Chapter 11: Serum Albumin and Serum Bicarbonate

Summary

- The method of measurement of serum albumin has a major effect on the interpretation of differences between centres and changes with time. The centres using BCP have lower serum albumins. This is most apparent within the peritoneal dialysis population, in whom the albumin concentrations overall are significantly lower. The BCG method will overestimate serum albumin concentration by several grams per litre below 30g/L (as assessed by BCG).

- For haemodialysis patients, there was a variation in the median serum albumin within both the BCP group (overall median = 34 g/L, units ranging from 33 to 37 g/L) and the BCG group (overall median = 38 g/L, units ranging from 34 to 41 g/L).

- For peritoneal dialysis patients, the median serum albumin was 30 g/L by BCP (units varying between 27 and 32 g/L) and 35 g/L by BCG (units varying between 33 and 37 g/L).

- For haemodialysis patients, median serum bicarbonate varied from 18 to 26 mmol/L between centres. More detailed information concerning sample handling by laboratories and units is required to explore the difference in results before any suggestion that this is the result of differences in clinical practice can be considered. There appears to be no relationship between analytical method and median bicarbonate level. Sixty-two per cent of patients achieved the recommended Standard, the large majority of PD patients achieving the standard.

Serum albumin

Albumin measurement

In general, serum albumin is measured by one of two methods, both of which utilise a colour change induced by a dye binding to albumin:

1. **BCG** (bromocresol green) is the most commonly used agent, but this has been criticised for the fact BCG binds to a range of proteins other than albumin such that, at low albumin concentrations, there may be a significant overestimation of the albumin concentration
2. **BCP** (bromocresol purple) is slightly more expensive than BCG and is available on fewer clinical laboratory analysers. The advantage of BCP is that it predominantly binds to albumin and thus gives a more accurate measure of albumin concentration, especially below 30g/L.

Immunoassay can also be employed. The reference procedure for serum albumin measurement is to use a specific antibody along with either immunonephelometric or immunoturbidimetric detection.

Most of the above statements with regard to the relative performance of BCG and BCP hold true even in uraemic serum where uraemic toxins (unknown) bind to albumin and alter the ability of other substances, for example drugs and dyes such as BCP and BCG, to bind.

The remaining issue related to albumin in previous Registry reports was the variation in reference range reported by laboratories and the different sources that had been used to obtain them. In principle, and supported by most manufacturers and published sources, there should be no great difference in the reference ranges that would be appropriate for use with the BCG and BCP methodologies. As can be seen from Table 11.1, most laboratories are using broadly similar reference ranges, only two out 34 showing a significant difference at the low end. One laboratory previously having a lower limit of 30 g/L has now increased this to 34 g/L following the introduction of a new analyser. Consensus within the laboratory community is moving towards the adoption of common laboratory reference ranges for many analytes.

City	Hospital	Method	Ref range
Birmingham	Heartlands Hospital	BCG	35–48
Bradford	St Luke's Hospital	BCG	37–49
Bristol	Southmead Hospital	BCG	35–50
Cardiff	University of Wales Hospital	BCG	35–50
Carlisle	Cumberland Infirmary	BCG	36–47
Carshalton	St Helier Hospital	BCG	35–50
Coventry	Walsgrave Hospital	**BCP**	34–48
Derby	Derby District General	**BCP**	30–45
Exeter	Royal Devon and Exeter Hospital	BCG	34–48
Gloucester	Gloucester Road Infirmary	**BCP**	35–53
Hull	Hull Royal Infirmary	**BCP**	36–48
Leeds	St James's Hospital	BCG	37–49
Leeds	LGI	BCG	37–49
Leicester	Leicester General Hospital	BCG	35–55
Liverpool	Liverpool Royal Hospital	BCG	34–45
London	Guys St Thomas'	**BCP**	35–45
Middlesborough	South Cleveland Hospital	BCG	35–50
Newcastle	Royal	BCG	34–50
Nottingham	Nottingham City Hospital	**BCP**	30–52
Oxford	Churchill Hospital	BCG	35–50
Plymouth	Derriford Hospital	BCG	35–50
Portsmouth	Queen Alex	BCG	37–50
Preston	Royal Preston Hospital	BCG	35–55
Reading	Royal Berkshire	BCG	35–49
Sheffield	Northern General Hospital	BCG	36–50
Stevenage	Lister Hospital	**BCP**	35–50
Stourbridge	Wordsley Hospital	BCG	35–47
Southend	Southend Hospital	BCG	35–50
Sunderland	Sunderland Royal Hospital	BCG	34–50
Swansea	Morriston	BCG	36–53
Truro	Royal Cornwall Hospital Trust	BCG	35–50
Wolverhampton	Newcross Hospital	BCG	36–52
Wrexham	Maelor General Hospital	**BCP**	35–50
York	York District Hospital	BCG	35–50

Table 11.1: Methods and ranges of albumin measurement
Conversion factor: g/dL = g/L × 0.1.

To study the influence of albumin assay methodology on the distribution of results for different centres, a large box symbol has been used in Figure 11.1 to highlight those supported by laboratories using BCP methodology.

The Renal Association Standard for albumin is that ***all patients should lie within the local normal range***.

Haemodialysis (HD)

