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Electrocardiographic Changes in Normal and Abnormal Canine Pregnancy

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Contents

The aim of this study was to describe the canine electrocardiographic changes in the course of normal and abnormal pregnancy. Twenty-three Brucellosis-negative pregnant bitches were retrospectively classified as normal (n = 12) or abnormal (n = 11). A control group of non-pregnant dioestrous bitches (n = 10) was also included. Normal pregnant females delivered healthy puppies at term while abnormal animals interrupted their pregnancy between days 52–60 (from estimated luteinizing hormone peak) or presented perinatal litter death higher than 60%. All the bitches were electrocardiographically evaluated every 10 days from day 0 to day 65 of the oestrous cycle, to parturition or abortion. Percentage heart rate change increased 31.3% from day 40 to 60 in normal gestation while it decreased −1.8% in dioestrous bitches, although it did not change in the abnormal group ($p < 0.01$). In the abnormal pregnant group but not in the others, percentage QRSa change fell to −34% on day 60 ($p < 0.01$). At the same time point, percentage QRSd change was 6.2% vs −4.9% in normal gestations and dioestrous animals, respectively ($p < 0.05$). Corrected QT interval augmented from day 40 onwards up to 9.9% and 4.3% in the normal pregnant and dioestrous groups, respectively, while it remained unchanged in abnormal gestations ($p < 0.05$). It is concluded that during normal canine pregnancy, some electrocardiographic parameters begin changing from day 40 onwards, and that pathological gestations differ from normality from day 30. The use of electrocardiography in canine obstetrics might contribute to identify abnormal outcomes before they become clinically evident.

Introduction

Canine pregnancy is a physiological state characterized by important adaptive changes, many of which occur in the cardiovascular system. These changes include an increase in total blood volume and cardiac output, associated with eccentric myocardial hypertrophy (Williams et al. 2007; Abbott 2010). Moreover, peripheral vascular resistance decreases and uterine blood flow augments (Blanco et al. 2010). These anatomical and functional adaptations are believed to modify cardiac conduction system. Other factors including variations in circulating hormones, modified autonomic tone and electrolyte levels may also contribute to these modifications (Gowda et al. 2003; Baumert et al. 2010).

Electric remodelling, which results from changes in cardiac morphology and gene expression, is particularly associated with action potential prolongation. This phenomenon can result from reduced fast transient outward of potassium current (Eghbali et al. 2006). For this reason, QT interval has been reported to augment during gestation (Eghbali et al. 2005).

The lack of these adaptive mechanisms of normal gestation may jeopardize the health of both mother and foetus. Pregnant women with pathological outcomes show alterations in heart rate and QT interval that precede clinical symptoms (Baumert et al. 2010). Furthermore, there is also evidence suggesting that pregnancy can exacerbate pre-existing arrhythmias or even cause them (Baumert et al. 2010).

In bitches, electrocardiographic assessment has been performed in the course of gestation to register maternal heart rate, demonstrating an increasing rate of this parameter from the third week onward (Olsson et al. 2003; Lúcio et al. 2009; Blanco et al. 2010).

While there are substantial data on cardiac structural changes and heart rate, little is known about other electrophysiological alterations during canine pregnancy. Furthermore, in this species, electrocardiographic monitoring has not been described during pathological gestation. It is worth noting that some aetiologic agents that cause abortion or perinatal death may also provoke systemic affection, including cardiac malfunction (Root Kustritz 2005). In these cases, electrocardigraphic modifications of normal trace may appear before other systemic or obstetric sympthoms develope (Flood and Hoover 2009).

A more detailed understanding of the electrophysiology underlying pregnancy is essential to harness its use for monitoring canine maternal and foetal health. Therefore, the aim of this study was to analyze the electrocardiographic changes in the course of normal and abnormal canine pregnancy.

Materials and Methods

Animals and follow up schedule

Thirty-three clinically healthy, 1–8 year-old (3.09 ± 1.7), 3–55 kg (17.15 ± 14.7) and cross- and pure-bred bitches were included in this study. The study included German Shepherd, Miniature Poodle, Yorkshire, Miniature Schnauzer, Canary dog and Rottweiller bitches.

