequency of thyrotoxicosis in Denmark, 1941–1945.* Copenhagen: Rosekilde and Bagger, 1948: 68.
4. Oehme C, Paal H. Untersuchungen mittels der Reid Huntschen Reaktion, besonders bei Asthma bronchiale. *Med Klin* 1930; **13:** 454–7.
5. Hirsch D. Beitrag zum Basedowproblem. *Deutsche Arch Klin Med* 1930; **168:** 331–46.
6. Jacobowitz H. Basedow und Jahreszeit. *Ztschr Klin Med* 1932; **122:** 307–15.
7. Stewart JC, Vidor GI, Buttfield IH, Hetzel BS. Epidemic thyrotoxicosis in Northern Tasmania: Studies of clinical features and iodine nutrition. *Aust NZ J Med* 1971; **3:** 203–11.
8. McGregor AM, Weetman T, Hall R. Effect of iodine on the immune response. In: *Thyroid disorders associated with iodine deficiency and excess.* Serono Symposium Series, 1984 (in press).
9. Broadhead GD, Pearson IB, Wilson GM. Seasonal changes in iodine metabolism 1. Iodine content of cows' milk. *Br Med J* 1965; **1:** 343–5.
10. Wenlock RW, Buss DH, Moxon RE, Bunton NG. Trace nutrients 4. Iodine in British food. *Br J Nutr* 1982; **47:** 381–90.