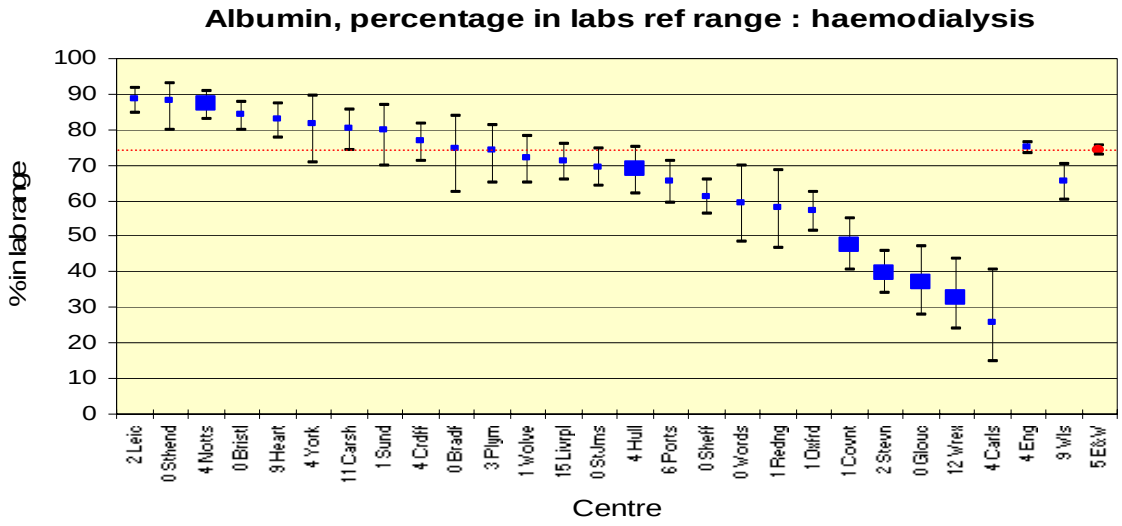

Figure 11.1: Percentage albumin in the laboratory reference range, HD

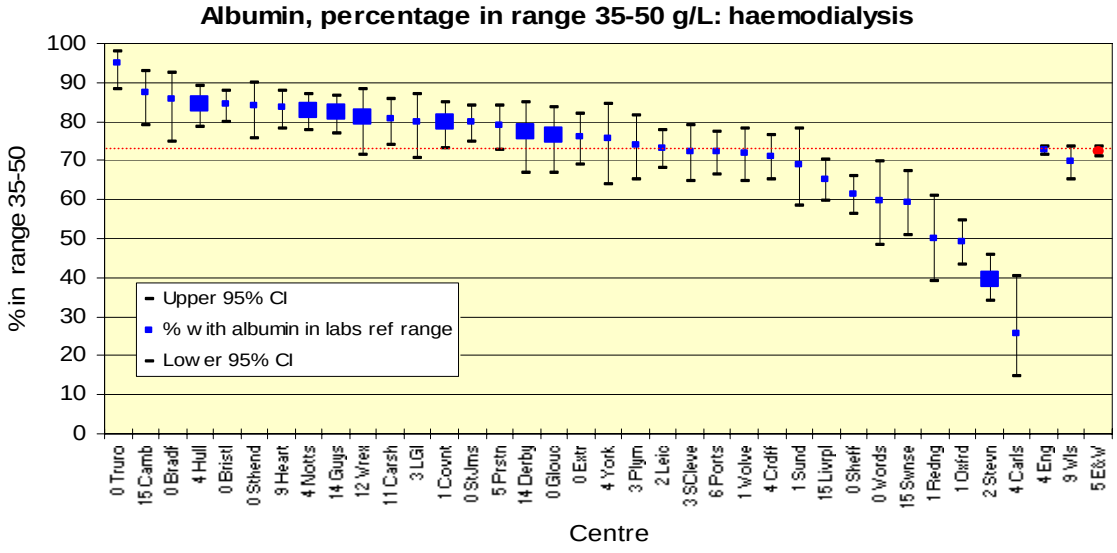

Figure 11.2: Percentage albumin in the range 35–50 g/L, HD

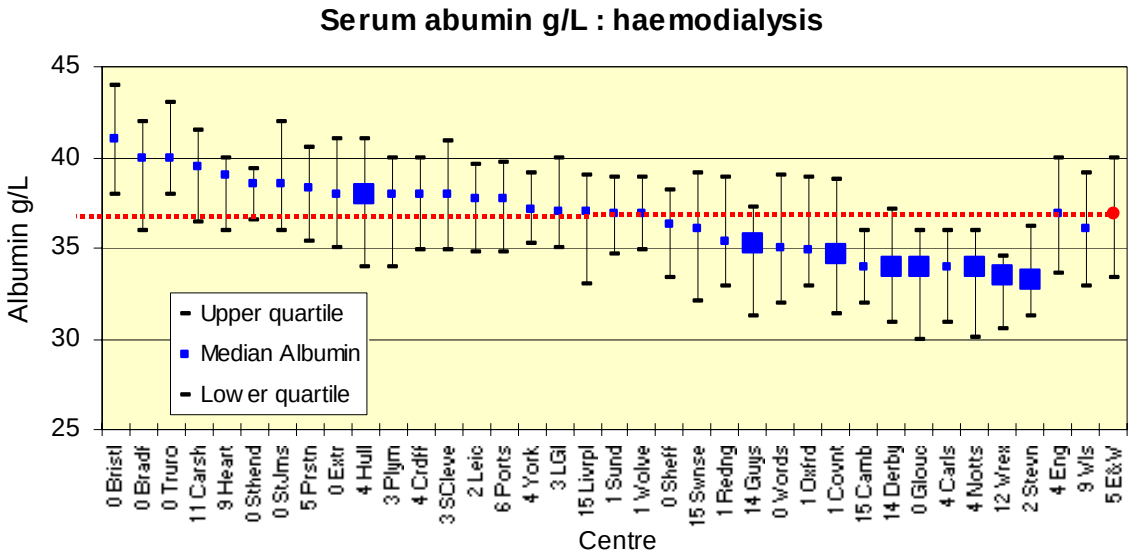

Figure 11.3: Serum albumin, HD

Figure 11.3 shows that there was a variation in the median serum albumin level within both the BCP group (overall median = 34 g/L, units ranging from 33 to 37g/L) and the BCG group (overall median = 38 g/L, units ranging from 34–41 g/L). Figure 11.1 above shows that no unit achieved the Renal Association Standard.

Data were incomplete for Figure 11.2 looking at the proportion of patients within the laboratories' reference range because, at the time of data analysis, reference ranges had not yet been provided. A comparison of Figures 11.2 and 11.3 would support the use of a common reference range as the BCP users were a less distinctive group in the latter Figure, in which 35–50 g/L was used.

Peritoneal dialysis (PD)

