

# Adherence or Antibodies

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## Background

Two cases of type 1 diabetics with initially good control. Case 1: 14-year old boy with increasing insulin requirement. Long-acting insulin was changed from Protaphane<sup>®</sup> (neutral protoamine Hagedorn insulin) to Basaglar (insulin glargine) with no improvement, but was controlled on continuous subcutaneous Humalog<sup>®</sup> (insulin lispro) infusion. Case 2: 8-year old girl with hypoglycaemic attacks on Actrapid<sup>®</sup> (regular human insulin), Protaphane<sup>®</sup> and Humalog<sup>®</sup>. Insulin measured 56mIU/L (2.6-24.9) during one attack. ~~The Queried~~ query was whether insulin antibodies were interfering with pharmacokinetics. Of interest was which insulins cross-react in our assay and how measured results relate to administered dose.

## Methods

Case 1: Performed the Ouchterlony technique to investigate for specific antibodies against Basaglar<sup>®</sup> as compared to Humalog<sup>®</sup>.

Case 2: Performed hourly insulin measurements for 13 hours to ascertain whether 56mIU/L was an outlier. Performed PEG precipitation and compared insulin measurement pre- and post-precipitation to determine the presence of insulin antibodies. Performed recovery studies to determine the relationship between administered dose and measured insulin.

## Results

We were unable to determine whether antibodies were present against Basaglar<sup>®</sup> due to precipitation of the formulation in the buffered agar gel.

Antibodies were present in Case 2 with 31% recovery post-PEG precipitation. Our immunoassay recovered approximately 100% of a human insulin dose but 0% of analogue. Measured insulin of 56mIU/L was not an outlier.

## Conclusions

Antibodies may develop against various epitopes relevant to insulin synthesis, bioavailability and action and may result in hyper- and hypoglycaemia. Antibody interference is a consideration in immunoassays and may lead to spurious results.