All the females were Brucellosis-negative and retrospectively classified as normal (n = 12) or abnormal (n = 11) pregnant bitches. A control group of non-pregnant dioestrous bitches (n = 10) was also included. Normal pregnant females delivered healthy puppies at term while abnormal animals interrupted their pregnancy between days 52 to 60 [from estimated luteinizing hormone (LH) peak; n = 5] or presented perinatal litter death higher than 60% (n = 6). All the bitches were electrocardiographically evaluated every 10 days from day 0 (estimated LH peak) to day 65 of the oestrous cycle, to parturition or abortion. Seven abnormal group bitches reach 60 days of gestation. Day 0 of the oestrous cycle was defined as the first day of typical oestrous vaginal cytology (Olson et al. 1984). This study was

approved by the Faculty Institutional Care and Animal Use Committee (IACUC).

Electrocardiograms

To record the electrocardiogram (ECG), patients were placed in right lateral recumbency on a rubber mat. They were gently restrained with the forelimbs held perpendicular with the body and slightly separated (Ferasin et al. 2010). The electrodes were attached to the skin with alligator clips. To accomplish proper contact of the electrodes, alcohol was locally used to improve electrical transmission. All the examinations were performed in the same room between 9 and 11 am, under the same environmental conditions. Electrocardiograms were recorded after 5 min of acclimatisation, on calibrated paper as previously reported (Kittleson 1998a). Leads I, II, III, aV_R, aV_L, aV_F, CV_{6LU}, CV_{6LL}, CV_{5RL} and V_{10} were recorded at a paper speed of 50 mm/s. Later, lead II was recorded at 25 mm/s to analyze heart rate (HR; bpm) and cardiac rhythm (normal sinus rhythm or sinus arrythmia). Following recording, the ECG was analyzed by a single trained operator. Mean electrical axis (MEA; degrees), P wave amplitude (Pa; mv) and duration (Pd; ms), P-R interval (PR; ms), QRS complex amplitude (QRSa; mv) and duration (QRSd; ms), Q-T interval (QT; ms), S-T segment (ST; mv) and T wave (T; smaller or greater than one fourth amplitude of R wave) were calculated manually at a paper speed of 50 mm/s (Tilley 1992). Three consecutive beats were measured and averaged. In case of marked sinus arrhythmia, six beats were averaged (Blanco et al. 2010). The RR interval immediately preceding each complex was recorded and QT interval was corrected (QTc) by Van de Water formula [QTc = QT−0.087 (RR−1000); Tattersall et al. 2006].

Statistical analysis

To manage the effect of different body weights, HR, MEA, Pa, Pd, PR, QRSa, QRSd, QT and QTc were transformed to percentage change [(Final value – initial value/initial value) × 100]. Comparisons between groups were carried out by ANOVA for repeated measures followed by Tukey test. Cardiac rhythm and T wave were analyzed by Chi-squared test (SPSS 17.0; SPSS Inc. Chicago, IL, USA). $p < 0.05$ was considered significant.

Results

There were no weight ($p > 0.1$), age ($p > 0.1$) nor breed ($p > 0.1$) differences among groups. Litter size did not differ between pregnant groups ($p > 0.1$). None of the animals presented severe arrhythmias during the experiment. Percentage HR ($p < 0.01$), Pa ($p < 0.01$), QRSa ($p < 0.01$), QRSd ($p < 0.05$) and QTc ($p < 0.05$) changes differently varied throughout time in the three groups.

In normal gestation, percentage HR change increased progressively from day 40 to 60 31.3% vs −1.8% in dioestrous bitches ($p < 0.01$; Fig. 1). Conversely, this parameter did not show the same rise in the abnormal group (Fig. 1). On day 50 of gestation, percentage Pa change diminished up to −20.1% and −17.8% in normal and abnormal pregnant bitches, respectively, while no decrease was observed in diestrous animals (Table 1). In the abnormal pregnant group but not in the others, percentage QRSa change fell to −34% on day 60 ($p < 0.01$; Fig. 2). At the same time point, percentage QRSd change was 6.2% vs −4.9% in normal gestations and dioestrous animals, respectively (Table 1). In the normal pregnant group, percentage QTc change augmented from day 40 onwards up to 9.9% vs 4.3% in the diestrous females, while this parameter remained unchanged in abnormal bitches (Fig. 3).