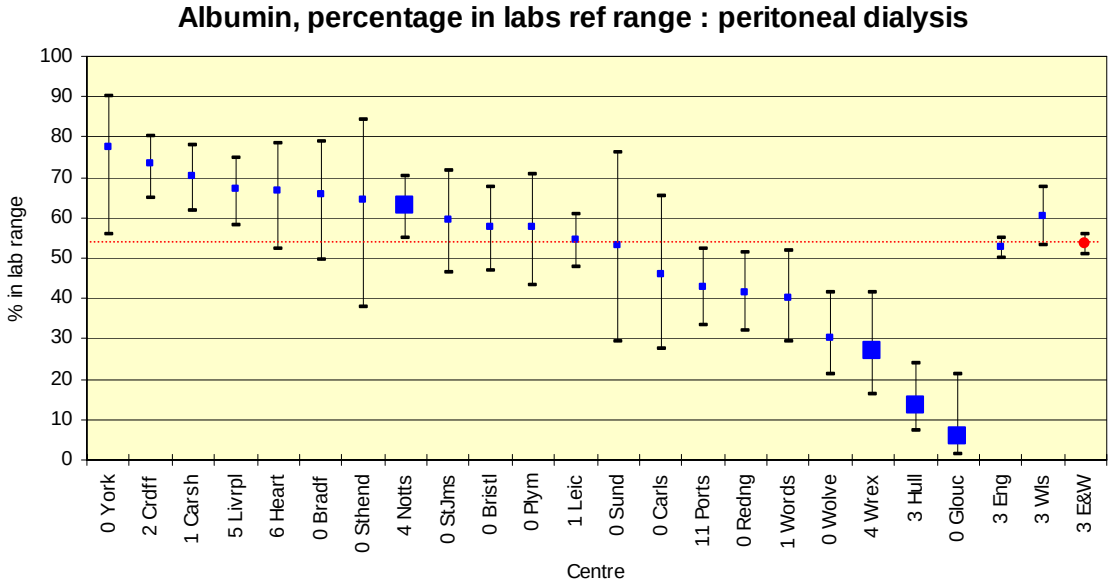

Figure 11.4: Percentage albumin in the laboratory reference range, PD

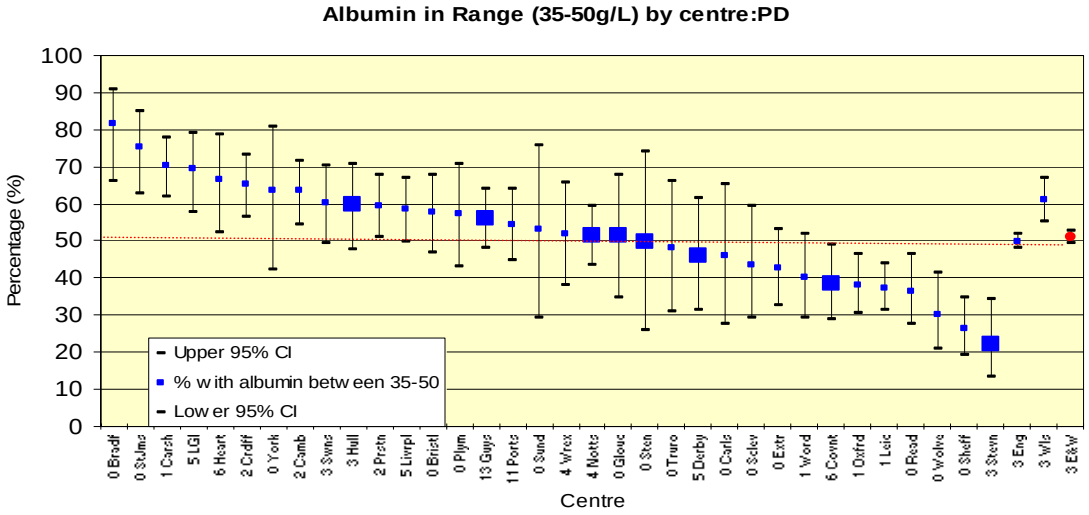

Figure 11.5: Percentage albumin in the range 35–50 g/L, PD

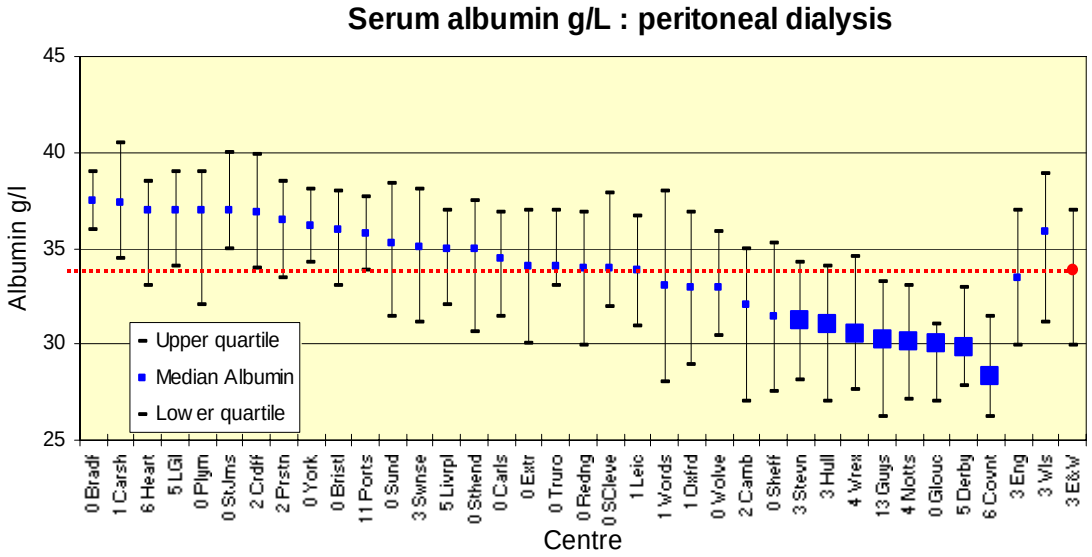

Figure 11.6: Serum albumin, PD

As shown in Figure 11.6, the median serum albumin was 30 g/L by BCP (units varying between 27 and 32 g/L) and 35 g/L by BCG (units varying between 33 and 37 g/L). Figure 11.4 shows that no unit achieved the Renal Association Standard. Data were incomplete for Figure 11.5 looking at proportion of patients within the laboratories' reference range because, at the time of data analysis, reference ranges had not yet been provided.

Discussion

The centres using BCP are clearly grouped towards one side of the figures, being most apparent within the PD population, in whom the albumin concentration overall is significantly lower. The BCG method will overestimate serum albumin concentration by several grams per litre below 30g/L (as assessed by BCG). Applying different reference ranges did not significantly modulate the relative positions. It is clear, within the PD population, that a significant proportion of the variation in albumin concentration arises from methodological factors.