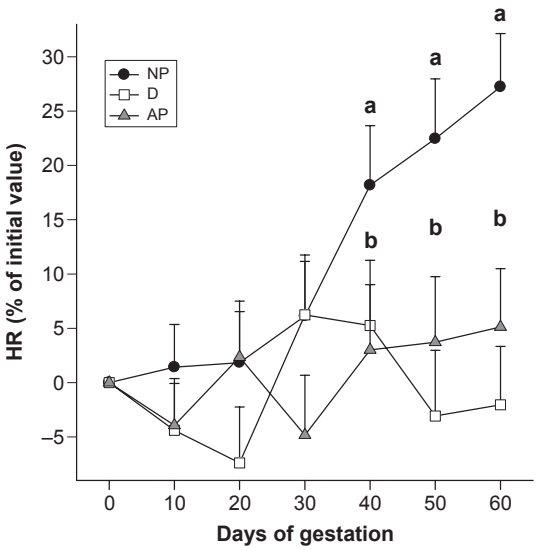

Fig. 1. Percentage heart rate change (mean ± SEM) of the same animal groups and experiment of Table 1. Letters a and b indicate *post hoc* differences ($p < 0.01$) between NP vs D and NP vs AP, respectively

On day 60 of pregnancy, most of the pregnant of both groups presented normal sinus rhythm in comparison with the dioestrous dogs, which mostly developed sinus arrythmia ($p < 0.05$; Fig. 4). Percentage MEA, Pd, PR and QT changes as well as ST and T did not differ among groups (Table 2 and Table 3).

Discussion

To our knowledge, this is the first report of serial electrocardiographic description and comparison during normal and abnormal canine gestation. The heart rate acceleration observed in normal bitches is a well-known phenomenon of canine pregnancy that guarantees increased cardiac output optimizing oxygen and nutrients supply (Wong et al. 2002; Olsson et al. 2003; Blanco et al. 2010). Interestingly, this adaptive mechanism did not characterize gestations having an adverse outcome. This finding is in line with previous reports in women, where heart rate in patients with abnormal uterine perfusion is slower compared with normal perfusion pregnancies (Baumert et al. 2010). Furthermore, in dogs, some systemic diseases, which provoke abortion or perinatal death, are associated with maternal heart rate decelerations (Kienle 1998). The

Table 1. Percentage P wave amplitude (Pa) and QRS complex duration (QRSd) changes (mean ± SEM) of 12 normal pregnant (NP), 11 abnormal pregnant (AP) and 10 dioetrous (D) bitches assessed every 10 days from estimated day of luteinizing hormone peak

	Days of gestation					
Parameter	10	20	30	40	50	60
Pa						
NP	0.4 ± 8.0	−18.7 ± 9.3	−15.9 ± 9.6	−5.5 ± 10.5	−20.1 ± 10.1[b]	−9.7 ± 7.9
AP	−7.1 ± 8.4	7.7 ± 9.7	−1.6 ± 10.0	−9.6 ± 10.9	−17.8 ± 10.5[b]	−30.9 ± 8.2
D	1.6 ± 8.8	−3.3 ± 10.2	−8.3 ± 10.5	−1.6 ± 11.5	1.6 ± 11.0[a]	−6.6 ± 8.6
QRSd						
NP	0.5 ± 3.7	−4.4 ± 3.3	−0.2 ± 4.9	−0.9 ± 5.8	3.8 ± 5.9	6.2 ± 4.7[b]
AP	2.2 ± 3.9	−6.0 ± 3.4	4.6 ± 5.1	−4.8 ± 6.1	3.0 ± 6.1	0.7 ± 4.9[b]
D	0.0 ± 4.1	8.9 ± 3.6	7.5 ± 4.5	1.0 ± 6.4	1.0 ± 6.4	−4.9 ± 5.1[a]

Different superscript letters within a same column indicate differences ($p < 0.05$) among groups.

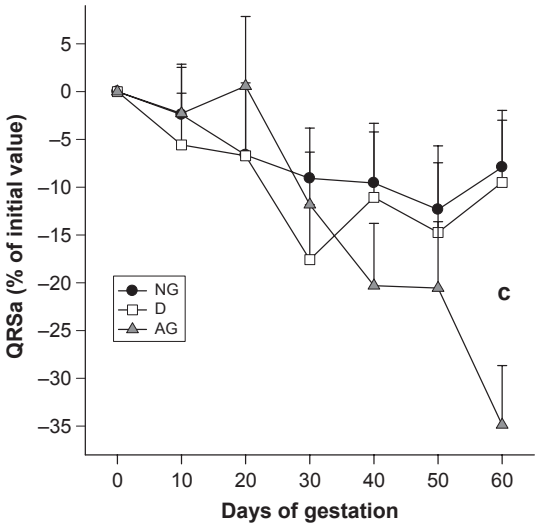

Fig. 2. Percentage QRS complex amplitude (QRSa) change (mean ± SEM) of the same animal groups and experiment of Fig. 1. Letter c indicates *post hoc* differences ($p < 0.01$) between NP and D vs AP

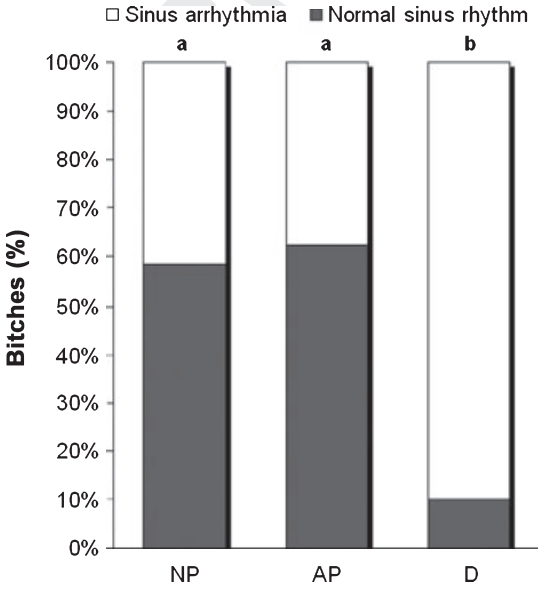

Fig. 4. Bitches (percentage) of Fig. 1 on day 60 of the study having different cardiac rhythms. Different letters over the columns indicate differences $p < 0.05$

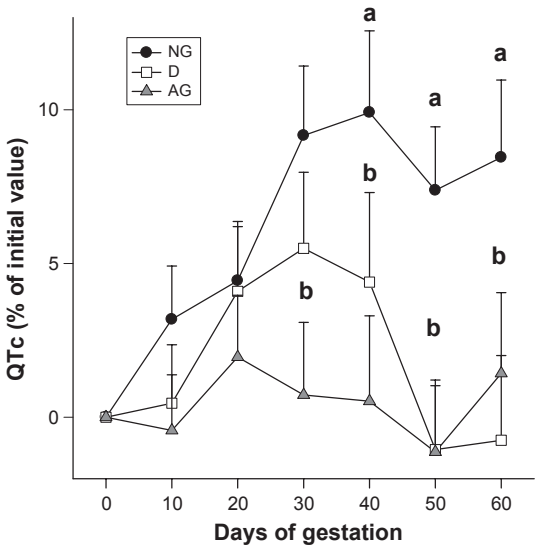

Fig. 3. Percentage corrected QT interval change (mean ± SEM) of the same animal groups and experiment of Fig. 1. Letters a and b indicate *post hoc* differences ($p < 0.05$) between NP vs D and NP vs AP, respectively

failure in maternal heart rate adaptation might cause an inadequate increase in cardiac output and therefore a decrease in conceptus perfusion (Blanco et al. 2010).

The decrease in Pa in both pregnant groups might be attributed to electrolyte modifications that occur in the course of gestation. In pregnant mice, myocardial cells develop a decrease in Ito-f, a molecular constituent of the fast transient outward of potassium current (Eghbali et al. 2005). It is worth noting that in hyperkalemic dogs, the atrial myocardium may lose its ability to depolarize (Kittleson 1998b; Ghaffari et al. 2009) explaining the lower Pa found in the pregnant animals. In addition, non-homogeneous and discontinuous conduction of the atrial impulse has been described during human pregnancy (Ozmen et al. 2006).