Changes in albumin 1998–2001

Haemodialysis

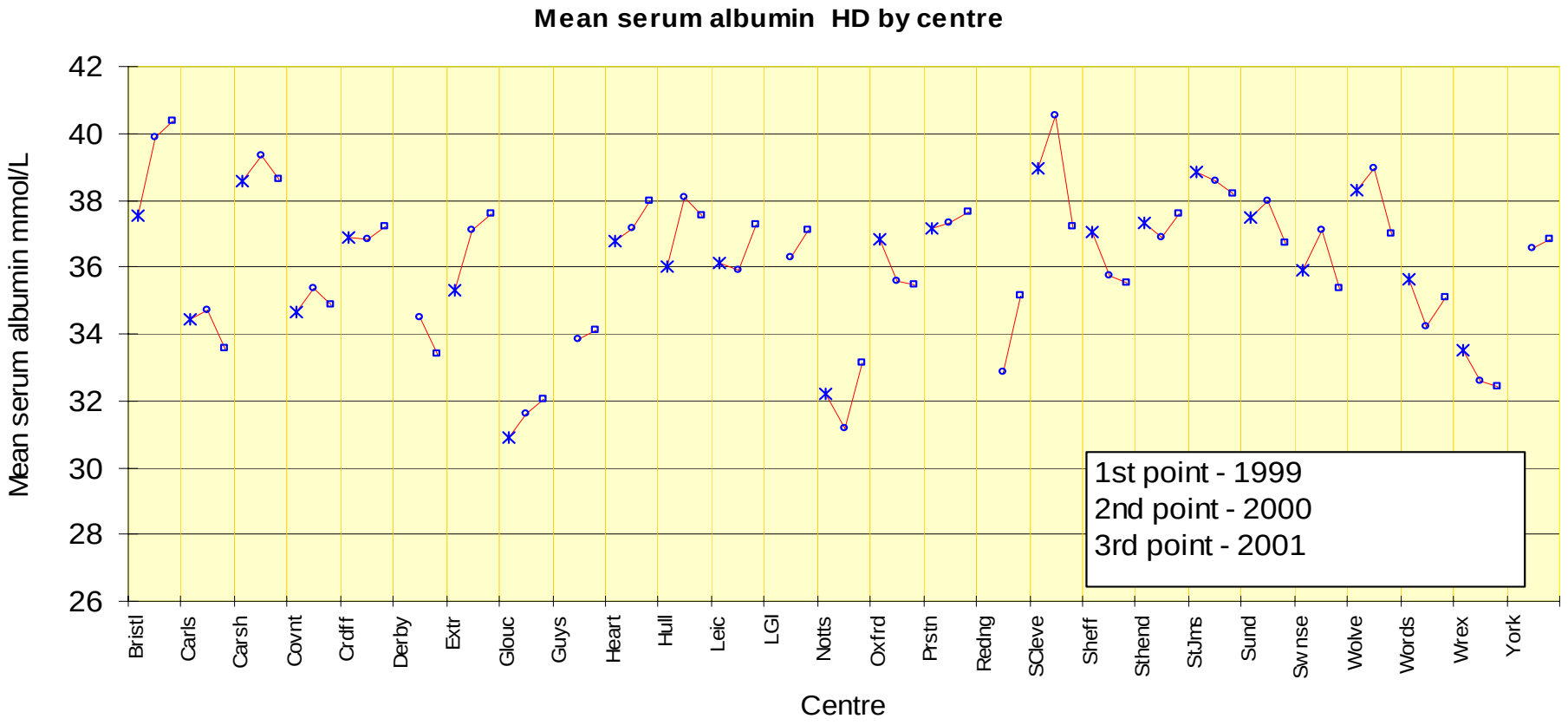

Figure 11.7: Mean serum albumin over 3 years, by centre, HD

Peritoneal dialysis

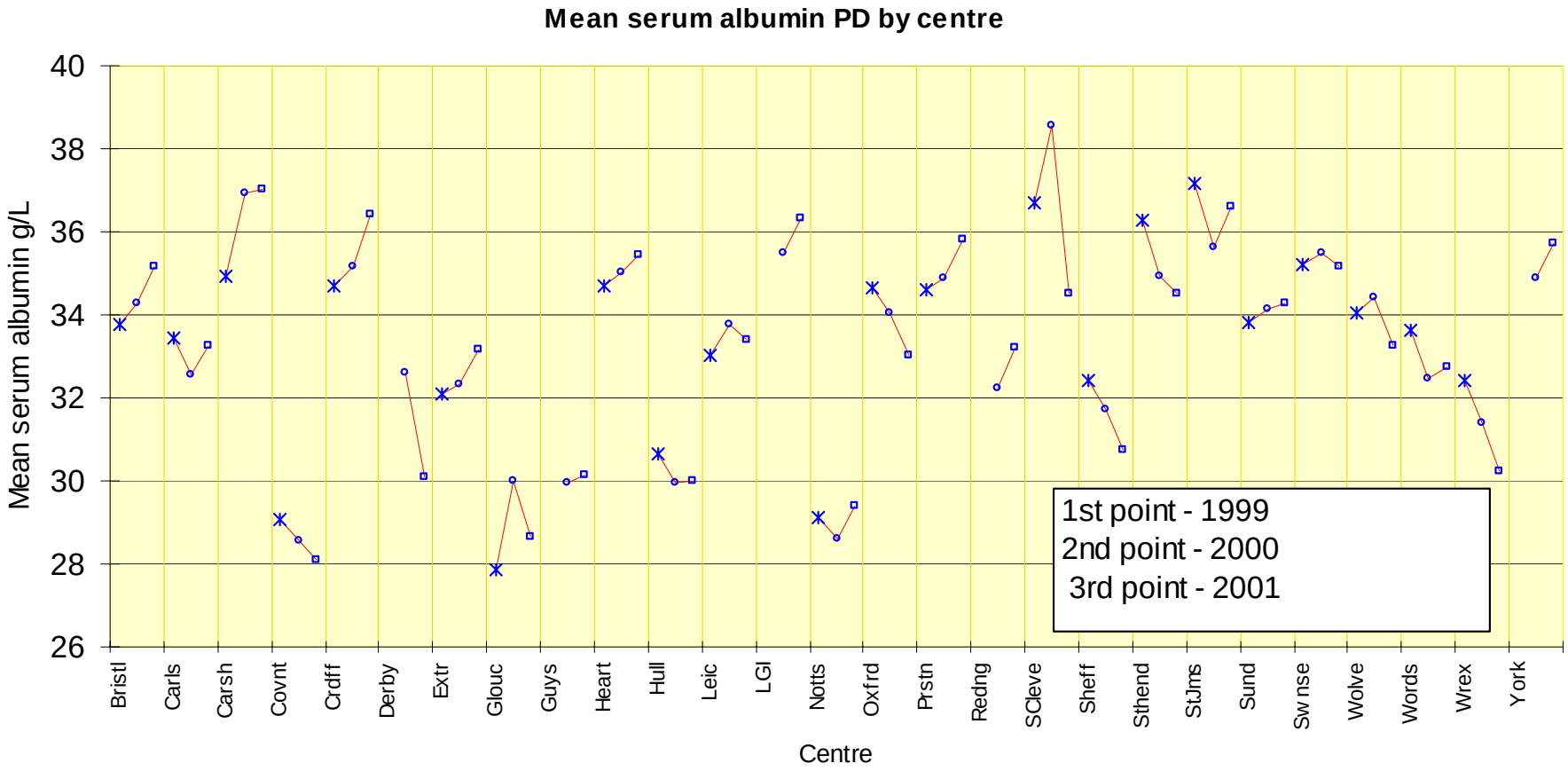

Figure 11.8: Mean albumin over 3 years, by centre, PD

Discussion

Figures 11.7 and 11.8 indicates the serial albumin level by centre over 3 years. From the laboratory survey carried out each year, the Registry is alerted to changes in laboratory methodology and instrumentation. Across the 3 year period shown here, Birmingham, Cardiff, Exeter, Preston and Wolverhampton all changed main-line analyser with only a minor change in median albumin concentration. Some centres appear to demonstrate an improvement in serial albumin measurement. In patients on PD, this may be due to a more careful selection of patients, and the Registry is undertaking further work to establish whether the changes in albumin concentration over time that are shown above are caused by changes in clinical practice or result from method performance.

Conclusion

The measurement of serum albumin and its value to nephrologists as a surrogate outcome measure is dependent upon the method used. This is particularly evident in PD patients, in whom the methodological differences are most pronounced. The relationship of BCP to BCG albumin concentration with mortality in this population is deserving of study.