Increased QRSd and QRSa are associated with ventricular enlargement in dogs (Kittleson 1998a). This morphologycal change has already been described in normal canine gestation, where cardiac eccentric hypertrophy is observed as a compensatory mechanism to volume overload (Blanco et al. 2010). The increase in QRSd might also be attributed to the augmented

Table 2. Percentage mean electrical axis (MEA), P wave duration (Pd), P-R interval (PR) and Q-T interval (QT) changes (mean ± SEM) of the same groups and experiment of Table 1

	Days of gestation					
Parameter	10	20	30	40	50	60
MEA						
NP	34.9 ± 15	16.7 ± 13	18.9 ± 18	7.9 ± 16	80.7 ± 48	43.4 ± 31
AP	7.0 ± 15	12.4 ± 13	−0.7 ± 19	−0.2 ± 17	−40.9 ± 51	−72.9 ± 33
D	13.4 ± 16	8.2 ± 14	7.9 ± 20	19.7 ± 18	9.0 ± 53	16.3 ± 34
Pd						
NP	−8.3 ± 2.7	−1.3 ± 4.9	−9.7 ± 3.8	−5.5 ± 3.4	−1.3 ± 4.3	−5.5 ± 3.7
AP	0 ± 2.8	3.1 ± 5.1	5.6 ± 4.0	2.5 ± 3.6	2.2 ± 4.5	7.1 ± 3.8
D	7.5 ± 3.0	5.0 ± 5.3	0.0 ± 4.2	0.0 ± 3.8	5.0 ± 4.8	5.0 ± 4.0
PR						
NP	−0.1 ± 2.2	3.0 ± 2.6	−2.0 ± 2.8	0.4 ± 3.0	−4.6 ± 3.6	−6.9 ± 3.2
AP	4.9 ± 2.3	1.8 ± 2.7	5.7 ± 2.9	3.5 ± 3.1	−1.2 ± 3.8	−2.1 ± 3.3
D	1.2 ± 2.5	1.7 ± 2.9	2.0 ± 3.1	4.2 ± 3.3	0.2 ± 4.0	4.1 ± 3.5
QT						
NP	3.4 ± 2.0	5.3 ± 2.3	9.5 ± 2.8	8.2 ± 3.0	4.3 ± 2.1	4.8 ± 2.8
AP	−0.7 ± 2.1	2.1 ± 2.4	6.2 ± 2.9	−1.3 ± 3.1	−3.0 ± 2.1	−2.8 ± 3.0
D	2.5 ± 2.2	7.4 ± 2.5	5.5 ± 3.1	4.0 ± 3.3	0.0 ± 2.3	0.0 ± 3.1

Table 3. S-T interval (ST; mean ± SEM) of the same groups and experiment of Table 1

	Days of gestation						
	0	10	20	30	40	50	60
ST							
NP	−0.01 ± 0.01	0 ± 0.01	−0.01 ± 0.05	−0.01 ± 0.05	0 ± 0.01	−0.02 ± 0.01	0 ± 0.01
AP	−0.02 ± 0.01	−0.02 ± 0.01	−0.01 ± 0.05	−0.01 ± 0.05	0 ± 0.01	0 ± 0.01	0 ± 0.01
D	−0.06 ± 0.01	−0.04 ± 0.01	−0.04 ± 0.05	−0.02 ± 0.05	−0.03 ± 0.01	−0.05 ± 0.01	−0.05 ± 0.01

potassium in myocardial cells described for other species. This phenomenon may in term cause a prolonged action potential in normal canine pregnancy. In pregnant women, QRSa remains constant throughout gestation (Gowda et al. 2003). In the present study, diminishing QRSa in the abnormal group might evidence the lack of the physiological cardiovascular adaptation in these animals. This result is in line with studies in women with peripartum cardiomyopathy, where low voltage complexes are frequently detected (Bhakta et al. 2007). Furthermore, this finding might also be an early subclinical indicator of systemic disease. To our knowledge, this is the first report of QRSd and QRSa in the course of abnormal gestation in domestic species.