Serum bicarbonate

Bicarbonate measurement

As can be seen from Table 11.2, there are two main methodologies in use for the measurement of bicarbonate. There is a variation in reference range, but this is not the only factor that will determine the distribution of results between centres. Bicarbonate is relatively unstable, and concentration changes will result from delayed analysis, as can happen with samples sent from GPs, home HD and possibly satellite dialysis units. Bicarbonate concentration can fall by as much as 6 mmol/L in an hour as the dissolved carbon dioxide in plasma is at a much greater concentration than it is in atmospheric air. Home HD patients have been excluded from the HD analysis. Another factor that will alter bicarbonate distribution will be the proportion of patients receiving acetate dialysis solutions.

Laboratory values for bicarbonate have not been harmonised for methodological differences.

City	Hospital	Method	Ref range
Birmingham	Heartlands Hospital	PEPC	22–30
Bradford	St Luke's Hospital	PEPC	23–32
Bristol	Southmead Hospital	PEPC	20–29
Cardiff	University of Wales Hospital	Enzymatic	22–30
Carlisle	Cumberland Infirmary	PEPC	23–30
Carshalton	St Helier Hospital	PEPC	24–30
Coventry	Walsgrave Hospital	PEPC	24–30
Derby	Derby District General	PEPC	23–30
Exeter	Royal Devon and Exeter Hospital	Electrode	23–30
Gloucester	Gloucester Road Infirmary	Electrode	24–32
Hull	Hull Royal Infirmary	Electrode	24–32
Leeds	St James's Hospital	PEPC	20–28
Leeds	LGI	PEPC	23–32
Leicester	Leicester General Hospital	PEPC	22–30

City	Hospital	Method	Ref range
Liverpool	Liverpool Royal Hospital	PEPC	22–33
London	Guys St Thomas'	Electrode	22–32
Middlesborough	South Cleveland Hospital	PEPC	22–29
Newcastle	Royal	PEPC	22–30
Nottingham	Nottingham City Hospital	PEPC	19–28
Oxford	Churchill Hospital	PEPC	24–30
Plymouth	Derriford Hospital	PEPC	23–31
Portsmouth	Queen Alex	PEPC	24–32
Preston	Royal Preston Hospital	Electrode	19–32
Reading	Royal Berkshire	PEPC	22–31
Sheffield	Northern General Hospital	PEPC	22–31
Stevenage	Lister Hospital	Electrode	20–30
Stourbridge	Wordsley Hospital	PEPC	22–29
Southend	Southend Hospital	PEPC	22–30
Sunderland	Sunderland Royal Hospital	PEPC	23–30
Swansea	Morriston	Enzymatic	20–35
Truro	Royal Cornwall Hospital Trust	Enzymatic	22–26
Wolverhampton	Newcross Hospital	PEPC	24–32
Wrexham	Maelor General Hospital	Electrode	24–32
York	York District Hospital	PEPC	22–26

Table 11.2: Bicarbonate methodology and reference ranges

Haemodialysis

The Renal Association Standard is that all patients ***should fall within the local normal range***.

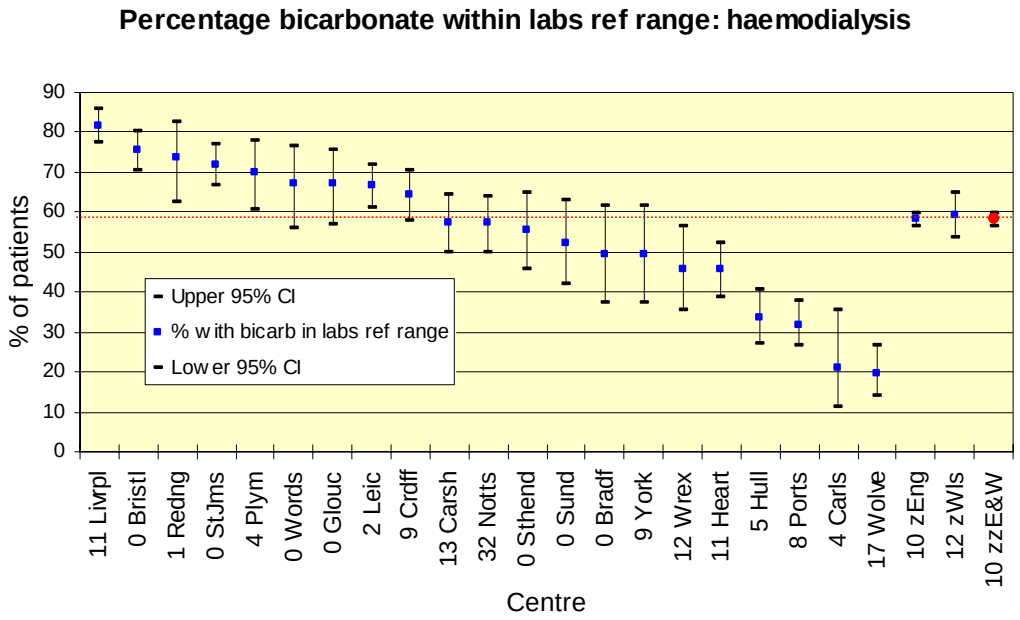

Figure 11.9: Percentage bicarbonate in the laboratory reference range, HD

There is a wide distribution in bicarbonate concentrations found to fall within the laboratory local reference range. This is not, however, entirely explained by different lower limits of normal as Nottingham has the lowest reference range of the units shown in Figure 11.9. In Figure 11.10, Bristol, Leeds, Nottingham, Stevenage, Wolverhampton and Preston (the lowest reference limits) are scattered across the dataset, again suggesting that reference limits cannot totally explain the distribution in results. No unit achieved the Renal Association Standard.

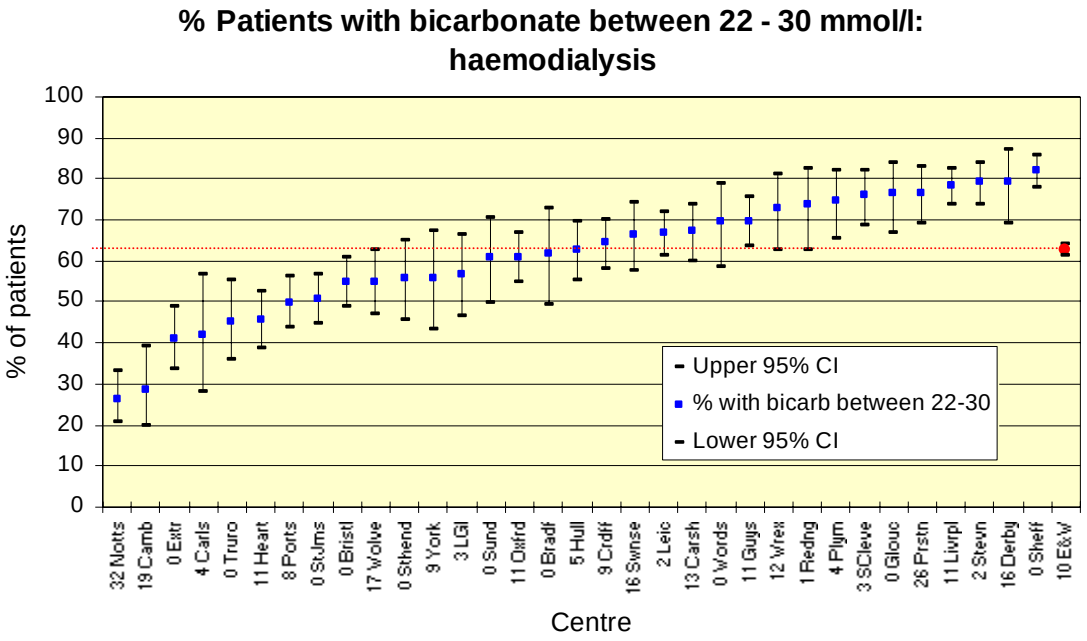

Figure 11.10: Percentage of patients with bicarbonate in the range 22–30 mmol/L, HD