In contrast to previous reports in pregnant mice (Eghbali et al. 2005), QT interval did not change during normal canine gestation. This is probably because of maternal HR acceleration. This acceleration normally occurs in conjunction with short QT intervals, and it could mask an inherent change in this interval (Tattersall et al. 2006).

When corrected for heart rate, QTc of pregnant dogs was higher than that of non-pregnant animals, suggesting that the time required for ventricular depolarization and repolarization is altered by normal pregnancy. This augmentation in QTc may be explained by the previously described prolonged action potential. In the second half of gestation, QTc of bitches with pathological pregnancy outcome differed from normality. This result is consistent with reports in women with hypertensive pregnancy disorders, where QT reflects an elevated sympathetic nerve activity (Baumert et al. 2010). It is interesting to note that in these dogs, like in women, this electrocardiographic finding appeared before the onset of clinical symptoms.

Heart rate correction of the QT has been reported in veterinary cardiology to evaluate Boxer familial ventricular arrhythmias, although, it did not appear to be a useful non-invasive diagnostic tool (Spier et al. 2001). Nevertheless, in our study, this correction revealed significant differences among groups. Further studies in healthy dogs are necessary to determine whether this conversion gives profitable information or not.

Respiratory sinus arrhythmia diminished at the end of both normal and abnormal gestations suggesting that the vagal neural outflow to the sinoatrial node is decreased during pregnancy (Baumert et al. 2010). This is in line with what Lúcio et al. (2009) described for canine pregnancy and parturition, where the majority of bitches had normal sinus rhythm (Lúcio et al. 2009). Although non-specific changes in the ST segments and T waves are seen in 4 to 14% of normal human pregnancies (Kron and Conti 2007), these parameters did not change during both normal and abnormal canine gestation.

In this study, cardiovascular dissimilarities between normal and abnormal pregnant bitches preceded the appearance of complications. For this reason, the use of electrocardiography in canine obstetrics might contribute to identify pathologycal outcomes before they become clinically evident. It is concluded that during normal canine pregnancy, some electrochardiographic parameters begin to change from day 40 onwards, and that pathological gestations begin to electrocardiographically differ from normality from day 30 onwards. Therefore, monitoring the maternal electrocardiogram

during pregnancy might be important to support medical decision making in canine obstetrics.

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Conflict of interest

None of the authors have any conflict of interest to declare.

Author contributions

All authors contributed equally.

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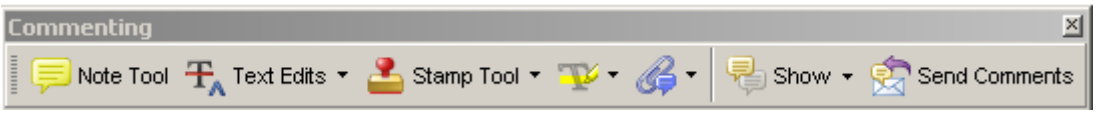

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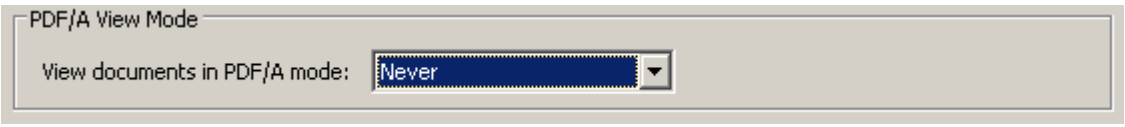

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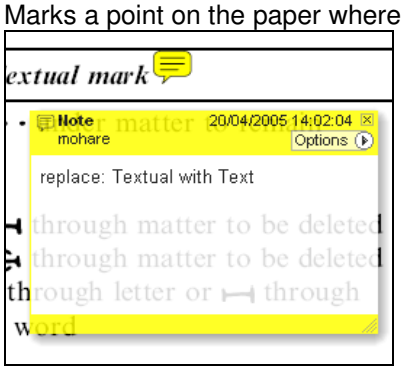