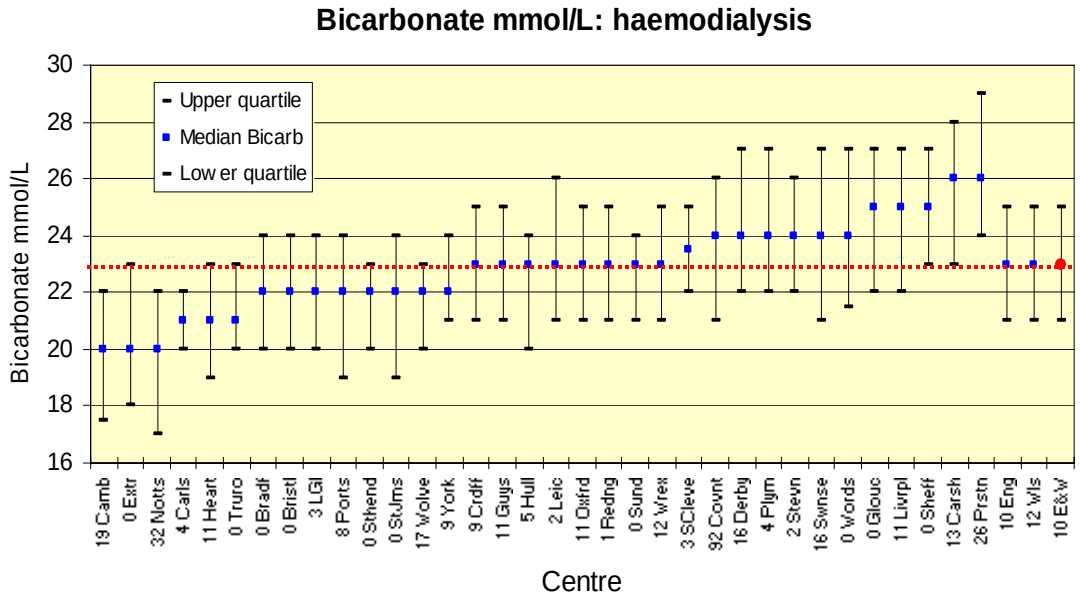

Figure 11.11: Median bicarbonate (mmol/L), HD

Median serum bicarbonate varied from 18 to 26 mmol/L between centres. More detailed information concerning sample handling by laboratories and units is required to explore the difference in results before any suggestion that this is due to differences in clinical practice can be considered. There appears to be no relationship between analytical method and median bicarbonate level. The Welsh External Quality Assurance Scheme (WEQAS) bicarbonate scheme data suggest that a variation in bicarbonate concentration of at least ±2 mmol/L could be expected to arise from method performance.

Peritoneal dialysis

The Renal Association Standard is that patients should have a serum bicarbonate between ***the lower local normal and upper local normal +3mmol/L.***

In England & Wales 78% of patients on peritoneal dialysis achieved the Standard (figure 11.12). There was significant variation between centres (Chi squared p = <.001)

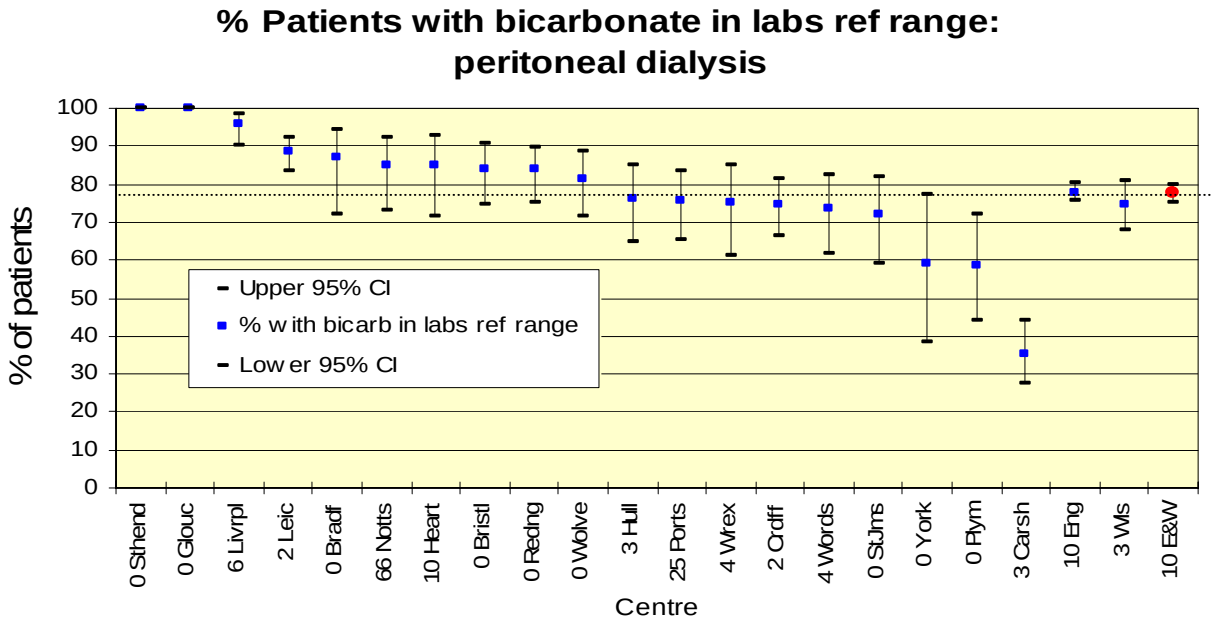

Figure 11.12: Percentage of patients with bicarbonate in the laboratory reference range, PD

In figure 11.14, the median serum bicarbonate varied between 24 and 31 mmol/L. Unlike the HD results, most units achieved the Renal Association PD Standard for bicarbonate

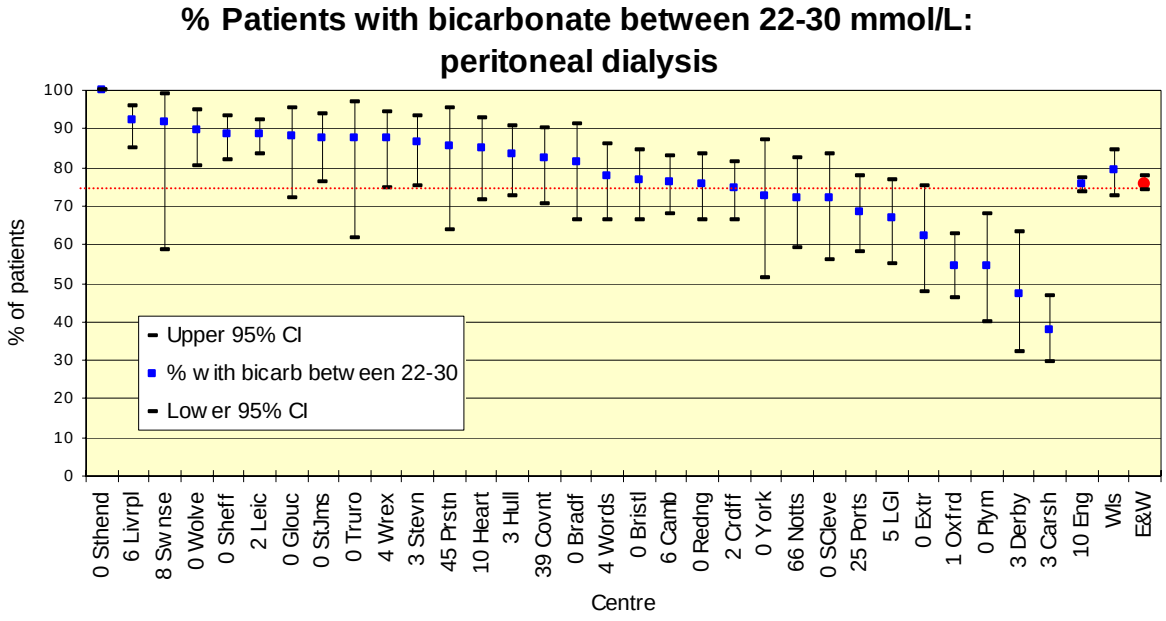

Figure 11.13: Percentage of patients with bicarbonate in the range 22–30 mmol/L, PD

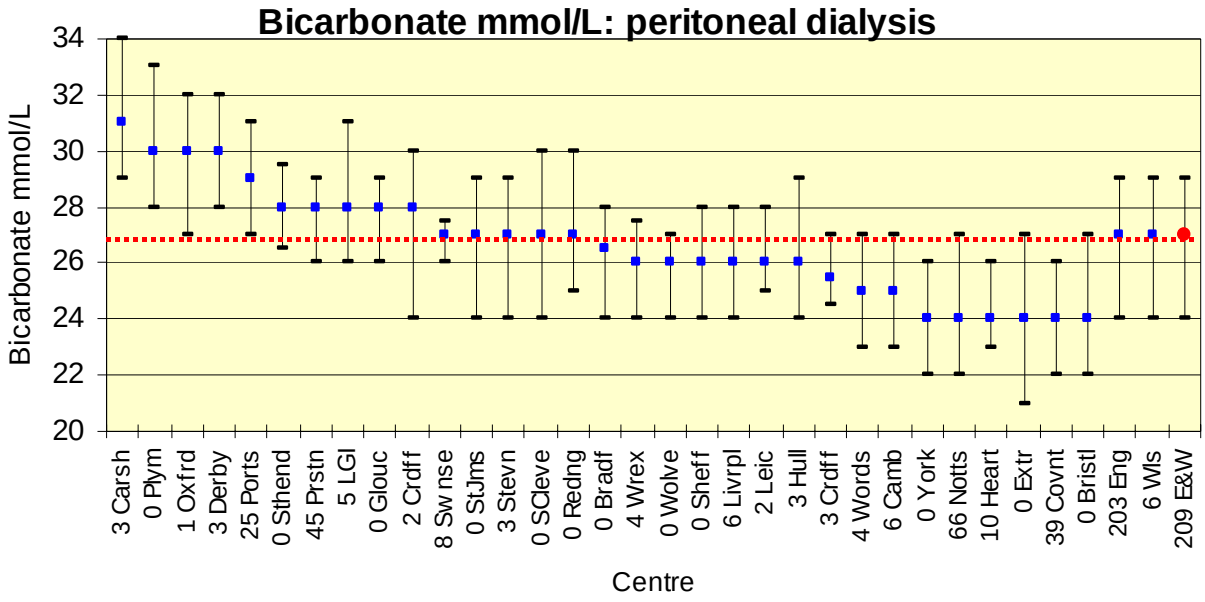

Figure 11.14: Median serum bicarbonate, PD

Changes in serum bicarbonate 1999 – 2001

In figures 11.15 and 11.16, there are large variations shown in serum bicarbonate results across these time periods. Some, but not all, of these variations may be caused by changes in the main-line analyser, which occurred at Birmingham, Cardiff, Exeter, Preston and Wolverhampton. The Welsh QA scheme, WEQAS, organises a bicarbonate service, and these data will now be used to explore the significance of changes in bicarbonate concentration between laboratories

It is hard to interpret these changes without further information. The large changes seen at Carshalton are mirrored both in the haemodialysis and peritoneal dialysis population indicating a methodology change In contrast, the Bristol renal unit showed a change in bicarbonate levels in 2000 for haemodialysis patients only indicating a dialysis technique change.

As the renal units have been identified this year, it will be useful if each centre could discuss these changes observed with their supporting laboratories to identify any possible explanations. These could include transport of samples to the laboratory from satellite units and changes in laboratory practice. There may also be changes in patient mix, the use of dialysis fluids and the use of dialysis technology (e.g. ambulatory PD). This could then be fed back to the Registry and discussed at the annual users' meeting.

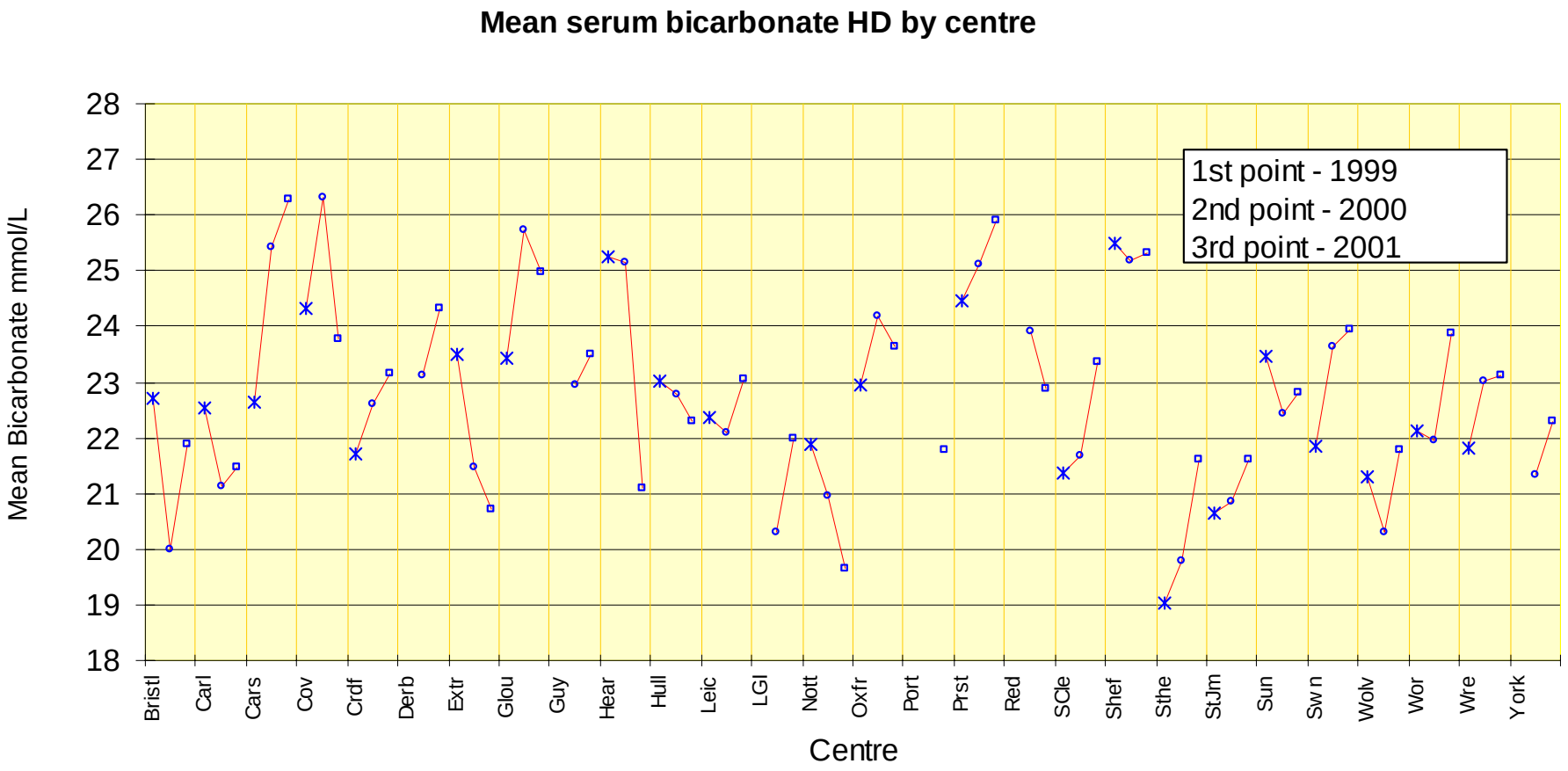

Figure 11.15: Mean serum bicarbonate, by centre, HD

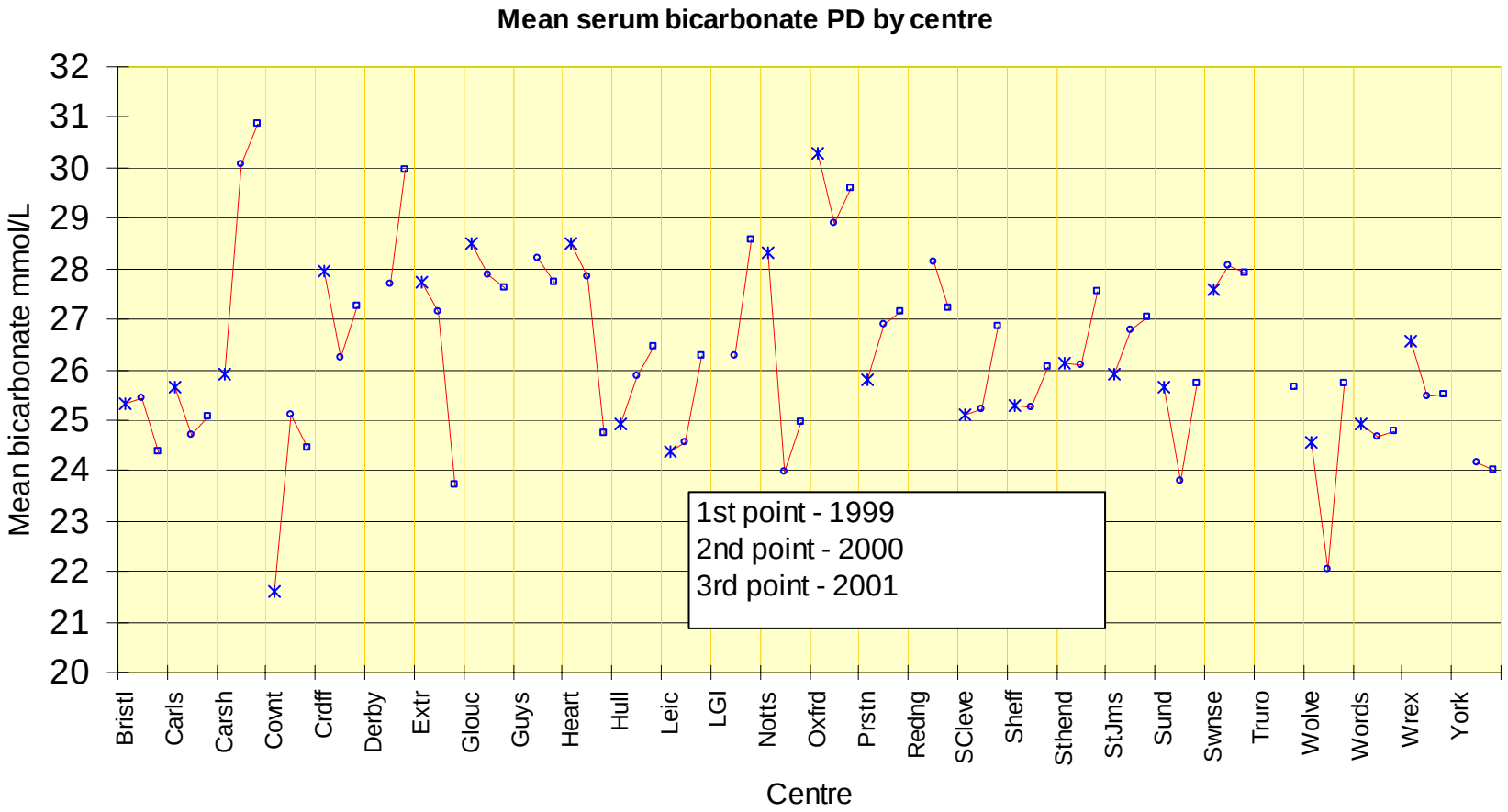

Figure 11.16: Mean serum bicarbonate, by centre, on PD