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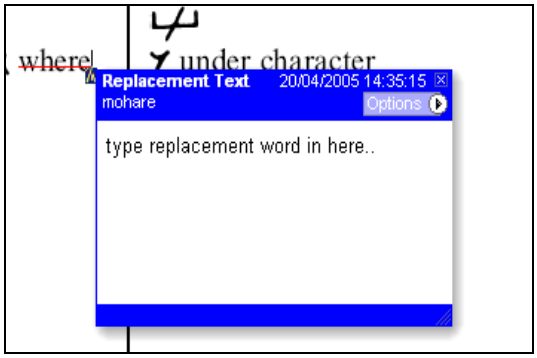

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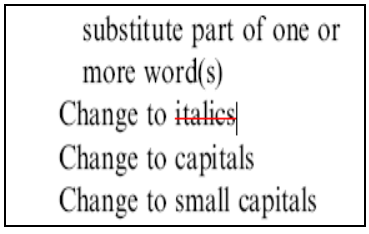
Cross out text tool — For deleting text when there is nothing to replace selection

Strikes through text in a red line.



How to use it:

1. Select cursor from toolbar
2. Highlight word or sentence
3. Right click
4. Select Cross Out Text

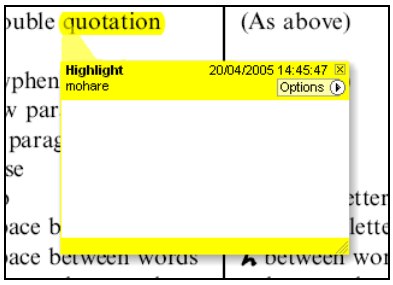
Approved tool — For approving a proof and that no corrections at all are required.

How to use it:

1. Click on the Stamp Tool in the toolbar
2. Select the Approved rubber stamp from the 'standard business' selection
3. Click on the text where you want to rubber stamp to appear (usually first page)

Highlight tool — For highlighting selection that should be changed to bold or italic.

Highlights text in yellow and opens up a text box.

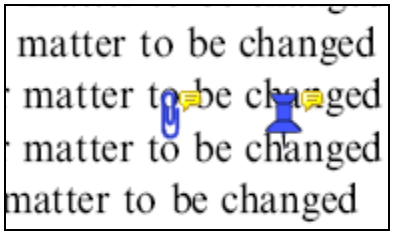


How to use it:

1. Select Highlighter Tool from the commenting toolbar
2. Highlight the desired text
3. Add a note detailing the required change

Attach File Tool — For inserting large amounts of text or replacement figures as a files.

Inserts symbol and speech bubble where a file has been inserted.

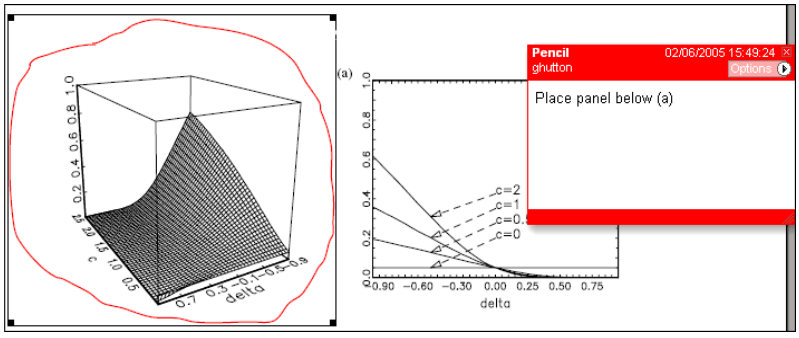


How to use it:

1. Click on paperclip icon in the commenting toolbar
2. Click where you want to insert the attachment
3. Select the saved file from your PC/network
4. Select appearance of icon (paperclip, graph, attachment or tag) and close

Pencil tool — For circling parts of figures or making freeform marks

Creates freeform shapes with a pencil tool. Particularly with graphics within the proof it may be useful to use the Drawing Markups toolbar. These tools allow you to draw circles, lines and comment on these marks.



How to use it:

1. Select Tools > Drawing Markups > Pencil Tool
2. Draw with the cursor
3. Multiple pieces of pencil annotation can be grouped together
4. Once finished, move the cursor over the shape until an arrowhead appears and right click
5. Select Open Pop-Up Note and type in a details of required change
6. Click the X in the top right hand corner of the note box to close.

Help

For further information on how to annotate proofs click on the Help button to activate a list of instructions: